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(54) **Title:** COMBINATION THERAPIES COMPRISING ANTIBODY MOLECULES TO LAG-3

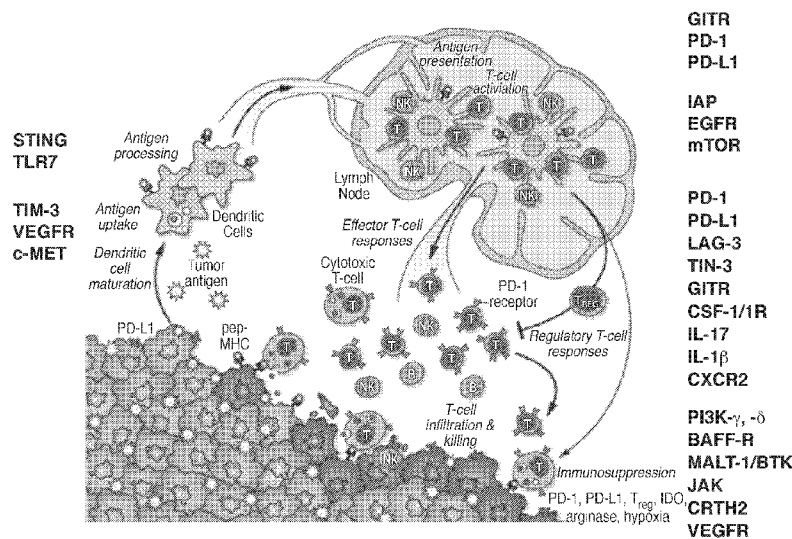


FIGURE 15

(57) **Abstract:** Combination therapies comprising antibody molecules that specifically bind to LAG-3 are disclosed. The combination therapies can be used to treat, prevent and/or diagnose cancerous or infectious disorders.

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COMBINATION THERAPIES COMPRISING
ANTIBODY MOLECULES TO LAG-3

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 62/198,492, filed July 29, 2015, the content of the aforementioned application is hereby incorporated by reference in their entirety.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on July 25, 2016, is named C2160-7010WO_SL.txt and is 323,665 bytes in size.

BACKGROUND

Lymphocyte Activation Gene-3, or LAG-3 (also known as CD223), is a member of the immunoglobulin supergene family, and is expressed on activated T cells (Huard *et al.* (1994) *Immunogenetics* 39:213), NK cells (Triebel *et al.* (1990) *J. Exp. Med.* 171:1393-1405), regulatory T cells (Huang *et al.* (2004) *Immunity* 21:503-513; Camisaschi *et al.* (2010) *J Immunol.* 184:6545-6551; Gagliani *et al.* (2013) *Nat Med* 19:739-746), and plasmacytoid dendritic cells (DCs) (Workman *et al.* (2009) *J Immunol* 182:1885-1891). LAG-3 is a membrane protein encoded by a gene located on chromosome 12, and is structurally and genetically related to CD4.

Similar to CD4, LAG-3 can interact with MHC class II molecules on the cell surface (Baixeras *et al.* (1992) *J. Exp. Med.* 176:327-337; Huard *et al.* (1996) *Eur. J. Immunol.* 26:1180-1186). It has been suggested that the direct binding of LAG-3 to MHC class II plays a role in down-regulating antigen-dependent stimulation of CD4⁺ T lymphocytes (Huard *et al.* (1994) *Eur. J. Immunol.* 24:3216-3221) and LAG-3 blockade has also been shown to reinvigorate CD8⁺ lymphocytes in both tumor or self-antigen (Gross *et al.* (2007) *J Clin Invest.* 117:3383-3392) and viral models (Blackburn *et al.* (2009) *Nat. Immunol.* 10:29-37). Further, the intra-cytoplasmic region of LAG-3 can interact with LAP (LAG-3-associated protein), which is a signal

transduction molecule involved in the downregulation of the CD3/TCR activation pathway (Iouzalén *et al.* (2001) *Eur. J. Immunol.* 31:2885-2891). Moreover, CD4⁺CD25⁺ regulatory T cells (T_{reg}) have been shown to express LAG-3 upon activation, which contributes to the suppressor activity of T_{reg} cells (Huang, C. *et al.* (2004) *Immunity* 21:503-513). LAG-3 can also negatively regulate T cell homeostasis by T_{reg} cells in both T cell-dependent and independent mechanisms (Workman, C. J. and Vignali, D. A. (2005) *J. Immunol.* 174:688-695).

Given the importance of LAG-3 in downregulating an immune response, the need exists for developing novel agents that modulate its activity to activate the immune system. Such agents can be used, *e.g.*, for cancer immunotherapy and treatment of other conditions, such as chronic infection.

SUMMARY

Disclosed herein, at least in part, are methods and compositions comprising a combination of two, three or more therapeutic agents chosen from one, two, or all of the following categories (i)-(iii): (i) an agent that enhances antigen presentation (*e.g.*, tumor antigen presentation); (ii) an agent that enhances an effector cell response (*e.g.*, B cell and/or T cell activation and/or mobilization); or (iii) an agent that decreases tumor immunosuppression. In some embodiments, the combination includes an inhibitor of Lymphocyte Activation Gene-3 (LAG-3) (*e.g.*, an anti-LAG-3 antibody molecule as described herein).

Without wishing to be bound by theory, it is believed that therapeutic approaches that enhance anti-tumor immunity work more effectively when the immune response is optimized by targeting multiple components at one or more stages of an immune response, *e.g.*, an anti-tumor immune response. For example, approaches that enhance antigen presentation, *e.g.*, by activation and/or maturation of dendritic cells, combined with approaches that enhance cellular and humoral immune responses (*e.g.*, by stimulating, *e.g.*, disinhibiting, phagocytes and/or tumor infiltrating lymphocytes (*e.g.*, NK cells and T cells)), while blocking tumor immunosuppressive signaling (*e.g.*, by increasing macrophage polarization, increasing T_{reg} depletion and/or decreasing myeloid-derived suppressive cells (MDSCs)) can result in a more effective and/or prolonged therapeutic response. Accordingly, disclosed herein are combination therapies that optimize one, two, or all of: (i) antigen presentation, *e.g.*, increasing antigen presentation (*e.g.*, by enhancing one or more of dendritic cell activity or maturation, antigen uptake, or antigen

processing); (ii) effector cell response, *e.g.*, increasing effector cell response (*e.g.*, enhancing B cell and/or T cell activation and/or mobilization, *e.g.*, in the lymph node); or (iii) tumor immunosuppression, *e.g.*, decreasing tumor immunosuppression (*e.g.*, increasing T cell infiltration and tumor cell killing). The combinations described herein can provide a superior beneficial effect, *e.g.*, in the treatment of a disorder, such as an enhanced anti-cancer effect, reduced toxicity and/or reduced side effects, compared to monotherapy administration of the therapeutic agents in the combination. For example, one or more of the therapeutic agents in the combination can be administered at a lower dosage, or for a shorter period of administration, than would be required to achieve the same therapeutic effect compared to the monotherapy administration. Thus, compositions and methods for treating cancer and other immune disorders using the aforesaid combination therapies are disclosed.

Accordingly, in one aspect, the invention features a method of treating (*e.g.*, inhibiting, reducing, ameliorating, or preventing) a disorder, *e.g.*, a hyperproliferative condition or disorder (*e.g.*, a cancer) in a subject. The method includes administering to the subject a combination of two, three or more therapeutic agents chosen from one, two or all of the following categories (i)-(iii): (i) an agent that enhances antigen (*e.g.*, tumor antigen) presentation; (ii) an agent that enhances an effector cell response (*e.g.*, B cell and/or T cell activation and/or mobilization); or (iii) an agent that decreases tumor immunosuppression, thereby treating the disorder, *e.g.*, the hyperproliferative condition or disorder (*e.g.*, the cancer). In some embodiments, the combination includes a LAG-3 inhibitor (*e.g.*, an anti-LAG-3 antibody molecule as described herein). The cancer treated can be, *e.g.*, a cancer described herein, such as a lung cancer, a melanoma, a renal cancer, a liver cancer, a myeloma, a prostate cancer, a breast cancer, a head and neck cancer, a colorectal cancer, a pancreatic cancer, a hematological cancer, a non-Hodgkin's lymphoma, or a leukemia, or a metastatic lesion of the cancer.

In another aspect, the invention features a method of reducing an activity (*e.g.*, growth, survival, or viability, or all), of a hyperproliferative (*e.g.*, a cancer) cell. The method includes contacting the cell with a combination of two, three or more therapeutic agents chosen from one, two or all of the following categories (i)-(iii): (i) an agent that enhances antigen (*e.g.*, tumor antigen) presentation; (ii) an agent that enhances an effector cell response (*e.g.*, B cell and/or T

cell activation and/or mobilization); or (iii) an agent that decreases tumor immunosuppression, thereby reducing an activity in the hyperproliferative cell. In some embodiments, the combination includes a LAG-3 inhibitor (*e.g.*, an anti-LAG-3 antibody molecule as described herein). The method can be performed in a subject, *e.g.*, as part of a therapeutic protocol. The cancer cell can be, *e.g.*, a cell from a cancer described herein, such as a lung cancer, a melanoma, a renal cancer, a liver cancer, a myeloma, a prostate cancer, a breast cancer, a head and neck cancer, a colorectal cancer, a pancreatic cancer, a hematological cancer, a non-Hodgkin's lymphoma, or a leukemia, or a metastatic lesion of the cancer.

In certain embodiments of the methods disclosed herein, the method further includes determining the level of an immune cell (*e.g.*, a T cell) infiltrate (*e.g.*, the level of tumor infiltrating lymphocytes (TIL)) in the subject. In one embodiment, the level of the immune cell infiltrate is determined *in vivo*, *e.g.*, non-invasively (*e.g.*, by detecting an antibody to a T cell marker detectably labeled using a suitable imaging technique, *e.g.*, positron emission tomography (PET) scan). In other embodiments, the level of the immune cell infiltrate is determined in a sample (*e.g.*, a tumor biopsy) acquired from the subject (*e.g.*, using immunohistochemical techniques). In embodiments, responsive to a low level of, or no detectable, tumor infiltrate in the subject, one or more agents of categories (i) or (ii), or both (i) and (ii), is/are administered. In other embodiments, responsive to a detectable level, or an elevated level, of tumor infiltrate in the subject, one or more agents of category (iii) is/are administered. The detection steps can also be used, *e.g.*, to monitor the effectiveness of a therapeutic agent described herein. For example, the detection step can be used to monitor the effectiveness of therapeutic agents of categories (i), (ii) and/or (iii).

In another aspect, the invention features a composition (*e.g.*, one or more compositions or dosage forms), that includes a combination of two, three or more therapeutic agents chosen from one, two or all of the following categories (i)-(iii): (i) an agent that enhances antigen (*e.g.*, tumor antigen) presentation; (ii) an agent that enhances an effector cell response (*e.g.*, activation and/or mobilization of B cell and/or T cell); or (iii) an agent that decreases tumor immunosuppression. In some embodiments, the combination includes a LAG-3 inhibitor (*e.g.*, an anti-LAG-3 antibody molecule as described herein).

In yet another aspect, the invention features a composition (*e.g.*, one or more compositions or dosage forms as described hereom), for use in treating a disorder, *e.g.*, a cancer. In embodiments, the composition for use includes a combination of two, three or more therapeutic agents chosen from one, two or all of the following categories (i)-(iii): (i) an agent that enhances antigen (*e.g.*, tumor antigen) presentation; (ii) an agent that enhances an effector cell response (*e.g.*, activation and/or mobilization of B cell and/or T cell); or (iii) an agent that decreases tumor immunosuppression. In some embodiments, the combination used includes a LAG-3 inhibitor (*e.g.*, an anti-LAG-3 antibody molecule as described herein). The cancer can be, *e.g.*, a cancer described herein, such as lung a lung cancer, a melanoma, a renal cancer, a liver cancer, a myeloma, a prostate cancer, a breast cancer, a head and neck cancer, a colorectal cancer, a pancreatic cancer, a hematological cancer, a non-Hogdkin's lymphoma, or a leukemia, or a metastatic lesion of the cancer.

Formulations, *e.g.*, dosage formulations, and kits, *e.g.*, therapeutic kits, that include a combination of two, three or more therapeutic agents chosen from one, two or all of the following categories (i)-(iii): (i) an agent that enhances antigen (*e.g.*, tumor antigen) presentation; (ii) an agent that enhances an effector cell response (*e.g.*, activation and/or mobilization of B cell and/or T cell); or (iii) an agent that decreases tumor immunosuppression, thereby reducing an activity in the cell, and (optionally) instructions for use, are also disclosed. In some embodiments, the combination includes a LAG-3 inhibitor (*e.g.*, an anti-LAG-3 antibody molecule as described herein).

The combinations of therapeutic agents disclosed herein include two or more therapeutic agents described herein. The therapeutic agents in the combination can belong to the same category, *e.g.*, two or more therapeutic agents of category (i), or can include at least one agent of two or more categories (*e.g.*, a therapeutic agent of category (i) combined with a therapeutic agent of category (ii)), as described below. Certain therapeutic agents can belong to two or more categories of categories (i)-(iii). For example, a therapeutic agent (*e.g.*, a GITR agonist, an IDO antagonist, a TGF-b inhibitor, among others) can act as a therapeutic agent in multiple categories.

Additional features or embodiments of the methods, compositions, dosage formulations, and kits described herein include one or more of the following:

Combinations

In certain embodiments, the combination includes one, two, three, four or more therapeutic agents that enhance antigen (*e.g.*, tumor antigen) presentation (referred to herein as an “antigen-presentation combination”). In certain embodiments, the antigen presentation combination includes one or more of: an agent that enhances antigen presentation (*e.g.*, a vaccine, *e.g.*, a cell- or antigen-based vaccine); an agent that enhances lysis of tumor cells (*e.g.*, an oncolytic virus); an agent that stimulates (*e.g.*, disinhibits) a phagocyte, *e.g.*, a Type I interferon (IFN) activator (*e.g.*, a TLR agonist, a RIG-I-like receptor agonist (RLRs)), and/or an agent that activates and/or recruits a dendritic cell or a macrophage (*e.g.*, a macrophage I), *e.g.*, a bi- or tri-specific cell engager.

In some embodiments, the antigen-presentation combination includes one, two, three, four, five or more therapeutic agents chosen from: (i) an agonist of Stimulator of Interferon Genes (a STING agonist), (ii) an agonist of a Toll-like receptor (TLR) (*e.g.*, an agonist of TLR-3, -4, -5, -7, -8, or -9), (iii) a TIM-3 modulator (*e.g.*, an anti-TIM-3 antibody molecule), (iv) a vascular endothelial growth factor receptor (VEGFR) inhibitor, (v) a c-Met inhibitor, (vi) a TGFb inhibitor (*e.g.*, an anti-TGFb antibody), (vii) an IDO/TDO inhibitor, (viii) an A2AR antagonist, (ix) an oncolytic virus, (x) a vaccine (*e.g.*, a scaffold vaccine), or (xi) a bi- or tri-specific cell engager. Any combination of the aforesaid agents (i)-(xi) can be used in the antigen-presentation combination. In one exemplary embodiment, the antigen-presentation combination includes a STING agonist. In another exemplary embodiment, the antigen-presentation combination includes a TLR agonist (*e.g.*, a TLR7 agonist). In another exemplary embodiment, the antigen-presentation combination includes a STING agonist and a TLR agonist (*e.g.*, a TLR7 agonist). In some embodiments, the antigen presentation combination is chosen from a STING agonist, a TLR agonist, an A2AR antagonist, or an oncolytic virus or a combination thereof, and optionally, one or more of (iii)-(vii) or (x)-(xi). In some embodiments, the antigen presentation combination is chosen from a STING agonist or a TLR agonist, or a combination of both, and optionally, one or more of (iii)-(xi). In another embodiment, the

antigen-presentation combination includes a STING agonist, a TLR agonist (*e.g.*, a TLR7 agonist) and a TIM-3 modulator (*e.g.*, an anti-TIM-3 inhibitor). In another embodiment, the antigen-presentation combination includes a STING agonist, a TLR agonist (*e.g.*, a TLR7 agonist) and a VEGFR inhibitor. In another embodiment, the antigen-presentation combination includes a STING agonist, a TLR agonist (*e.g.*, a TLR7 agonist) and a c-MET inhibitor. In yet other embodiments, the antigen-presenting combination includes an oncolytic virus. In other embodiments, the antigen-presenting combination includes an oncolytic virus and a cytokine, *e.g.*, an oncolytic virus expressing one or more of GM-CSF, or a CSF (*e.g.*, CSF1, or CSF2). In some embodiments, the antigen-presenting combination includes a bi- or tri-specific cell engager, *e.g.*, a bi- or tri-specific antibody molecule to CD47 and CD19, with or without an Fc domain. In some embodiments, the antigen-presenting combination includes a TGFb inhibitor (*e.g.*, an anti-TGFb antibody). In other embodiments, the antigen-presenting combination includes an IDO/TDO inhibitor. In yet other embodiments, the antigen-presenting combination includes an A2AR antagonist. In yet other embodiments, the antigen-presenting combination includes a vaccine (*e.g.*, IL-2 in combination with MUC1, or a dendritic cell based vaccine (*e.g.*, Provenge®)). In yet other embodiments, the antigen-presenting combination includes a vaccine and a TLR agonist (*e.g.*, a TLR agonist as described herein). In certain embodiment, the antigen-presentation combination includes a vaccine and a STING agonist. In certain embodiment, the antigen-presentation combination includes a vaccine, a STING agonist and a TLR agonist.

In certain embodiments, the combination includes one, two, three, four, five or more therapeutic agents that enhance an effector cell response (referred to herein as an “effector cell combination”). In some embodiments, the effector cell combination includes a lymphocyte activator, *e.g.*, an NK cell activator and/or a T cell activator. In some embodiments, the effector cell combination activates (*e.g.*, disinhibits) a tumor infiltrating lymphocyte (TIL), *e.g.*, an NK cell or a T cell. In some embodiments, the effector cell combination includes an NK cell modulator chosen from a modulator (*e.g.*, an antibody molecule) of an NK receptor (*e.g.*, a modulator of one or more of NKG2A, KIR3DL, NKp46, MICA or CEACAM1); an interleukin or an interleukin variant (*e.g.*, IL-2, IL-15, IL-21, IL-13R or IL-12 cytokine or variant thereof, or a combination thereof); a bi- or tri-specific cell engager (*e.g.*, a bispecific antibody molecule of NKG2A and CD138, or a bispecific antibody molecule of CD3 and TCR); an NK cell therapy; or

a vaccine that includes NK cells and an antigen/immune stimulant. In some embodiments, the effector cell combination includes an immunomodulator (*e.g.*, one or more of: an activator of a costimulatory molecule or an inhibitor of an immune checkpoint molecule as described herein). In some embodiments, the effector cell combination includes a T cell modulator chosen from an inhibitor of a checkpoint inhibitor (*e.g.*, an inhibitor of one or more of: PD-1, PD-L1, TIM-3, LAG-3, VISTA, DKG- α , B7-H3, B7-H4, TIGIT, CTLA4, BTLA, CD160, TIM1, IDO, LAIR1, IL-12, or a combination thereof, *e.g.*, an inhibitor of LAG-3 and PD-1, or an inhibitor of LAG-3 and TIM-3). In one embodiment, the inhibitor of the checkpoint inhibitor is an antibody molecule (*e.g.*, a mono- or bispecific antibody or fragment thereof as described herein). For example, the inhibitor of the checkpoint inhibitor is an antibody molecule against PD-1, PD-L1, TIM-3, LAG-3, VISTA, B7-H4, CTLA-4 or TIGIT, or any combination thereof (*e.g.* a combination as described herein). In some embodiments, the effector cell combination includes a T cell modulator chosen from an agonist or an activator of a costimulatory molecule. In one embodiment, the agonist of the costimulatory molecule is chosen from an agonist (*e.g.*, an agonistic antibody or antigen-binding fragment thereof, or a soluble fusion) of GITR, OX40, ICOS, SLAM (*e.g.*, SLAMF7), HVEM, LIGHT, CD2, CD27, CD28, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), CD30, CD40, BAFFR, CD7, NKG2C, NKp80, CD160, B7-H3, or CD83 ligand. In other embodiments, the effector cell combination includes a bispecific T cell engager (*e.g.*, a bispecific antibody molecule that binds to CD3 and a tumor antigen (*e.g.*, EGFR, PSCA, PSMA, EpCAM, HER2 among others).

In some embodiments, the effector cell combination includes one, two, three, four, five or more therapeutic agents chosen from: (i) a GITR modulator (*e.g.*, a GITR agonist), (ii) a PD-1 inhibitor (*e.g.*, an anti-PD-1 antibody molecule as described herein), (iii) a PD-L1 inhibitor, (iv) an inhibitor of IAP (Inhibitor of Apoptosis Protein), (v) an inhibitor of EGFR (Epidermal Growth Factor Receptor), (vi) an inhibitor of target of rapamycin (mTOR), (vii) IL-15 or a variant thereof, (viii) a CTLA-4 inhibitor, (ix) a bispecific T cell engager (*e.g.*, a bispecific antibody molecule that binds to CD3 and a tumor antigen (*e.g.*, EGFR, PSCA, PSMA, EpCAM, HER2 among others), (x) a CD40 agonist (*e.g.*, an anti-CD40 antibody molecule), (xi) an OX40 agonist (*e.g.*, an anti-OX40 antibody molecule), or (xii) a CD27 agonist (*e.g.*, an anti-CD27 antibody molecule). Any combination of the aforesaid agents can be used in the effector cell

combination. In one exemplary embodiment, the effector cell combination includes a GITR agonist. In another embodiment, the effector cell combination includes a PD-1 inhibitor (*e.g.*, an anti-PD-1 antibody molecule as described herein). In another embodiment, the effector cell combination includes a PD-L1 inhibitor. In other embodiments, the effector cell combination includes a GITR agonist and a PD-1 inhibitor (*e.g.*, an anti-PD-1 antibody molecule as described herein). In other embodiments, the effector cell combination includes a GITR agonist and a PD-L1 inhibitor. In other embodiments, the effector cell combination includes a GITR agonist, a PD-1 inhibitor (*e.g.*, an anti-PD-1 antibody molecule as described herein), and a PD-L1 inhibitor. In other embodiments, the effector cell combination includes a PD-1 inhibitor (*e.g.*, an anti-PD-1 antibody molecule as described herein), and a PD-L1 inhibitor. In one embodiment, the effector cell combination includes a GITR agonist and an inhibitor of IAP. In another embodiment, the effector cell combination includes a GITR agonist and an inhibitor of an EGFR inhibitor. In yet another embodiment, the effector cell combination includes a GITR agonist and an inhibitor of an mTOR inhibitor. In one embodiment, the effector cell combination includes IL-15 or a variant thereof. In one embodiment, the effector cell combination includes a CTLA-4 inhibitor. In one embodiment, the effector cell combination includes a bispecific T cell engager (*e.g.*, a bispecific antibody molecule that binds to CD3 and a tumor antigen (*e.g.*, EGFR, PSCA, PSMA, EpCAM, HER2 among others)). In one embodiment, the effector cell combination includes a CD40 agonist (*e.g.*, an anti-CD40 antibody molecule). In one embodiment, the effector cell combination includes an OX40 agonist (*e.g.*, an anti-OX40 antibody molecule). In one embodiment, the effector cell combination includes a CD27 agonist (*e.g.*, an anti-CD27 antibody molecule).

In certain embodiments, the combination includes one, two, three, four, five or more therapeutic agents that decrease tumor immunosuppression (referred to herein as an “anti-tumor immunosuppression combination”). In some embodiments, the combination modulates the activity or level of one or more of T_{reg} , macrophage 2 or MDSCs. In some embodiments, the combination increases one or more of M2 polarization, T_{reg} depletion, or T cell recruitment. In some embodiments, the anti-tumor immunosuppression combination includes one, two, three, four, five or more therapeutic agents chosen from: (i) an immunomodulator (*e.g.*, one or more of: an activator of a costimulatory molecule (*e.g.*, a GITR agonist), or an inhibitor of an immune

checkpoint molecule (*e.g.*, one or more of PD-1, PD-L1, LAG-3, TIM-3 or CTLA-4), as described herein), (ii) a CSF-1/1R inhibitor (*e.g.*, an inhibitor of macrophage colony-stimulating factor (M-CSF)), (iii) an IL-17 inhibitor, (iv) an IL-1 β inhibitor, (v) a CXCR2 inhibitor, (vi) an inhibitor of a phosphoinositide 3-kinase (PI3K, *e.g.*, PI3K γ or PI3K δ), (vii) a BAFF-R inhibitor, (viii) a MALT-1/BTK inhibitor, (ix) a JAK inhibitor, (x) a CRTH2 inhibitor, (xi) a VEGFR inhibitor, (xiii) an IL-15 or a variant thereof, (xiv) a CTLA-4 inhibitor, (xv) an IDO/TDO inhibitor, (xvi) an A2AR antagonist, (xvii) a TGF β inhibitor, or (xviii) a PFKFB3 inhibitor. In certain embodiments, the immunomodulator is an inhibitor of an immune checkpoint molecule (*e.g.*, an inhibitor of PD-1, PD-L1, LAG-3, TIM-3, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), or CTLA-4, or any combination thereof). Any combination of the aforesaid agents can be used in the tumor immunosuppression combination. In one exemplary embodiment, the anti-tumor immunosuppression combination includes one, two, three, four, five or more therapeutic agents chosen from a LAG-3 inhibitor (*e.g.*, an anti-LAG-3 antibody molecule as described herein), a PD-1 inhibitor, a PD-L1 inhibitor, a TIM-3 modulator (*e.g.*, an anti-TIM-3 inhibitor), a GITR agonist, a CSF-1/1R inhibitor (*e.g.*, an M-CSF inhibitor), an IL-17 inhibitor, an IL-1 β inhibitor, or a CXCR2 inhibitor. In one embodiment, the anti-tumor immunosuppression combination includes one, two, or all of a CSF-1/1R inhibitor (*e.g.*, an M-CSF inhibitor), an IL-17 inhibitor, an IL-1 β inhibitor. In one embodiment, the anti-tumor immunosuppression combination includes an IL-17 inhibitor, a CXCR2 inhibitor, a CRTH2 inhibitor, an A2AR antagonist, or a PFKFB3 inhibitor, or a combination thereof.

In some embodiments, the combination includes one or more therapeutic agents of the antigen-presentation combination. In other embodiments, the combination includes one or more therapeutic agents of the effector cell combination. In yet other embodiments, the combination includes one or more therapeutic agents of the anti-tumor immunosuppression combination. In other embodiments, the combination includes one or more therapeutic agents of the antigen-presentation combination and one or more therapeutic agents of the effector cell combination. In other embodiments, the combination includes one or more therapeutic agents of the antigen-presentation combination and one or more therapeutic agents of the anti-tumor immunosuppression combination. In other embodiments, the combination includes one or more therapeutic agents of the antigen-presentation combination, one or more therapeutic agents of the

effector cell combination and one or more therapeutic agents of the anti-tumor immunosuppression combination. In other embodiments, the combination includes one or more therapeutic agents of the antigen-presentation combination, one or more therapeutic agents of the effector cell combination and one or more therapeutic agents of the anti-tumor immunosuppression combination.

In certain embodiments, the combination includes:

(i) one or more therapeutic agents of the antigen-presentation combination chosen from one, two or all of a STING agonist, a TLR agonist (*e.g.*, a TLR7 agonist), or a TIM-3 modulator (*e.g.*, a TIM-3 inhibitor);

(ii) one or more therapeutic agents of the effector cell combination chosen from one, two or all of a GITR modulator (*e.g.*, a GITR agonist), a PD-1 inhibitor (*e.g.*, an anti-PD-1 antibody molecule as described herein), or a PD-L1 inhibitor;

(iii) one or more therapeutic agents of the anti-tumor immunosuppression combination chosen from one, two or all of a CSF-1/1R inhibitor (*e.g.*, an M-CSF inhibitor), an IL-17 inhibitor, or an IL-1 β inhibitor:

(iv) a combination of (i) and (ii);

(v) a combination of (i) and (iii);

(vi) a combination of (ii) and (iii); or

(vii) a combination of (i), (ii) and (iii).

The combination can be used to treat a cancer as described herein, such as a lung cancer, a melanoma, a renal cancer, a liver cancer, a myeloma, a prostate cancer, a breast cancer, a head and neck cancer, a colorectal cancer, a pancreatic cancer, a hematological cancer, a non-Hodgkin's lymphoma, or a leukemia, or a metastatic lesion of the cancer.

In other embodiments, the combination includes a therapeutic agent from the antigen-presentation combination (*e.g.*, one or more of a STING agonist, a TLR agonist, a vaccine or an oncolytic virus) in combination with a therapeutic agent from the effector cell and/or anti-tumor immunosuppression combination (*e.g.*, an inhibitor of a checkpoint inhibitor, *e.g.*, an inhibitor of PD-1, PD-L1, LAG-3, TIM-3, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), or CTLA-4, or any combination thereof. In one embodiment, one or more of a STING agonist, a TLR agonist, a

vaccine or an oncolytic virus is administered in combination with an anti-LAG-3 antibody molecule as described herein. In one embodiment, a STING agonist and/or a vaccine is administered in combination with an anti-LAG-3 antibody molecule as described herein. In one embodiment, an oncolytic virus is administered in combination with an anti-LAG-3 antibody molecule as described herein. The combination can be used to treat a cancer as described herein, such as a lung cancer, a melanoma, a renal cancer, a liver cancer, a myeloma, a prostate cancer, a breast cancer, a head and neck cancer, a colorectal cancer, a pancreatic cancer, a hematological cancer, a non-Hodgkin's lymphoma, or a leukemia, or a metastatic lesion of the cancer.

In certain embodiments, the combination includes a combination of therapeutic agents as provided in the section entitled "Exemplary Combinations of Antigen-Presentation Combinations, Effector Cell Combinations and Anti-tumor Immunosuppression Combinations" provided in the Detailed Description.

The combinations disclosed herein can be administered together in a single composition or administered separately in two or more different compositions, *e.g.*, compositions or dosage forms as described herein. The administration of the therapeutic agents can be in any order. The first agent and the additional agents (*e.g.*, second, third agents) can be administered via the same administration route or via different administration routes. For example, a first therapeutic agent can be administered concurrently with, prior to, or subsequent to, the additional agent. In certain embodiments, a first agent is administered locally, *e.g.*, a therapeutic agent of any of categories (i)-(iii) can be coupled to a tumor targeting agent, *e.g.*, a tumor-targeting antibody (*e.g.*, to form an antibody-drug conjugate), or any other delivery agent (*e.g.*, a formulation such as a targeted formulation) such that administration of the first agent is localized to a desired site, *e.g.*, a tumor site (*e.g.*, a dendritic cell-enriched site). In one embodiment, the therapeutic agent is an antigen (*e.g.*, a vaccine, *e.g.*, an *in situ* cancer vaccine), which is targeted to the tumor environment, thus resulting in activation of dendritic cells. The therapeutic agent also can be locally administered, *e.g.*, injected, at a tumor site (*e.g.*, intratumoral or peritumoral administration). Localized delivery or administration of the therapeutic agent can reduce one or more side effects or toxicities that would otherwise be associated with systemic administration of the therapeutic agent. In one exemplary embodiment, a therapeutic agent (*e.g.*, STING or a TLR) can be

conjugated to a tumor-binding antibody (*e.g.*, an antibody that binds to HER2), thereby delivering the therapeutic agent to a HER-2-expressing cell.

When administered in combination, the first agent, the additional agent (*e.g.*, second or third agent), or all, can be administered in an amount or dose that is higher, lower or the same than the amount or dosage of each agent used individually, *e.g.*, as a monotherapy. In certain embodiments, the administered amount or dosage of the first agent, the additional agent (*e.g.*, second or third agent), or all, is lower (*e.g.*, at least 20%, at least 30%, at least 40%, or at least 50%) than the amount or dosage of each agent used individually, *e.g.*, as a monotherapy. In other embodiments, the amount or dosage of the first agent, the additional agent (*e.g.*, second or third agent), or all, that results in a desired effect (*e.g.*, treatment of cancer) is lower (*e.g.*, at least 20%, at least 30%, at least 40%, or at least 50% lower).

In one embodiment, the anti-LAG-3 antibody molecule is administered, alone or in combination (*e.g.*, in combination with an anti-PD-1 antibody molecule), at a dose of less than, or about, 5 mg/kg; less than, or about, 4 mg/kg; less than, or about, 3 mg/kg; less than, or about, 2 mg/kg; less than, or about, 1 mg/kg, every other week. In one embodiment, the anti-LAG-3 antibody molecule is administered at a dose of 1 to 5 mg/kg every other week; 1 to 4 mg/kg every other week, 1 to 3 mg/kg every other week, or 1 to 2 mg/kg every other week. In one embodiment, the anti-PD-1 antibody molecule is administered, alone or in combination (*e.g.*, in combination with an anti-LAG-3 antibody molecule) at a dose of 1 to 5 mg/kg every other week; 1 to 4 mg/kg every other week, 1 to 3 mg/kg every other week, or 1 to 2 mg/kg every other week.

In certain embodiments, the combinations can be in the form of an antibody molecule, *e.g.*, a bi- or tri-specific molecule, against one or more therapeutic agents chosen from the antigen-presentation combination, the effector cell combination, or the anti-tumor immunosuppression combination, or any combination thereof. For example, a bispecific molecule against two or more checkpoint inhibitors (*e.g.*, an anti-LAG-3 and anti-PD-1 antibody molecule). In other embodiments, the combinations can be in the form of an antibody molecule, *e.g.*, a bi- or tri-specific molecule, against one or more therapeutic agents chosen from two or all of the antigen-presentation combination, the effector cell combination, and/or the anti-tumor immunosuppression combination. In one embodiment, the antibody molecule is a full antibody

or fragment thereof (*e.g.*, a Fab, F(ab')₂, Fv, or a single chain Fv fragment (scFv)). In yet other embodiments, the antibody molecule has a heavy chain constant region (Fc) chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE; particularly, chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4, more particularly, the heavy chain constant region of IgG1 or IgG4 (*e.g.*, human IgG1 or IgG4). In one embodiment, the heavy chain constant region is human IgG1 or human IgG4. In one embodiment, the constant region is altered, *e.g.*, mutated, to modify the properties of the antibody molecule (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function). In certain embodiments, the antibody molecule is in the form of a bispecific or multispecific antibody molecule, *e.g.*, a bispecific, trispecific antibody molecule as described herein.

Certain exemplary therapeutic agents and combinations thereof are provided herein below. A more detailed description of the therapeutic agents used in the combinations is provided in the Detailed Description.

Immunomodulators

In certain embodiments, the immunomodulator used in the combinations disclosed herein (*e.g.*, in combination with a therapeutic agent chosen from an antigen-presentation combination) is an inhibitor of an immune checkpoint molecule. In one embodiment, the immunomodulator is an inhibitor of PD-1, PD-L1, PD-L2, CTLA-4, TIM-3, LAG-3, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and/or TGF beta. In one embodiment, the inhibitor of an immune checkpoint molecule inhibits PD-1, PD-L1, LAG-3, TIM-3, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), CTLA-4, or any combination thereof.

Inhibition of an inhibitory molecule can be performed at the DNA, RNA or protein level. In embodiments, an inhibitory nucleic acid (*e.g.*, a dsRNA, siRNA or shRNA), can be used to inhibit expression of an inhibitory molecule. In other embodiments, the inhibitor of an inhibitory signal is, a polypeptide *e.g.*, a soluble ligand (*e.g.*, PD-1-Ig or CTLA-4 Ig), or an antibody or antigen-binding fragment thereof, that binds to the inhibitory molecule; *e.g.*, an antibody or fragment thereof (also referred to herein as “an antibody molecule”) that binds to

PD-1, PD-L1, PD-L2, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), CTLA-4, TIM-3, LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and/or TGF beta, or a combination thereof.

In certain embodiments, the antibody molecule is in the form of a bispecific or a multispecific antibody molecule. In one embodiment, the bispecific antibody molecule has a first binding specificity for LAG-3 and a second binding specificity for PD-1, TIM-3, CEACAM (*e.g.*, CEACAM-1 and/or CEACAM-5), PD-L1 or PD-L2. In one embodiment, the bispecific antibody molecule binds to LAG-3 and PD-1. In another embodiment, the bispecific antibody molecule binds to LAG-3 and TIM-3. In another embodiment, the bispecific antibody molecule binds to LAG-3 and CEACAM (*e.g.*, CEACAM-1, -3 and/or CEACAM-5). In another embodiment, the bispecific antibody molecule binds to LAG-3 and CEACAM-1. In still another embodiment, the bispecific antibody molecule binds to LAG-3 and CEACAM-3. In yet another embodiment, the bispecific antibody molecule binds to LAG-3 and CEACAM-5. In another embodiment, the bispecific antibody molecule binds to LAG-3 and PD-L1. In yet another embodiment, the bispecific antibody molecule binds to LAG-3 and PD-L2. Any combination of the aforesaid molecules can be made in a multispecific antibody molecule, *e.g.*, a trispecific antibody that includes a first binding specificity to LAG-3, and a second and third binding specificity to one or more of: PD-1, TIM-3, CEACAM (*e.g.*, CEACAM-1, -3, and/or CEACAM-5), PD-L1 or PD-L2.

In other embodiments, the immunomodulator is an inhibitor of LAG-3, *e.g.*, human LAG-3. In one embodiment, the inhibitor of LAG-3 is an antibody molecule to LAG-3. The LAG-3 inhibitor can be administered alone, or in combination with other immunomodulators, *e.g.*, in combination with an inhibitor of CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), TIM-3, PD-1, PD-L1 or CTLA-4. In an exemplary embodiment, the inhibitor of LAG-3, *e.g.*, the anti-LAG-3 antibody molecule, is administered in combination with a PD-1 inhibitor, *e.g.*, an anti-PD-1 antibody molecule. In an exemplary embodiment, the inhibitor of LAG-3, *e.g.*, the anti-LAG-3 antibody molecule, is administered in combination with a PD-L1 inhibitor, *e.g.*, an anti-PD-L1 antibody molecule. In another embodiment, the inhibitor of LAG-3, *e.g.*, the anti-LAG-3 antibody molecule, is administered in combination with a TIM-3 inhibitor, *e.g.*, an anti-TIM-3 antibody molecule. In another embodiment, the inhibitor of LAG-3, *e.g.*, the anti-LAG-3 antibody molecule, is administered in combination with a CEACAM inhibitor (*e.g.*, CEACAM-1, -3 and/or -5 inhibitor), *e.g.*, an anti-CEACAM antibody molecule. In another embodiment, the

inhibitor of LAG-3, *e.g.*, the anti-LAG-3 antibody molecule, is administered in combination with a CEACAM-1 inhibitor, *e.g.*, an anti-CEACAM-1 antibody molecule. In another embodiment, the inhibitor of LAG-3, *e.g.*, the anti-LAG-3 antibody molecule, is administered in combination with a CEACAM-5 inhibitor, *e.g.*, an anti-CEACAM-5 antibody molecule. In yet other embodiments, the inhibitor of LAG-3, *e.g.*, the anti-LAG-3 antibody molecule, is administered in combination with a PD-1 inhibitor, *e.g.*, an anti-PD-1 antibody molecule, and a TIM-3 inhibitor, *e.g.*, an anti-TIM-3 antibody molecule. Other combinations of immunomodulators with a LAG-3 inhibitor (*e.g.*, one or more of PD-1, PD-L1, PD-L2, CTLA-4, TIM-3, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and/or TGF beta) are also within the present invention. Any of the antibody molecules known in the art or disclosed herein can be used in the aforesaid combinations of inhibitors of checkpoint molecule

In certain embodiments, the immunomodulator is an inhibitor of PD-1, *e.g.*, human PD-1. In another embodiment, the immunomodulator is an inhibitor of PD-L1, *e.g.*, human PD-L1. In one embodiment, the inhibitor of PD-1 or PD-L1 is an antibody molecule to PD-1 or PD-L1. The PD-1 or PD-L1 inhibitor can be administered alone, or in combination with other immunomodulators, *e.g.*, in combination with an inhibitor of LAG-3, TIM-3, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5) or CTLA-4. In an exemplary embodiment, the inhibitor of PD-1 or PD-L1, *e.g.*, the anti-PD-1 or PD-L1 antibody molecule, is administered in combination with a LAG-3 inhibitor, *e.g.*, an anti-LAG-3 antibody molecule. In another embodiment, the inhibitor of PD-1 or PD-L1, *e.g.*, the anti-PD-1 or PD-L1 antibody molecule, is administered in combination with a TIM-3 inhibitor, *e.g.*, an anti-TIM-3 antibody molecule. In another embodiment, the inhibitor of PD-1 or PD-L1, *e.g.*, the anti-PD-1 or PD-L1 antibody molecule, is administered in combination with a CEACAM inhibitor (*e.g.*, CEACAM-1, -3 and/or -5 inhibitor), *e.g.*, an anti-CEACAM antibody molecule. In another embodiment, the inhibitor of PD-1 or PD-L1, *e.g.*, the anti-PD-1 or PD-L1 antibody molecule, is administered in combination with a CEACAM-1 inhibitor, *e.g.*, an anti-CEACAM-1 antibody molecule. In another embodiment, the inhibitor of PD-1 or PD-L1, *e.g.*, the anti-PD-1 or PD-L1 antibody molecule, is administered in combination with a CEACAM-5 inhibitor, *e.g.*, an anti-CEACAM-5 antibody molecule. In yet other embodiments, the inhibitor of PD-1 or PD-L1, *e.g.*, the anti-PD-1 antibody molecule, is administered in combination with a LAG-3 inhibitor, *e.g.*, an anti-LAG-3 antibody molecule, and a TIM-3 inhibitor, *e.g.*, an anti-TIM-3 antibody molecule. Other

combinations of immunomodulators with a PD-1 inhibitor (*e.g.*, one or more of PD-L2, CTLA-4, TIM-3, LAG-3, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and/or TGF beta) are also within the present invention. Any of the antibody molecules known in the art or disclosed herein can be used in the aforesaid combinations of inhibitors of checkpoint molecule.

In other embodiments, the immunomodulator is an inhibitor of CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), *e.g.*, human CEACAM (*e.g.*, CEACAM-1, -3 and/or -5). In one embodiment, the immunomodulator is an inhibitor of CEACAM-1, *e.g.*, human CEACAM-1. In another embodiment, the immunomodulator is an inhibitor of CEACAM-3, *e.g.*, human CEACAM-3. In another embodiment, the immunomodulator is an inhibitor of CEACAM-5, *e.g.*, human CEACAM-5. In one embodiment, the inhibitor of CEACAM (*e.g.*, CEACAM-1, -3 and/or -5) is an antibody molecule to CEACAM (*e.g.*, CEACAM-1, -3 and/or -5). The CEACAM (*e.g.*, CEACAM-1, -3 and/or -5) inhibitor can be administered alone, or in combination with other immunomodulators, *e.g.*, in combination with an inhibitor of LAG-3, TIM-3, PD-1, PD-L1 or CTLA-4.

In other embodiments, the immunomodulator is an inhibitor of TIM-3, *e.g.*, human TIM-3. In one embodiment, the inhibitor of TIM-3 is an antibody molecule to TIM-3. The TIM-3 inhibitor can be administered alone, or in combination with other immunomodulators, *e.g.*, in combination with an inhibitor of CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), LAG-3, PD-1, PD-L1 or CTLA-4.

In certain embodiments, the immunomodulator used in the combinations disclosed herein (*e.g.*, in combination with a therapeutic agent chosen from an antigen-presentation combination) is an activator or agonist of a costimulatory molecule. In one embodiment, the agonist of the costimulatory molecule is chosen from an agonist (*e.g.*, an agonistic antibody or antigen-binding fragment thereof, or a soluble fusion) of OX40, CD2, CD27, CD28, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3, or CD83 ligand.

In other embodiments, the immunomodulator is a GITR agonist. In one embodiment, the GITR agonist is an antibody molecule to GITR. The GITR agonist can be administered alone, or in combination with other immunomodulators, *e.g.*, in combination with an inhibitor of PD-1, PD-L1, CTLA-4, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), TIM-3 or LAG-3. In some

embodiments, the anti-GITR antibody molecule is a bispecific antibody that binds to GITR and PD-1, PD-L1, CTLA-4, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), TIM-3 or LAG-3. In one exemplary embodiment, the anti-GITR antibody molecule is administered in combination with an anti-PD-1 antibody molecule (*e.g.*, an anti-PD-1 molecule as described herein). The GITR antibody molecule and the anti-PD-1 antibody molecule may be in the form of separate antibody composition, or as a bispecific antibody molecule. In other embodiments, a GITR agonist can be administered in combination with other costimulatory molecule, *e.g.*, an agonist of OX40, CD2, CD27, CD28, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3, or CD83 ligand.

In other embodiments, the immunomodulator is an activator of a costimulatory molecule (*e.g.*, an OX40 agonist). In one embodiment, the OX40 agonist is an antibody molecule to OX40. The OX40 agonist can be administered alone, or in combination with other immunomodulators, *e.g.*, in combination with an inhibitor of PD-1, PD-L1, CTLA-4, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), TIM-3 or LAG-3. In some embodiments, the anti-OX40 antibody molecule is a bispecific antibody that binds to GITR and PD-1, PD-L1, CTLA-4, CEACAM (*e.g.*, CEACAM-1, -3 and/or -5), TIM-3 or LAG-3. In one exemplary embodiment, an OX40 antibody molecule is administered in combination with an anti-PD-1 antibody molecule (*e.g.*, an anti-PD-1 molecule as described herein). The OX40 antibody molecule and the anti-PD-1 antibody molecule may be in the form of separate antibody composition, or as a bispecific antibody molecule. In other embodiments, the OX40 agonist can be administered in combination with other costimulatory molecule, *e.g.*, an agonist of GITR, CD2, CD27, CD28, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3, or CD83 ligand.

It is noted that only exemplary combinations of inhibitors of checkpoint inhibitors or agonists of costimulatory molecules are provided herein. Additional combinations of these agents are within the scope of the present invention.

Antibody Molecules to LAG-3

In one embodiment, the LAG-3 inhibitor is an anti-LAG-3 antibody molecule as described in U.S. Patent Application Publication No. US 2015/0259420 (USSN 14/657,260),

entitled “Antibody Molecules to LAG-3 and Uses Thereof,” incorporated by reference in its entirety.

In one embodiment, the anti-LAG-3 antibody molecule comprises at least one antigen-binding region, *e.g.*, a variable region or an antigen-binding fragment thereof, from an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In another embodiment, the anti-LAG-3 antibody molecule comprises at least one, two, three or four variable regions from an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences. In one

embodiment, the antibody molecule includes a substitution (*e.g.*, a Cys to Ser substitution at position 84) in the heavy chain framework region 3 (VHFW3) (*e.g.*, as shown in Tables 1 and 2).

In yet another embodiment, the anti-LAG-3 antibody molecule comprises at least one or two heavy chain variable regions from an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In yet another embodiment, the anti-LAG-3 antibody molecule comprises at least one or two light chain variable regions from an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In yet another embodiment, the anti-LAG-3 antibody molecule includes a heavy chain constant region for an IgG4, *e.g.*, a human IgG4. In one embodiment, the human IgG4 includes a substitution at position 228 according to EU numbering (*e.g.*, a Ser to Pro substitution). In still another embodiment, the anti-LAG-3 antibody molecule includes a heavy chain constant region for an IgG1, *e.g.*, a human IgG1. In one embodiment, the human IgG1 includes a substitution at position 297 according to EU numbering (*e.g.*, an Asn to Ala substitution). In one embodiment, the human IgG1 includes a substitution at position 265 according to EU numbering, a substitution at position 329 according to EU numbering, or both (*e.g.*, an Asp to Ala substitution at position 265 according to EU numbering and/or a Pro to Ala substitution at position 329 according to EU numbering). In one embodiment, the human IgG1 includes a substitution at position 234 according to EU numbering, a substitution at position 235 according to EU numbering, or both (*e.g.*, a Leu to Ala substitution at position 234 according to EU numbering and/or a Leu to Ala substitution at position 235 according to EU numbering). In one embodiment, the heavy chain constant region comprises an amino sequence set forth in Table 3, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto.

In yet another embodiment, the anti-LAG-3 antibody molecule includes a kappa light chain constant region, *e.g.*, a human kappa light chain constant region. In one embodiment, the light chain constant region comprises an amino sequence set forth in Table 3, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto.

In another embodiment, the anti-LAG-3 antibody molecule includes a heavy chain constant region for an IgG4, *e.g.*, a human IgG4, and a kappa light chain constant region, *e.g.*, a human kappa light chain constant region, *e.g.*, a heavy and light chain constant region comprising an amino sequence set forth in Table 3, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto. In one embodiment, the constant region is a mutated IgG4, *e.g.*, a mutated human IgG4 (*e.g.*, has a mutation at position 228 according to EU numbering (*e.g.*, a S228P mutation). In yet another embodiment, the anti-LAG-3 antibody molecule includes a heavy chain constant region for an IgG1, *e.g.*, a human IgG1, and a kappa light chain constant region, *e.g.*, a human kappa light chain constant region, *e.g.*, a heavy and light chain constant region comprising an amino

sequence set forth in Table 3, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto. In one embodiment, the human IgG1 includes a substitution at position 297 according to EU numbering (*e.g.*, an Asn to Ala substitution). In one embodiment, the human IgG1 includes a substitution at position 265 according to EU numbering, a substitution at position 329 according to EU numbering, or both (*e.g.*, an Asp to Ala substitution at position 265 according to EU numbering and/or a Pro to Ala substitution at position 329 according to EU numbering). In one embodiment, the human IgG1 includes a substitution at position 234 according to EU numbering, a substitution at position 235 according to EU numbering, or both (*e.g.*, a Leu to Ala substitution at position 234 according to EU numbering and/or a Leu to Ala substitution at position 235 according to EU numbering).

In another embodiment, the anti-LAG-3 antibody molecule includes a heavy chain variable domain and a constant region, a light chain variable domain and a constant region, or both, comprising the amino acid sequence of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences. The anti-LAG-3 antibody molecule, optionally, comprises a leader sequence from a heavy chain, a light chain, or both, as shown in Table 4; or a sequence substantially identical thereto.

In yet another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07,

BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs shown in Table 1.

In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

In yet another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, or three complementarity determining regions (CDRs) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J;

or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs shown in Table 1.

In yet another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

In another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid shown in Table 1, or encoded by a nucleotide sequence shown in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs shown in Table 1.

In another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

In one embodiment, the anti-LAG-3 antibody molecule includes all six CDRs from an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-

hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1, or closely related CDRs, *e.g.*, CDRs which are identical or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs shown in Table 1. In one embodiment, the anti-LAG-3 antibody molecule may include any CDR described herein.

In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three CDRs according to Kabat (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in Table 1) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two,

three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Kabat shown in Table 1.

In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three CDRs according to Kabat (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in Table 1) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Kabat shown in Table 1.

In yet another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, three, four, five, or six CDRs according to Kabat (*e.g.*, at least one, two, three, four, five, or six CDRs according to the Kabat definition as set out in Table 1) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser,

BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to at least one, two, three, four, five, or six CDRs according to Kabat *et al.* shown in Table 1. In one embodiment, the anti-LAG-3 antibody molecule may include any CDR described herein.

In yet another embodiment, the anti-LAG-3 antibody molecule includes all six CDRs according to Kabat (*e.g.*, all six CDRs according to the Kabat definition as set out in Table 1) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to Kabat *et al.* shown in Table 1. In one embodiment, the anti-LAG-3 antibody molecule may include any CDR described herein.

In another embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three hypervariable loops (*e.g.*, at least one, two, or three hypervariable loops according to the Chothia definition as set out in Table 1) from a heavy chain variable region of an antibody

described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, according to Chothia (*e.g.*, at least one, two, or three hypervariable loops according to the Chothia definition as set out in Table 1); or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three hypervariable loops according to Chothia shown in Table 1.

In another embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three hypervariable loops according to Chothia (*e.g.*, at least one, two, or three CDRs according to the Chothia definition as set out in Table 1) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J,; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at

least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three hypervariable loops according to Chothia shown in Table 1.

In yet another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, three, four, five, or six hypervariable loops (*e.g.*, at least one, two, three, four, five, or six hypervariable loops according to the Chothia definition as set out in Table 1) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or at least the amino acids from those hypervariable loops that contact LAG-3. In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two, three, four, five, or six Chothia hypervariable loops of Table 1.

In one embodiment, the anti-LAG-3 antibody molecule includes all six hypervariable loops (*e.g.*, all six hypervariable loops according to the Chothia definition as set out in Table 1) of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser,

BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, or closely related hypervariable loops, *e.g.*, hypervariable loops which are identical or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six hypervariable loops shown in Table 1. In one embodiment, the anti-LAG-3 antibody molecule may include any hypervariable loop described herein.

In still another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, or three hypervariable loops that have the same canonical structures as the corresponding hypervariable loop of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, *e.g.*, the same canonical structures as at least loop 1 and/or loop 2 of the heavy and/or light chain variable domains of an antibody described herein. *See, e.g.*, Chothia *et al.*, (1992) *J. Mol. Biol.* 227:799-817; Tomlinson *et al.*, (1992) *J. Mol. Biol.* 227:776-798 for descriptions of hypervariable loop canonical structures. These structures can be determined by inspection of the tables described in these references.

In certain embodiments, the anti-LAG-3 antibody molecule includes a combination of CDRs or hypervariable loops defined according to the Kabat *et al.* and Chothia *et al.*

In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three CDRs or hypervariable loops from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13,

BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, according to the Kabat and Chothia definition (*e.g.*, at least one, two, or three CDRs or hypervariable loops according to the Kabat and Chothia definition as set out in Table 1); or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs or hypervariable loops according to Kabat and/or Chothia shown in Table 1.

For example, the anti-LAG-3 antibody molecule can include VH CDR1 according to Kabat *et al.* or VH hypervariable loop 1 according to Chothia *et al.*, or a combination thereof, *e.g.*, as shown in Table 1. In one embodiment, the combination of Kabat and Chothia CDR of VH CDR1 comprises the amino acid sequence GFTLTNYGMN (SEQ ID NO: 286), or an amino acid sequence substantially identical thereto (*e.g.*, having at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions)). The anti-LAG-3 antibody molecule can further include, *e.g.*, VH CDRs 2-3 according to Kabat *et al.* and VL CDRs 1-3 according to Kabat *et al.*, *e.g.*, as shown in Table 1. Accordingly, in some embodiments, framework regions are defined based on a combination of CDRs defined according to Kabat *et al.* and hypervariable loops defined according to Chothia *et al.* For example, the anti-LAG-3 antibody molecule can include VH FR1 defined based on VH hypervariable loop 1 according to Chothia *et al.* and VH FR2 defined based on VH CDRs 1-2 according to Kabat *et al.*, *e.g.*, as shown in Table 1. The anti-LAG-3 antibody molecule can further include, *e.g.*, VH FRs 3-4 defined based on VH CDRs 2-3 according to Kabat *et al.* and VL FRs 1-4 defined based on VL CDRs 1-3 according to Kabat *et al.*

The anti-LAG-3 antibody molecule can contain any combination of CDRs or hypervariable loops according to the Kabat and Chothia definitions. In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three CDRs from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, according to the Kabat and Chothia definition (*e.g.*, at least one, two, or three CDRs according to the Kabat and Chothia definition as set out in Table 1).

In one embodiment, the anti-LAG-3 antibody includes:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15;

(b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15; or

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3;

and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12.

In the combinations therein, in another embodiment, the antibody molecule comprises (i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and (ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12.

In the combination therein, in yet another embodiment, the antibody molecule includes: (i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and (ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15.

In an embodiment, *e.g.*, an embodiment comprising a variable region, CDR (*e.g.*, CDR or Kabat CDR), or other sequence referred to herein, *e.g.*, in Table 1, the antibody molecule is a monospecific antibody molecule, a bispecific antibody molecule, or is an antibody molecule that comprises an antigen binding fragment of an antibody, *e.g.*, a half antibody or antigen binding fragment of a half antibody. In certain embodiments, the antibody molecule is a bispecific antibody molecule having a first binding specificity for LAG-3 and a second binding specificity for PD-1, TIM-3, CEACAM (*e.g.*, CEACAM-1, CEACAM-3, and/or CEACAM-5), PD-L1 or PD-L2. . In one embodiment, the bispecific antibody molecule binds to LAG-3 and TIM-3. In another embodiment, the bispecific antibody molecule binds to LAG-3 and PD-1. In another embodiment, the bispecific antibody molecule binds to LAG-3 and CEACAM (*e.g.*, CEACAM-1, CEACAM-3, and/or CEACAM-5). In another embodiment, the bispecific antibody molecule binds to LAG-3 and CEACAM-1. In yet another embodiment, the bispecific antibody molecule binds to LAG-3 and CEACAM-5. In another embodiment, the bispecific antibody molecule binds to LAG-3 and PD-L1. In yet another embodiment, the bispecific antibody molecule binds to LAG-3 and PD-L2. Any combination of the aforesaid molecules can be made in a multispecific antibody molecule, *e.g.*, a trispecific antibody that includes a first binding

specificity to LAG-3, and a second and third binding specificity to one or more of: TIM-3, PD-1, CEACAM (*e.g.*, CEACAM-1, CEACAM-3, or CEACAM-5), PD-L1 or PD-L2.

In other embodiments, the anti-LAG-3 antibody molecule is used in combination with a bispecific molecule comprising one or more of: TIM-3, PD-1, CEACAM (*e.g.*, CEACAM-1, CEACAM-3, or CEACAM-5), PD-L1 or PD-L2. In one embodiment, the bispecific antibody molecule used in combination binds to CEACAM (*e.g.*, CEACAM-1, CEACAM-3, and/or CEACAM-5) and PD-1. In another embodiment, the bispecific antibody molecule used in combination binds to CEACAM (*e.g.*, CEACAM-1, CEACAM-3, and/or CEACAM-5) and TIM-3. In another embodiment, the bispecific antibody molecule used in combination binds to PD-1 and TIM-3.

Uses of the Combination Therapies

The combinations disclosed herein can result in one or more of: an increase in antigen presentation, an increase in effector cell function (*e.g.*, one or more of T cell proliferation, IFN- γ secretion or cytolytic function), inhibition of regulatory T cell function, an effect on the activity of multiple cell types, such as regulatory T cell, effector T cells and NK cells), an increase in tumor infiltrating lymphocytes, an increase in T-cell receptor mediated proliferation, and a decrease in immune evasion by cancerous cells. In one embodiment, the use of a LAG-3 inhibitor in the combinations inhibits, reduces or neutralizes one or more activities of LAG-3, resulting in blockade or reduction of an immune checkpoint. Thus, such combinations can be used to treat or prevent disorders where enhancing an immune response in a subject is desired.

Accordingly, in another aspect, a method of modulating an immune response in a subject is provided. The method comprises administering to the subject a combination disclosed herein (*e.g.*, a combination comprising a therapeutically effective amount of an anti-LAG-3 antibody molecule), alone or in combination with one or more agents or procedures, such that the immune response in the subject is modulated. In one embodiment, the antibody molecule restores, enhances, stimulates or increases an immune response in the subject.

The subject can be a mammal, *e.g.*, a primate, preferably a higher primate, *e.g.*, a human (*e.g.*, a patient having, or at risk of having, a disorder described herein). In one embodiment, the subject is in need of enhancing an immune response. In some embodiments, the anti-LAG-3 antibody molecule restores, enhances or stimulates an antigen-specific T cell response, *e.g.*,

interleukin-2 (IL-2) or interferon-gamma (IFN- γ) production in an antigen-specific T cell response, in the subject. In some embodiments, the immune response is an anti-tumor response. In one embodiment, the subject has, or is at risk of, having a disorder described herein, *e.g.*, a cancer or an infectious disorder as described herein. In certain embodiments, the subject is, or is at risk of being, immunocompromised. For example, the subject is undergoing or has undergone a chemotherapeutic treatment and/or radiation therapy. Alternatively, or in combination, the subject is, or is at risk of being, immunocompromised as a result of an infection.

In one aspect, a method of treating (*e.g.*, one or more of reducing, inhibiting, or delaying progression) a cancer or tumor in a subject is provided. The method comprises administering to the subject an anti-LAG-3 antibody molecule described herein (*e.g.*, a combination comprising a therapeutically effective amount of an anti-LAG-3 antibody molecule).

In certain embodiments, the cancer treated with the combination, includes but is not limited to, a solid tumor, a hematological cancer (*e.g.*, leukemia, lymphoma, myeloma), and a metastatic lesion thereof. In one embodiment, the cancer is a solid tumor. Examples of solid tumors include malignancies, *e.g.*, sarcomas and carcinomas (*e.g.*, adenocarcinomas), of the various organ systems, such as those affecting lung, breast, lymphoid, gastrointestinal or colorectal, genitals and genitourinary tract (*e.g.*, renal, urothelial, bladder cells), pharynx, CNS (*e.g.*, brain, neural or glial cells), skin (*e.g.*, melanoma), head and neck (*e.g.*, head and neck squamous cell carcinoma (HNSCC)), and pancreas. For example, the cancer can be chosen from a skin cancer (*e.g.*, a melanoma or a Merkel cell carcinoma), a colon cancer, a gastric cancer, a rectal cancer, a kidney cancer (*e.g.*, a renal cancer (*e.g.*, renal-cell carcinoma)), a breast cancer (*e.g.*, a breast cancer that does not express one, two or all of estrogen receptor, progesterone receptor, or Her2/neu, *e.g.*, a triple negative breast cancer), a liver cancer, a lung cancer (*e.g.*, a non-small cell lung cancer (NSCLC) (*e.g.*, a NSCLC with squamous and/or non-squamous histology) or small cell lung cancer), a prostate cancer, a cancer of head or neck (*e.g.*, HPV+ squamous cell carcinoma), a cancer of the small intestine, a brain cancer (*e.g.*, a glioblastoma), an endometrial cancer, or a cancer of the esophagus. Examples of hematological cancer include, but is not limited to, leukemia (*e.g.*, a myeloid leukemia, lymphoid leukemia, or chronic lymphocytic leukemia (CLL)), lymphoma (*e.g.*, Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), Diffuse large B-cell lymphoma (DLBCL), T-cell lymphoma, or mantle cell

lymphoma (MCL)), and myeloma, *e.g.*, multiple myeloma. The cancer may be at an early, intermediate, late stage or metastatic cancer.

In some embodiments, the cancer is chosen from a colorectal cancer (*e.g.*, CRC), melanoma, *e.g.*, advanced stage melanoma (*e.g.*, stage II-IV melanoma) or HLA-A2 positive-melanoma; a pancreatic cancer, *e.g.*, advanced pancreatic cancer; a breast cancer, *e.g.*, metastatic breast carcinoma or triple negative breast cancer; a head and neck cancer (*e.g.*, HNSCC); an esophageal cancer; a renal cell carcinoma (RCC), *e.g.*, clear renal cell carcinoma (ccRCC) or metastatic renal cell carcinoma (MRCC); a lung cancer (*e.g.*, NSCLC); a cervical cancer; bladder cancer; or a hematologic malignancy, *e.g.*, a leukemia (*e.g.*, a lymphocytic leukemia), or a lymphoma (*e.g.*, a Hodgkin's lymphoma (HL), a non-Hodgkin's lymphoma (NHL), a diffuse large B-cell lymphoma (DLBCL), a mantle cell lymphoma (MCL), or a CLL, *e.g.*, a relapsed or refractory chronic lymphocytic leukemia).

In some embodiments, the cancer is MSI-high (high microsatellite instability) cancer (*e.g.*, an MSI-high endometrial cancer). In other embodiments, the cancer is an EBV+ cancer. In certain embodiments, the cancer is a FoxP3-expressing cancer (*e.g.*, a FoxP3-expressing non-small cell lung cancer or a head and neck squamous cell carcinoma). In other embodiments, the cancer is EGFR mutated or cMET positive (*e.g.*, an EGFR mutated or cMET positive non-small cell lung cancer). In other embodiments, the cancer has a KRAS mutation (*e.g.*, a non-small cell lung cancer having a KRAS mutation).

In one embodiment, the cancer is an advanced or unresectable melanoma that does not respond to other therapies. In other embodiments, the cancer is a melanoma with a BRAF mutation (*e.g.*, a BRAF V600 mutation). In yet other embodiments, the combination disclosed herein (*e.g.*, the combination comprising the anti-LAG-3 antibody molecule) is administered alone, or in combination with one or more second agents (*e.g.*, a BRAF inhibitor). In one embodiment, the combination disclosed herein (*e.g.*, the combination comprising the anti-LAG-3 antibody molecule) is administered in combination with (*e.g.*, before or after treatment or simultaneously with) an inhibitor of an immune checkpoint modulator (*e.g.*, a PD-1 inhibitor, a PD-L1 inhibitor, a TIM-3 inhibitor, a CEACAM (*e.g.*, CEACAM-1, -3 and/or CEACAM-5) inhibitor, or a CTLA-4 inhibitor (*e.g.*, an anti-CTLA-4 antibody, *e.g.*, ipilimumab)) with or without a BRAF inhibitor (*e.g.*, vemurafenib or dabrafenib) to treat a melanoma. In one embodiment, the combination disclosed herein (*e.g.*, the combination comprising the anti-LAG-3

antibody molecule) is administered in combination with a PD-1 or a PD-L1 inhibitor, *e.g.*, an anti-PD-1 or an anti-PD-L1 antibody molecule, to treat a melanoma as described herein.

In one embodiment, the combination disclosed herein (*e.g.*, the combination comprising the anti-LAG-3 antibody molecule) is administered alone, or in combination with an inhibitor of an immune checkpoint modulator (*e.g.*, a PD-1 inhibitor (*e.g.*, an anti-PD-1 antibody molecule), a PD-L1 inhibitor (*e.g.*, an anti-PD-L1 antibody molecule), a TIM-3 inhibitor (*e.g.*, an anti-TIM-3 antibody molecule), a CEACAM (*e.g.*, CEACAM1 and/or CEACAM5) inhibitor (*e.g.*, an anti-CEACAM antibody molecule), or a CTLA-4 inhibitor (*e.g.*, an anti-CTLA4 antibody) to treat a head and neck cancer (*e.g.*, HNSCC). In one embodiment, the combination disclosed herein (*e.g.*, the combination comprising the anti-LAG-3 antibody molecule) is administered in combination with a PD-1 or a PD-L1 inhibitor, *e.g.*, an anti-PD-1 or anti-PD-L1 antibody molecule, to treat a head and neck cancer as described herein.

In one embodiment, the combination disclosed herein (*e.g.*, the combination comprising the anti-LAG-3 antibody molecule) is administered alone, or in combination with an inhibitor or activator of an immune checkpoint modulator (*e.g.*, a PD-1 inhibitor (*e.g.*, an anti-PD-1 antibody molecule), a PD-L1 inhibitor (*e.g.*, an anti-PD-L1 antibody molecule), a TIM-3 modulator (*e.g.*, a TIM-3 activator or inhibitor, *e.g.*, an anti-TIM-3 antibody molecule), a CEACAM (*e.g.*, CEACAM1 and/or CEACAM5) inhibitor (*e.g.*, an anti-CEACAM antibody molecule), or a CTLA-4 inhibitor (*e.g.*, an anti-CTLA4 antibody) to treat a lung cancer (*e.g.*, a NSCLC). In one embodiment, the combination disclosed herein (*e.g.*, the combination comprising the anti-LAG-3 antibody molecule) is administered in combination with a PD-1 or a PD-L1 inhibitor, *e.g.*, an anti-PD-1 or anti-PD-L1 antibody molecule, to treat a lung cancer (*e.g.*, a NSCLC) as described herein.

In one embodiment, the combination disclosed herein (*e.g.*, the combination comprising the anti-LAG-3 antibody molecule) is administered alone, or in combination with an inhibitor of an immune checkpoint modulator (*e.g.*, a PD-1 inhibitor (*e.g.*, an anti-PD-1 antibody molecule), a PD-L1 inhibitor (*e.g.*, an anti-PD-L1 antibody molecule), a TIM-3 inhibitor (*e.g.*, an anti-TIM-3 antibody molecule), a CEACAM (*e.g.*, CEACAM1 and/or CEACAM5) inhibitor (*e.g.*, an anti-CEACAM antibody molecule), or a CTLA-4 inhibitor (*e.g.*, an anti-CTLA4 antibody) to treat a gastric cancer. In one embodiment, the combination disclosed herein (*e.g.*, the combination comprising the anti-LAG-3 antibody molecule) is administered in combination with a PD-1 or a

PD-L1 inhibitor, *e.g.*, an anti-PD-1 or anti-PD-L1 antibody molecule, to treat a gastric cancer as described herein.

In one embodiment, the combination disclosed herein (*e.g.*, the combination comprising the anti-LAG-3 antibody molecule) is administered alone, or in combination with an inhibitor of an immune checkpoint modulator (*e.g.*, a PD-1 inhibitor (*e.g.*, an anti-PD-1 antibody molecule), a PD-L1 inhibitor (*e.g.*, an anti-PD-L1 antibody molecule), a TIM-3 inhibitor (*e.g.*, an anti-TIM-3 antibody molecule), a CEACAM (*e.g.*, CEACAM1 and/or CEACAM5) inhibitor (*e.g.*, an anti-CEACAM antibody molecule), or a CTLA-4 inhibitor (*e.g.*, an anti-CTLA4 antibody) to treat a lymphoma (*e.g.*, Hodgkin's lymphoma (HL), non-Hodgkin's lymphoma (NHL), Diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), or CLL, *e.g.*, a relapsed or refractory chronic lymphocytic leukemia). In one embodiment, the combination disclosed herein (*e.g.*, the combination comprising the anti-LAG-3 antibody molecule) is administered in combination with a PD-1 or a PD-L1 inhibitor, *e.g.*, an anti-PD-1 or anti-PD-L1 antibody molecule, to treat a lymphoma as described herein.

In one aspect, a method of treating a cancer in a subject is provided. The method comprises administering to the subject a combination of two, three or more therapeutic agents chosen from two or all of the following categories (i)-(iii):

(i) an agent that enhances tumor antigen presentation chosen from a STING agonist, a TLR agonist, an A2AR antagonist, or an oncolytic virus, or a combination thereof, and, optionally, one or more of: a TIM-3 modulator, a vascular endothelial growth factor receptor (VEGFR) inhibitor, a c-Met inhibitor, a TGF β inhibitor, an IDO/TDO inhibitor, a vaccine, or a bi- or tri-specific cell engager;

(ii) (optionally) an agent that enhances an effector cell response chosen from one or more of: a GITR agonist, a PD-1 inhibitor, a PD-L1 inhibitor, an inhibitor of IAP (Inhibitor of Apoptosis Protein), an inhibitor of EGFR (Epidermal Growth Factor Receptor), an inhibitor of target of rapamycin (mTOR), IL-15 or a variant thereof, a CTLA-4 inhibitor, a bispecific antibody molecule that binds to CD3 and a tumor antigen, a CD40 agonist, an OX40 agonist, or a CD27 agonist; or

(iii) an agent that decreases tumor immunosuppression chosen from an anti-LAG-3 antibody molecule, and, optionally, one or more of: a GITR agonist, an inhibitor of an immune

checkpoint molecule chosen from one or more of PD-L1, PD-1, TIM-3 or CTLA-4, a CSF-1/1R inhibitor, an IL-17 inhibitor, an IL-1 β inhibitor, a CXCR2 inhibitor, an inhibitor of PI3K γ or PI3K δ), (vii) a BAFF-R inhibitor, a MALT-1/BTK inhibitor, a JAK inhibitor, a CRTH2 inhibitor, a VEGFR inhibitor, an IL-15 or a variant thereof, a CTLA-4 inhibitor, an IDO/TDO inhibitor, an A2AR antagonist, a TGF β inhibitor, or a PFKFB3 inhibitor,

wherein the anti-LAG-3 antibody molecule, comprises:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15;

(b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15; or

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12.

In some embodiments, the anti-LAG-3 antibody molecule comprises:

(a) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 32;

(b) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 36;

(c) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 40;

(d) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 44;

(e) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 48;

(f) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 52;

(g) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 56;

(h) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60;

(i) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 36;

(j) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 40;

(k) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 56;

(l) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60.

(m) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 68 or SEQ ID NO: 108; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 36;

(n) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 72 or SEQ ID NO: 8; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 40;

(o) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 72 or SEQ ID NO: 8; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60.

(p) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 76; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60;

(q) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 80; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 84;

(r) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 88;

(s) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 92; or

(t) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 96.

In some embodiments, the cancer is chosen from a cancer described herein, *e.g.*, a lung cancer, a melanoma, a renal cancer, a liver cancer, a myeloma, a prostate cancer, a breast cancer, a head and neck cancer, a colorectal cancer, a pancreatic cancer, a hematological cancer, a non-Hodgkin's lymphoma, or a leukemia, or a metastatic lesion of the cancer. In certain embodiments, the cancer is chosen from a melanoma, pancreatic cancer, breast cancer, a head and neck cancer, or a renal cell carcinoma.

In one embodiment, the cancer microenvironment has an elevated level of PD-L1 expression. Alternatively, or in combination, the cancer microenvironment can have increased IFN γ and/or CD8 expression.

In some embodiments, the subject has, or is identified as having, a tumor that has one or more of high PD-L1 level or expression, or as being Tumor Infiltrating Lymphocyte (TIL)+ (*e.g.*, as having an increased number of TILs), or both. In certain embodiments, the subject has, or is identified as having, a tumor that has high PD-L1 level or expression and that is TIL+. In some embodiments, the methods described herein further include identifying a subject based on having a tumor that has one or more of high PD-L1 level or expression or as being TIL+, or both. In certain embodiments, the methods described herein further include identifying a subject based on having a tumor that has high PD-L1 level or expression and as being TIL+. In some embodiments, tumors that are TIL+ are positive for CD8 and IFN γ . In some embodiments, the subject has, or is identified as having, a high percentage of cells that are positive for one, two or more of PD-L1, CD8, and/or IFN γ . In certain embodiments, the subject has or is identified as having a high percentage of cells that are positive for all of PD-L1, CD8, and IFN γ .

In some embodiments, the methods described herein further include identifying a subject based on having a high percentage of cells that are positive for one, two or more of PD-L1, CD8, and/or IFN γ . In certain embodiments, the methods described herein further include identifying a subject based on having a high percentage of cells that are positive for all of PD-L1, CD8, and IFN γ . In some embodiments, the subject has, or is identified as having, one, two or more of PD-L1, CD8, and/or IFN γ , and one or more of a lung cancer, *e.g.*, squamous cell lung cancer or lung adenocarcinoma; a head and neck cancer; a squamous cell cervical cancer; a stomach cancer; an esophageal cancer; a thyroid cancer; a melanoma, and/or a nasopharyngeal cancer (NPC). In certain embodiments, the methods described herein further describe identifying a subject based on having one, two or more of PD-L1, CD8, and/or IFN γ , and one or more of a lung cancer, *e.g.*, squamous cell lung cancer or lung adenocarcinoma; a head and neck cancer; a squamous cell cervical cancer; a stomach cancer; a thyroid cancer; a melanoma, and or a nasopharyngeal cancer.

Methods and compositions disclosed herein are useful for treating metastatic lesions associated with the aforementioned cancers.

In a further aspect, the invention provides a method of treating an infectious disease in a subject, comprising administering to a subject a therapeutically effective amount of an anti-LAG-3 antibody molecule described herein, alone or in combination with one or more agents or procedures. The antibodies of the invention are preferred for use in the method although other anti-LAG-3 antibodies, or antigen-binding fragments thereof, can be used instead (or in combination with an anti-LAG-3 antibody molecule described herein).

In one embodiment, the infectious disease is hepatitis (*e.g.*, hepatitis B infection). In certain embodiment, the anti-LAG-3 antibody molecule is administered in combination with a hepatitis B antigen or vaccine, and optionally in combination with an aluminum-containing adjuvant.

In another embodiment, the infectious disease is influenza. In certain embodiment, the anti-LAG-3 antibody molecule is administered in combination with an influenza antigen or vaccine.

Still further, the invention provides a method of enhancing an immune response to an antigen in a subject, comprising administering to the subject: (i) the antigen; and (ii) an anti-LAG-3 antibody molecule, such that an immune response to the antigen in the subject is enhanced. The antigen can be, for example, a tumor antigen, a viral antigen, a bacterial antigen or an antigen from a pathogen.

The anti-LAG-3 antibody molecule, alone or in combination, can be administered to the subject systemically (*e.g.*, orally, parenterally, subcutaneously, intravenously, rectally, intramuscularly, intraperitoneally, intranasally, transdermally, or by inhalation or intracavitary installation), topically, or by application to mucous membranes, such as the nose, throat and bronchial tubes.

Dosages and therapeutic regimens of the therapeutic agents disclosed herein can be determined by a skilled artisan. In certain embodiments, the anti-LAG-3 antibody molecule is administered by injection (*e.g.*, subcutaneously or intravenously) at a dose of about 1 to 30 mg/kg, *e.g.*, about 5 to 25 mg/kg, about 10 to 20 mg/kg, about 1 to 10 mg/kg, or about 1 mg/kg, 3 mg/kg, or 10 mg/kg. The dosing schedule can vary from *e.g.*, once a week to once every 2, 3, or 4 weeks. In one embodiment, the anti-LAG-3 antibody molecule is administered at a dose from about 10 to 20 mg/kg every other week. In one embodiment, the anti-LAG-3 antibody molecule is administered (*e.g.*, intravenously) at a dose from about 3 to 800 mg, *e.g.*, about 3, 20,

80, 240, or 800 mg. In certain embodiments, the anti-LAG-3 antibody molecule is administered alone at a dose from about 20 to 800 mg, *e.g.*, about 3, 20, 80, 240, or 800 mg. In other embodiments, the anti-LAG-3 antibody molecule is administered at a dose from about 3 to 240 mg, *e.g.*, about 3, 20, 80, or 240 mg, when it is combined with a second agent or therapeutic modality, *e.g.*, a second agent or therapeutic modality described herein. In one embodiment, the anti-LAG-3 antibody molecule is administered every 2 weeks (*e.g.*, during weeks 1, 3, 5, 7) during each 8 week cycle, *e.g.*, up to 96 weeks.

In one embodiment, the anti-LAG-3 antibody molecule is administered, alone or in combination (*e.g.*, in combination with an anti-PD-1 antibody molecule), at a dose of less than, or about, 5 mg/kg; less than, or about, 4 mg/kg; less than, or about, 3 mg/kg; less than, or about, 2 mg/kg; less than, or about, 1 mg/kg, every other week. In one embodiment, the anti-LAG-3 antibody molecule is administered at a dose of 1 to 5 mg/kg every other week; 1 to 4 mg/kg every other week, 1 to 3 mg/kg every other week, or 1 to 2 mg/kg every other week. In one embodiment, the anti-PD-1 antibody molecule is administered, alone or in combination (*e.g.*, in combination with an anti-LAG-3 antibody molecule) at a dose of 1 to 5 mg/kg every other week; 1 to 4 mg/kg every other week, 1 to 3 mg/kg every other week, or 1 to 2 mg/kg every other week.

The antibody molecules described herein are preferred for use in the methods described herein, although other anti-LAG-3 antibodies can be used instead, or in combination with an anti-LAG-3 antibody molecule of the invention.

Further Combination Therapies

The methods and compositions described herein can be used in combination with other agents or therapeutic modalities. In one embodiment, the methods described herein include administering to the subject a combination comprising an anti-LAG-3 antibody molecule as described herein, in combination with an agent or therapeutic procedure or modality, in an amount effective to treat or prevent a disorder. The anti-LAG-3 antibody molecule and the agent or therapeutic procedure or modality can be administered simultaneously or sequentially in any order. Any combination and sequence of the anti-LAG-3 antibody molecules and other therapeutic agents, procedures or modalities (*e.g.*, as described herein) can be used. The antibody molecule and/or other therapeutic agents, procedures or modalities can be administered during periods of active disorder, or during a period of remission or less active disease. The

antibody molecule can be administered before the other treatment, concurrently with the treatment, post-treatment, or during remission of the disorder.

In certain embodiments, the methods and compositions described herein are administered in combination with one or more of other antibody molecules, chemotherapy, other anti-cancer therapy (*e.g.*, targeted anti-cancer therapies, gene therapy, viral therapy, RNA therapy, bone marrow transplantation, nanotherapy, or oncolytic drugs), cytotoxic agents, immune-based therapies (*e.g.*, cytokines or cell-based immune therapies), surgical procedures (*e.g.*, lumpectomy or mastectomy) and/or radiation procedures, or a combination of any of the foregoing. The additional therapy may be in the form of adjuvant or neoadjuvant therapy. In some embodiments, the additional therapy is an enzymatic inhibitor (*e.g.*, small molecule enzymatic inhibitor) or a metastatic inhibitor.

Exemplary cytotoxic agents that can be administered in combination with include antimicrotubule agents, topoisomerase inhibitors, anti-metabolites, mitotic inhibitors, alkylating agents, anthracyclines, vinca alkaloids, intercalating agents, agents capable of interfering with a signal transduction pathway, agents that promote apoptosis, proteasome inhibitors, and radiation (*e.g.*, local or whole body irradiation (*e.g.*, gamma irradiation)). In other embodiments, the additional therapy is surgery or radiation, or a combination thereof. In other embodiments, the additional therapy is a therapy targeting one or more of PI3K/AKT/mTOR pathway, an HSP90 inhibitor, or a tubulin inhibitor. Exemplary other antibody molecules that can be administered in combination include, but are not limited to, checkpoint inhibitors (*e.g.*, anti-PD-1, anti-PD-L1); antibodies that stimulate an immune cell (*e.g.*, agonistic GITR or CD137 antibodies); anti-cancer antibodies (*e.g.*, rituximab (Rituxan® or MabThera®), trastuzumab (Herceptin®), cetuximab (Erbix®), among others.

Alternatively, or in combination with the aforesaid combinations, the methods and compositions described herein can be administered in combination with one or more of: an immunomodulator (*e.g.*, an activator of a costimulatory molecule or an inhibitor of an immunoinhibitory molecule, *e.g.*, an immune checkpoint molecule); a vaccine, *e.g.*, a therapeutic cancer vaccine; or other forms of cellular immunotherapy.

Exemplary non-limiting combinations and uses of the anti-LAG-3 antibody molecules include the following.

In certain embodiments, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with a modulator of a costimulatory molecule (*e.g.*, an agonist of a costimulatory molecule) or a modulator of an inhibitory molecule (*e.g.*, an inhibitor of an immune checkpoint inhibitor).

In one embodiment, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with a modulator, *e.g.*, an agonist, of a costimulatory molecule. In one embodiment, the agonist of the costimulatory molecule is chosen from an agonist (*e.g.*, an agonistic antibody or soluble fusion) of OX40, CD2, CD27, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3 or CD83 ligand.

In one embodiment, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with an inhibitor of an inhibitory (or immune checkpoint) molecule chosen from PD-1, PD-L1, PD-L2, CTLA-4, TIM-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CEACAM (*e.g.*, CEACAM-1, CEACAM-3 and/or CEACAM-5), VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and/or TGF beta. Inhibition of an inhibitory molecule can be performed by inhibition at the DNA, RNA or protein level. In embodiments, an inhibitory nucleic acid (*e.g.*, a dsRNA, siRNA or shRNA), can be used to inhibit expression of an inhibitory molecule. In other embodiments, the inhibitor of an inhibitory signal is, a polypeptide *e.g.*, a soluble ligand, or an antibody or antibody fragment, that binds to the inhibitory molecule. In one embodiment, the inhibitor is a soluble ligand (*e.g.*, a CTLA-4-Ig), or an antibody or antibody fragment that binds to PD-1, PD-L1, PD-L2 or CTLA-4.

For example, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, can be administered in combination with an inhibitor of, *e.g.*, an antibody or antibody fragment that binds to, PD-1, PD-L1, PD-L2 or CTLA-4, to treat a cancer (*e.g.*, a cancer chosen from: a colorectal cancer (*e.g.*, CRC); a melanoma, *e.g.*, advanced stage melanoma (*e.g.*, stage II-IV melanoma) or HLA-A2 positive-melanoma; a pancreatic cancer, *e.g.*, advanced pancreatic cancer; a breast cancer, *e.g.*, metastatic breast carcinoma or triple negative breast cancer; a head and neck cancer (*e.g.*, HNSCC); an esophageal cancer; a renal cell carcinoma (RCC), *e.g.*, clear renal cell carcinoma (ccRCC) or metastatic renal cell carcinoma (MRCC); a lung cancer (*e.g.*, NSCLC); a cervical cancer; a bladder cancer; or a hematologic

malignancy, *e.g.*, a leukemia (*e.g.*, a lymphocytic leukemia), or a lymphoma (*e.g.*, a Hodgkin's lymphoma (HL), a non-Hodgkin's lymphoma (NHL), a diffuse large B-cell lymphoma (DLBCL), a mantle cell lymphoma (MCL), or a CLL, *e.g.*, a relapsed or refractory chronic lymphocytic leukemia).

In one embodiment, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with (*e.g.*, before, with, or after) treatment with an anti-CTLA4 antibody (*e.g.*, ipilimumab) with or without a BRAF inhibitor (*e.g.*, vemurafenib or dabrafenib).

In another embodiment, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with an anti-PD-1 antibody (*e.g.*, Nivolumab or Pembrolizumab) or antigen-binding fragment thereof. In another embodiment, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with an anti-TIM-3 antibody or antigen-binding fragment thereof. In still another embodiment, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with an anti-PD-L1 antibody or antigen-binding fragment thereof.

In yet other embodiments, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with an anti-PD-1 antibody and an anti-TIM-3 antibody (or antigen-binding fragments thereof). In certain embodiments, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with an anti-PD-1 antibody and an anti-PD-L1 antibody (or antigen-binding fragments thereof). In certain embodiments, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with an anti-TIM-3 antibody and an anti-PD-L1 antibody (or antigen-binding fragments thereof).

In another embodiment, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with a CEACAM inhibitor (*e.g.*, CEACAM-1 and/or CEACAM-5 inhibitor), *e.g.*, an anti-CEACAM antibody molecule. In another embodiment, the anti-LAG-3 antibody molecule is administered in combination with a CEACAM-1 inhibitor, *e.g.*, an anti-CEACAM-1 antibody molecule. In another embodiment, the

anti-LAG-3 antibody molecule is administered in combination with a CEACAM-5 inhibitor, *e.g.*, an anti-CEACAM-5 antibody molecule.

In yet other embodiments, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with an anti-CEACAM (*e.g.*, anti-CEACAM-1 and/or anti-CEACAM-5) antibody molecule and an anti-PD-1 antibody molecule. In yet other embodiments, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule is administered in combination with an anti-CEACAM (*e.g.*, anti-CEACAM-1 and/or anti-CEACAM-5) antibody molecule and an anti-TIM-3 antibody molecule. In yet other embodiments, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule is administered in combination with an anti-CEACAM (*e.g.*, anti-CEACAM-1 and/or anti-CEACAM-5) antibody molecule and an anti-PD-L1 antibody molecule.

The combination of antibodies recited herein can be administered separately, *e.g.*, as separate antibodies or antigen-binding fragments thereof, or linked, *e.g.*, as a bispecific or trispecific antibody molecule. In one embodiment, a bispecific antibody that includes an anti-LAG-3 antibody molecule and one of: an anti-TIM-3 antibody, anti-CEACAM (*e.g.*, anti-CEACAM-1 and/or anti-CEACAM-5) antibody, anti-PD-L1 antibody, or anti-PD-1 antibody, or an antigen-binding fragment thereof, is administered. In certain embodiments, the combination of antibodies recited herein is used to treat a cancer, *e.g.*, a cancer as described herein (*e.g.*, a solid tumor or a hematological malignancy). In one embodiment, the anti-LAG-3 antibody molecule is administered in combination with an anti-PD-1 or anti-PD-L1 antibody to treat a solid tumor.

In other embodiments, the combination disclosed herein, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule, is administered in combination with a cytokine. The cytokine can be administered as a fusion molecule to the anti-LAG-3 antibody molecule, or as separate compositions. In one embodiment, the anti-LAG-3 antibody is administered in combination with one, two, three or more cytokines, *e.g.*, as a fusion molecule or as separate compositions. In one embodiment, the cytokine is an interleukin (IL) chosen from one, two, three or more of IL-1, IL-2, IL-12, IL-12, IL-15 or IL-21. In one embodiment, a bispecific antibody molecule has a first binding specificity to a first target (*e.g.*, to LAG-3), a second binding specificity to a second target (*e.g.*, PD-1, TIM-3, or PD-L1), and is optionally linked to an interleukin (*e.g.*, IL-12)

domain *e.g.*, full length IL-12 or a portion thereof. In certain embodiments, the combination of anti-LAG-3 antibody molecule and the cytokine described herein is used to treat a cancer, *e.g.*, a cancer as described herein (*e.g.*, a solid tumor).

In other embodiments, the anti-LAG-3 antibody molecule is administered in combination with a vaccine, *e.g.*, a therapeutic cancer vaccine, or other forms of cellular immunotherapy. In one embodiment, the vaccine is peptide-based, DNA-based, RNA-based, or antigen-based, or a combination thereof. In embodiments, the vaccine comprises one or more peptides, nucleic acids (*e.g.*, DNA or RNA), antigens, or a combination thereof. In certain embodiments, the cancer vaccine comprises an adjuvant (*e.g.*, aluminium phosphate or aluminum hydroxide). In some embodiments, the methods described herein are administered in combination with one or more of surgical removal of a tissue, chemotherapy, or other anti-cancer therapy and the primary or sole target will be metastatic lesions, *e.g.*, metastases in the bone marrow or lymph nodes.

In one embodiment, the cancer is a melanoma, *e.g.*, an advanced stage melanoma (*e.g.*, stage II-IV melanoma) or HLA-A2 positive melanoma. In certain embodiment, the anti-LAG-3 antibody molecule is administered in combination with a tumor antigenic peptide, *e.g.*, one or more HLA-A2 peptides, and optionally in combination with an adjuvant, *e.g.*, Montanide™. Exemplary tumor peptides that can be administered in combination with the anti-LAG-3 antibody molecule include one or more of Tyrosinase.A2, MAGE-C2.A2, NY-ESO-1b.A2, MAGE-4.A2, MAGE-3.A2, MAGE-1.A2, NA17.A2 (GnTV), and MAGE-10.A2.

In another embodiment, the cancer is a pancreatic cancer, *e.g.*, advanced pancreatic cancer. In certain embodiment, the antibody molecule can be administered in combination with a chemotherapeutic agent, *e.g.*, gemcitabine.

In another embodiment, the cancer is a breast cancer, *e.g.*, metastatic breast carcinoma or triple negative breast cancer. In certain embodiment, the antibody molecule can be administered in combination with a chemotherapeutic agent, *e.g.*, paclitaxel.

In another embodiment, the cancer is a renal cell carcinoma, *e.g.*, clear cell carcinoma, advanced (*e.g.*, stage IV) or metastatic renal cell carcinoma (MRCC).

In another embodiment, the cancer is a cancer of head or neck, *e.g.*, HPV+ squamous cell carcinoma.

In another embodiment, the anti-LAG-3 antibody molecule is administered in combination with an antigen. For example, the anti-LAG-3 antibody molecule can be combined

with a hepatitis B antigen (*e.g.*, Engerix B). In other embodiments, the anti-LAG-3 antibody molecule is administered in combination with a flu antigen.

The anti-LAG-3 antibody molecule can be used alone in unconjugated form, or can be bound to a substance, *e.g.*, a cytotoxic agent or moiety (*e.g.*, a therapeutic drug; a compound emitting radiation; molecules of plant, fungal, or bacterial origin; or a biological protein (*e.g.*, a protein toxin) or particle (*e.g.*, a recombinant viral particle, *e.g.*, via a viral coat protein). For example, the antibody can be coupled to a radioactive isotope such as an α -, β -, or γ -emitter, or a β - and γ -emitter.

Additional Combination Therapies

The methods and compositions described herein (*e.g.*, LAG-3 antibodies and methods of using them) can be used in combination with other agents or therapeutic modalities, *e.g.*, a second therapeutic agent chosen from one or more of the agents listed in Table 7.

In some embodiments, the additional therapeutic agent is chosen from one or more of: 1) a protein kinase C (PKC) inhibitor; 2) a heat shock protein 90 (HSP90) inhibitor; 3) an inhibitor of a phosphoinositide 3-kinase (PI3K) and/or target of rapamycin (mTOR); 4) an inhibitor of cytochrome P450 (*e.g.*, a CYP17 inhibitor or a 17 α -Hydroxylase/C17-20 Lyase inhibitor); 5) an iron chelating agent; 6) an aromatase inhibitor; 7) an inhibitor of p53, *e.g.*, an inhibitor of a p53/Mdm2 interaction; 8) an apoptosis inducer; 9) an angiogenesis inhibitor; 10) an aldosterone synthase inhibitor; 11) a smoothed (SMO) receptor inhibitor; 12) a prolactin receptor (PRLR) inhibitor; 13) a Wnt signaling inhibitor; 14) a CDK4/6 inhibitor; 15) a fibroblast growth factor receptor 2 (FGFR2)/fibroblast growth factor receptor 4 (FGFR4) inhibitor; 16) an inhibitor of macrophage colony-stimulating factor (M-CSF); 17) an inhibitor of one or more of c-KIT, histamine release, Flt3 (*e.g.*, FLK2/STK1) or PKC; 18) an inhibitor of one or more of VEGFR-2 (*e.g.*, FLK-1/KDR), PDGFRbeta, c-KIT or Raf kinase C; 19) a somatostatin agonist and/or a growth hormone release inhibitor; 20) an anaplastic lymphoma kinase (ALK) inhibitor; 21) an insulin-like growth factor 1 receptor (IGF-1R) inhibitor; 22) a P-Glycoprotein 1 inhibitor; 23) a vascular endothelial growth factor receptor (VEGFR) inhibitor; 24) a BCR-ABL kinase inhibitor; 25) an FGFR inhibitor; 26) an inhibitor of CYP11B2; 27) a HDM2 inhibitor, *e.g.*, an inhibitor of the HDM2-p53 interaction; 28) an inhibitor of a tyrosine kinase; 29) an inhibitor of c-MET; 30) an inhibitor of JAK; 31) an inhibitor of DAC; 32) an inhibitor of 11 β -hydroxylase;

33) an inhibitor of IAP; 34) an inhibitor of PIM kinase; 35) an inhibitor of Porcupine; 36) an inhibitor of BRAF, *e.g.*, BRAF V600E or wild-type BRAF; 37) an inhibitor of HER3; 38) an inhibitor of MEK; or 39) an inhibitor of a lipid kinase, *e.g.*, as described herein and in Table 7.

In one embodiment, the additional therapeutic agent is chosen from one or more of: Compound A8, Compound A17, Compound A23, Compound A24, Compound A27, Compound A29, Compound A33, and Compound A13.

In other embodiments, the additional therapeutic agent is chosen from one or more of: Compound A5, Compound A8, Compound A17, Compound A23, Compound A24, Compound A29, and Compound A40.

In other embodiments, the additional therapeutic agent is chosen from one or more of: Compound A9, Compound A16, Compound A17, Compound A21, Compound A22, Compound A25, Compound A28, Compound A48, and Compound 49.

In one embodiment, the cancer is chosen from a lung cancer (*e.g.*, a non-small cell lung cancer (NSCLC) (*e.g.*, a NSCLC with squamous and/or non-squamous histology, or a NSCLC adenocarcinoma), or disclosed in a publication listed in Table 7.

Additional Embodiments

Additional embodiments provide a method of treating a cancer, comprising: identifying in a sample (*e.g.*, a subject's sample comprising cancer cells and optionally immune cells such as TILs) the presence of one, two or all of PD-L1, CD8, or IFN- γ , thereby providing a value for one, two or all of PD-L1, CD8, and IFN- γ . The method can further include comparing the PD-L1, CD8, and/or IFN- γ values to a reference value, *e.g.*, a control value. If the PD-L1, CD8, and/or IFN- γ values are greater than the reference value, *e.g.*, the control values, administering a therapeutically effective amount of a combination as described herein (*e.g.*, a combination that includes an anti-LAG-3 antibody described herein), alone or in combination with an anti-PD-1 antibody molecule, an anti-PD-L1 antibody molecule, or both, to the subject, optionally in combination with one or more other agents, thereby treating the cancer. The cancer may be, *e.g.*, a cancer described herein, such as lung cancer (squamous), lung cancer (adenocarcinoma), head and neck cancer, cervical cancer (squamous), stomach cancer, thyroid cancer, melanoma, nasopharyngeal cancer, or breast cancer, *e.g.*, TN breast cancer, *e.g.*, IM-TN breast cancer. In some embodiments, the cancer is ER+ breast cancer or pancreatic cancer.

Also provided is a method of treating a cancer, comprising: testing a sample (*e.g.*, a subject's sample comprising cancer cells) for the presence of PD-L1, thereby identifying a PD-L1 value, comparing the PD-L1 value to a control value, and if the PD-L1 value is greater than the control value, administering a therapeutically effective amount of a combination as described herein (*e.g.*, a combination that includes an anti-LAG-3 antibody described herein), alone or in combination with an anti-PD-1 antibody molecule, an anti-PD-L1 antibody molecule, or both, to the subject, optionally in combination with one or more other agents, thereby treating the cancer. The cancer may be, *e.g.*, a cancer as described herein, such as cancer is non-small cell lung (NSCLC) adenocarcinoma (ACA), NSCLC squamous cell carcinoma (SCC), or hepatocellular carcinoma (HCC).

In another aspect, the invention features diagnostic or therapeutic kits that include the combination molecules described herein and instructions for use.

All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety.

Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 depicts the amino acid sequences of the light (SEQ ID NO: 16) and heavy (SEQ ID NO: 6) chain variable regions of murine anti-LAG-3 mAb BAP050. The light and heavy chain CDR sequences based on Kabat numbering are underlined. The light and heavy chain CDR sequences based on Chothia numbering are shown in bold italics.

Figure 2 depicts the amino acid sequences of the light (SEQ ID NO: 16) and heavy (SEQ ID NO: 6) chain variable regions of murine anti-LAG-3 mAb BAP050 aligned with the germline sequences (SEQ ID NOs: 290-291, respectively, in order of appearance). The upper and lower sequences are the germline (GL) and BAP050 (Mu mAb) sequences, respectively. The light and heavy chain CDR sequences based on Kabat numbering are underlined. The light and heavy chain CDR sequences based on Chothia numbering are shown in bold italics. “-” means identical amino acid residue.

Figure 3 depicts bar graphs showing the results of FACS binding analysis for the twenty humanized BAP050 clones (BAP050-hum01 to BAP050-hum20) and the chimeric mAb

(BAP050-chi). The antibody concentrations are 200, 100, 50, 25 and 12.5 ng/ml from the leftmost bar to the rightmost bar for each tested mAb.

Figure 4 depicts the structural analysis of the humanized BAP049 clones (a, b, c, d, e, f, g represent various types of framework region sequences). The concentrations of the mAbs in the samples are also shown.

Figure 5A-5B depicts the binding affinity and specificity of humanized mAbs measured in a competition binding assay using a constant concentration of FITC-labeled murine mAb, serial dilutions of the test antibodies, and LAG-3-expressing CHO cells. Experiment was performed twice, and the results are shown in Figures 5A and 5B, respectively.

Figure 6 depicts the ranking of humanized BAP050 clones based on FACS data, competition binding and structural analysis. The concentrations of the mAbs in the samples are also shown.

Figure 7 depicts the binding affinity and specificity of huBAP050(Ser) clones measured in a competition binding assay using a constant concentration of FITC-labeled murine mAb, serial dilutions of the test antibodies, and LAG-3-expressing CHO cells. HuBAP050(Ser) clones, such as, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum05-Ser, BAP050-hum09-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, and BAP050-hum13-Ser, were evaluated. Murine mAb BAP050, chimeric mAb BAP050-chi, and humanized BAP050-hum01, BAP050-hum02, BAP050-hum05, BAP050-hum09, BAP050-hum11, BAP050-hum12, and BAP050-hum13 were also included in the analyses.

Figure 8 depicts blocking of binding of LAG-3-Ig to Daudi cells by huBAP050(Ser) clones. HuBAP050(Ser) clones, such as, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum05-Ser, BAP050-hum09-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, and BAP050-hum13-Ser, were evaluated. Murine mAb BAP050 and chimeric mAb BAP050-chi were also included in the analyses.

Figures 9A-9B depict the alignment of heavy chain variable domain sequences for the twenty humanized BAP050 clones and BAP050 chimera (BAP050-chi). In Figure 9A, all of the sequences are shown (SEQ ID NOs: 20, 28, 28, 28, 28, 28, 28, 28, 28, 28, 28, 64, 64, 64, 64, 64, 68, 72, 72, 76 and 80, respectively, in order of appearance). In Figure 9B, only amino acid sequences that are different from mouse sequence are shown (SEQ ID NOs: 20, 28, 28, 28, 28,

28, 28, 28, 28, 28, 28, 64, 64, 64, 64, 64, 68, 72, 72, 76 and 80, respectively, in order of appearance).

Figures 10A-10B depict the alignment of light chain variable domain sequences for the twenty humanized BAP050 clones and BAP050 chimera (BAP050-chi). In Figure 10A, all of the sequences are shown (SEQ ID NOs: 24, 32, 36, 36, 36, 292, 292, 292, 44, 48, 52, 56, 56, 60, 60, 60, 84, 88, 92 and 96, respectively, in order of appearance). In Figure 10B, only amino acid sequences that are different from mouse sequence are shown (SEQ ID NOs: 24, 32, 36, 36, 36, 292, 292, 292, 44, 48, 52, 56, 56, 60, 60, 60, 60, 84, 88, 92 and 96, respectively, in order of appearance).

Figure 11 shows exemplary cancers having relatively high proportions of patients that are triple-positive for PD-L1/CD8/IFN- γ .

Figure 12 shows exemplary ER+ breast cancer and pancreatic cancer having relatively low proportions for patients that are triple positive for PD-L1/CD8/IFN- γ .

Figure 13 shows the proportion of exemplary breast cancer patients that are triple positive for PD-L1/CD8/IFN- γ .

Figure 14 shows the proportion of exemplary colon cancer patients that are triple positive for PD-L1/CD8/IFN- γ .

Figure 15 is a schematic diagram that outlines the antigen processing and presentation, effector cell responses and immunosuppression pathways targeted by the combination therapies disclosed herein.

BRIEF DESCRIPTION OF THE TABLES

Table 1 is a summary of the amino acid and nucleotide sequences for the murine, chimeric and humanized anti-LAG-3 antibody molecules. The antibody molecules include murine mAb BAP050 and chimeric mAbs BAP050-chi, humanized mAbs BAP050-hum01 to BAP050-hum20, BAP050-hum01-Ser to BAP050-hum15-Ser, BAP050-hum18-Ser to BAP050-hum20-Ser, and BAP050-Clone-F to BAP050-Clone-J. The amino acid and nucleotide sequences of the heavy and light chain CDRs, the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the amino acid and nucleotide sequences of the heavy and light chains are shown in this Table.

Table 2 depicts the amino acid and nucleotide sequences of the heavy and light chain framework regions for humanized mAbs BAP050-hum01 to BAP049-hum20, BAP050-hum01-Ser to BAP050-hum15-Ser, BAP050-hum18-Ser to BAP050-hum20-Ser, and BAP049-Clone-F to BAP049-Clone-J.

Table 3 depicts the constant region amino acid sequences of human IgG heavy chains and human kappa light chain.

Table 4 shows the amino acid sequences of the heavy and light chain leader sequences for humanized mAbs BAP050-Clone-F to BAP050-Clone-J.

Table 5 is a summary of yield, titre, monomer content and endotoxin levels for exemplary humanized BAP050 mAbs expressed in CHO cells.

Table 6 shows the charge isoforms as detected by Novex IEF analysis for exemplary humanized BAP050 mAbs expressed in CHO cells.

Table 7 is a summary of selected therapeutic agents that can be administered in combination with the anti-LAG-3 antibody molecules and other immunomodulators (*e.g.*, one or more of: an activator of a costimulatory molecule and/or an inhibitor of an immune checkpoint molecule) described herein. Table 7 provides from left to right the following: the Compound Designation of the second therapeutic agent, the Compound structure, and Patent publication(s) disclosing the Compound.

Table 8 provides an exemplary listing of the therapeutic agents from Antigen-Presentation Combinations (Category A), Effector Cell Combinations (Category B) and Anti-tumor Immunosuppression Combinations (Category C).

DETAILED DESCRIPTION

Disclosed herein, at least in part, are methods and compositions comprising a combination of two, three or more therapeutic agents chosen from one, two, or all of the following categories (i)-(iii): (i) an agent that enhances antigen presentation (*e.g.*, tumor antigen presentation) (*e.g.*, by enhancing one or more of dendritic cell activity or maturation, antigen uptake, or antigen processing); (ii) an agent that enhances an effector cell response (*e.g.*, an immune effector cell response, *e.g.*, B cell and/or T cell activation and/or mobilization, *e.g.*, in the lymph node); or (iii) an agent that decreases tumor immunosuppression (*e.g.*, increasing T cell infiltration and tumor cell killing). In some embodiments, the combination includes a PD-1

inhibitor (*e.g.*, an anti-PD-1 antibody molecule as described herein). Without wishing to be bound by theory, it is believed that therapeutic approaches that enhance anti-tumor immunity work more effectively when the immune response is optimized via multiple targets at different stages of the immune response. Each of these stages is depicted in schematic form in Figure 15. For example, approaches that result in activation of dendritic cells combined with approaches that enhance cellular and humoral immune can result in a more effective and/or prolonged therapeutic response.

Additional terms are defined below and throughout the application.

As used herein, the articles "a" and "an" refer to one or to more than one (*e.g.*, to at least one) of the grammatical object of the article.

The term "or" is used herein to mean, and is used interchangeably with, the term "and/or", unless context clearly indicates otherwise.

"About" and "approximately" shall generally mean an acceptable degree of error for the quantity measured given the nature or precision of the measurements. Exemplary degrees of error are within 20 percent (%), typically, within 10%, and more typically, within 5% of a given value or range of values.

By "a combination" or "in combination with," it is not intended to imply that the therapy or the therapeutic agents must be administered at the same time and/or formulated for delivery together, although these methods of delivery are within the scope described herein. The therapeutic agents in the combination can be administered concurrently with, prior to, or subsequent to, one or more other additional therapies or therapeutic agents. The therapeutic agents or therapeutic protocol can be administered in any order. In general, each agent will be administered at a dose and/or on a time schedule determined for that agent. It will further be appreciated that the additional therapeutic agent utilized in this combination may be administered together in a single composition or administered separately in different compositions. In general, it is expected that additional therapeutic agents utilized in combination be utilized at levels that do not exceed the levels at which they are utilized individually. In some embodiments, the levels utilized in combination will be lower than those utilized individually.

In embodiments, the additional therapeutic agent is administered at a therapeutic or lower-than therapeutic dose. In certain embodiments, the concentration of the second therapeutic

agent that is required to achieve inhibition, *e.g.*, growth inhibition, is lower when the second therapeutic agent is administered in combination with the first therapeutic agent, *e.g.*, the anti-PD-1 antibody molecule, than when the second therapeutic agent is administered individually. In certain embodiments, the concentration of the first therapeutic agent that is required to achieve inhibition, *e.g.*, growth inhibition, is lower when the first therapeutic agent is administered in combination with the second therapeutic agent than when the first therapeutic agent is administered individually. In certain embodiments, in a combination therapy, the concentration of the second therapeutic agent that is required to achieve inhibition, *e.g.*, growth inhibition, is lower than the therapeutic dose of the second therapeutic agent as a monotherapy, *e.g.*, 10-20%, 20-30%, 30-40%, 40-50%, 50-60%, 60-70%, 70-80%, or 80-90% lower. In certain embodiments, in a combination therapy, the concentration of the first therapeutic agent that is required to achieve inhibition, *e.g.*, growth inhibition, is lower than the therapeutic dose of the first therapeutic agent as a monotherapy, *e.g.*, 10-20%, 20-30%, 30-40%, 40-50%, 50-60%, 60-70%, 70-80%, or 80-90% lower.

The term “inhibition,” “inhibitor,” or “antagonist” includes a reduction in a certain parameter, *e.g.*, an activity, of a given molecule, *e.g.*, an immune checkpoint inhibitor. For example, inhibition of an activity, *e.g.*, a PD-1 or PD-L1 activity, of at least 5%, 10%, 20%, 30%, 40% or more is included by this term. Thus, inhibition need not be 100%.

The term “activation,” “activator,” or “agonist” includes an increase in a certain parameter, *e.g.*, an activity, of a given molecule, *e.g.*, a costimulatory molecule. For example, increase of an activity, *e.g.*, a costimulatory activity, of at least 5%, 10%, 25%, 50%, 75% or more is included by this term.

The term “anti-cancer effect” refers to a biological effect which can be manifested by various means, including but not limited to, *e.g.*, a decrease in tumor volume, a decrease in the number of cancer cells, a decrease in the number of metastases, an increase in life expectancy, decrease in cancer cell proliferation, decrease in cancer cell survival, or amelioration of various physiological symptoms associated with the cancerous condition. An “anti-cancer effect” can also be manifested by the ability of the peptides, polynucleotides, cells and antibodies in prevention of the occurrence of cancer in the first place.

The term “anti-tumor effect” refers to a biological effect which can be manifested by various means, including but not limited to, *e.g.*, a decrease in tumor volume, a decrease in the number of tumor cells, a decrease in tumor cell proliferation, or a decrease in tumor cell survival.

The term “cancer” refers to a disease characterized by the rapid and uncontrolled growth of aberrant cells. Cancer cells can spread locally or through the bloodstream and lymphatic system to other parts of the body. Examples of various cancers are described herein and include but are not limited to, breast cancer (*e.g.*, triple negative breast cancer), prostate cancer, ovarian cancer, cervical cancer, skin cancer (*e.g.*, melanoma), pancreatic cancer, colorectal cancer, renal cancer (*e.g.*, renal cell carcinoma), liver cancer (*e.g.*, hepatocellular carcinoma), brain cancer (*e.g.*, glioblastoma), head and neck cancer, endometrial cancer, nasopharyngeal cancer, bladder cancer, lymphoma, leukemia, lung cancer (*e.g.*, non-small cell lung cancer), and the like. The terms “tumor” and “cancer” are used interchangeably herein, *e.g.*, both terms encompass solid and liquid, *e.g.*, diffuse or circulating, tumors. As used herein, the term “cancer” or “tumor” includes premalignant, as well as malignant cancers and tumors.

The term “antigen presenting cell” or “APC” refers to an immune system cell such as an accessory cell (*e.g.*, a B-cell, a dendritic cell, and the like) that displays a foreign antigen complexed with major histocompatibility complexes (MHC's) on its surface. T-cells may recognize these complexes using their T-cell receptors (TCRs). APCs process antigens and present them to T-cells.

The term “costimulatory molecule” refers to the cognate binding partner on a T cell that specifically binds with a costimulatory ligand, thereby mediating a costimulatory response by the T cell, such as, but not limited to, proliferation. Costimulatory molecules are cell surface molecules other than antigen receptors or their ligands that are required for an efficient immune response. Costimulatory molecules include, but are not limited to, an MHC class I molecule, TNF receptor proteins, Immunoglobulin-like proteins, cytokine receptors, integrins, signaling lymphocytic activation molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, OX40, CD2, CD7, CD27, CD28, CD30, CD40, CDS, ICAM-1, LFA-1 (CD11a/CD18), 4-1BB (CD137), B7-H3, CDS, ICAM-1, ICOS (CD278), GITR, BAFER, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL,

CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, and a ligand that specifically binds with CD83.

“Immune effector cell,” or “effector cell” as that term is used herein, refers to a cell that is involved in an immune response, *e.g.*, in the promotion of an immune effector response. Examples of immune effector cells include T cells, *e.g.*, alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, mast cells, and myeloid-derived phagocytes.

“Immune effector” or “effector” “function” or “response,” as that term is used herein, refers to function or response, *e.g.*, of an immune effector cell, that enhances or promotes an immune attack of a target cell. *E.g.*, an immune effector function or response refers a property of a T or NK cell that promotes killing or the inhibition of growth or proliferation, of a target cell. In the case of a T cell, primary stimulation and co-stimulation are examples of immune effector function or response.

The term “effector function” refers to a specialized function of a cell. Effector function of a T cell, for example, may be cytolytic activity or helper activity including the secretion of cytokines.

As used herein, the terms “treat”, “treatment” and “treating” refer to the reduction or amelioration of the progression, severity and/or duration of a disorder, *e.g.*, a proliferative disorder, or the amelioration of one or more symptoms (preferably, one or more discernible symptoms) of the disorder resulting from the administration of one or more therapies. In specific embodiments, the terms “treat,” “treatment” and “treating” refer to the amelioration of at least one measurable physical parameter of a proliferative disorder, such as growth of a tumor, not necessarily discernible by the patient. In other embodiments the terms “treat”, “treatment” and “treating” -refer to the inhibition of the progression of a proliferative disorder, either physically by, *e.g.*, stabilization of a discernible symptom, physiologically by, *e.g.*, stabilization of a physical parameter, or both. In other embodiments the terms “treat”, “treatment” and “treating” refer to the reduction or stabilization of tumor size or cancerous cell count.

The compositions and methods of the present invention encompass polypeptides and nucleic acids having the sequences specified, or sequences substantially identical or similar thereto, *e.g.*, sequences at least 70%, 75%, 80%, 85%, 90%, 95% identical or higher to the sequence specified. In the context of an amino acid sequence, the term "substantially identical" is used herein to refer to a first amino acid that contains a sufficient or minimum number of amino acid residues that are i) identical to, or ii) conservative substitutions of aligned amino acid residues in a second amino acid sequence such that the first and second amino acid sequences can have a common structural domain and/or common functional activity. For example, amino acid sequences that contain a common structural domain having at least about 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, *e.g.*, a sequence provided herein.

In the context of nucleotide sequence, the term "substantially identical" is used herein to refer to a first nucleic acid sequence that contains a sufficient or minimum number of nucleotides that are identical to aligned nucleotides in a second nucleic acid sequence such that the first and second nucleotide sequences encode a polypeptide having common functional activity, or encode a common structural polypeptide domain or a common functional polypeptide activity. For example, nucleotide sequences having at least about 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, *e.g.*, a sequence provided herein.

The term "functional variant" refers to polypeptides that have a substantially identical amino acid sequence to the naturally-occurring sequence, or are encoded by a substantially identical nucleotide sequence, and are capable of having one or more activities of the naturally-occurring sequence.

Calculations of homology or sequence identity between sequences (the terms are used interchangeably herein) are performed as follows.

To determine the percent identity of two amino acid sequences, or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In a preferred embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%, preferably at least 40%, more preferably at least 50%, 60%, and even more preferably at least 70%, 80%, 90%, 100% of the length of the reference sequence. The amino acid residues

or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "homology").

The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) *J. Mol. Biol.* 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package (available at <http://www.gcg.com>), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at <http://www.gcg.com>), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used unless otherwise specified) are a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

The percent identity between two amino acid or nucleotide sequences can be determined using the algorithm of E. Meyers and W. Miller ((1989) *CABIOS*, 4:11-17) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to a nucleic acid (SEQ ID NO: 1) molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50,

wordlength = 3 to obtain amino acid sequences homologous to protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (1997) *Nucleic Acids Res.* 25:3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (*e.g.*, XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>.

As used herein, the term “hybridizes under low stringency, medium stringency, high stringency, or very high stringency conditions” describes conditions for hybridization and washing. Guidance for performing hybridization reactions can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6, which is incorporated by reference. Aqueous and nonaqueous methods are described in that reference and either can be used. Specific hybridization conditions referred to herein are as follows: 1) low stringency hybridization conditions in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by two washes in 0.2X SSC, 0.1% SDS at least at 50°C (the temperature of the washes can be increased to 55°C for low stringency conditions); 2) medium stringency hybridization conditions in 6X SSC at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 60°C; 3) high stringency hybridization conditions in 6X SSC at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 65°C; and preferably 4) very high stringency hybridization conditions are 0.5M sodium phosphate, 7% SDS at 65°C, followed by one or more washes at 0.2X SSC, 1% SDS at 65°C. Very high stringency conditions (4) are the preferred conditions and the ones that should be used unless otherwise specified.

It is understood that the molecules of the present invention may have additional conservative or non-essential amino acid substitutions, which do not have a substantial effect on their functions.

The term "amino acid" is intended to embrace all molecules, whether natural or synthetic, which include both an amino functionality and an acid functionality and capable of being included in a polymer of naturally-occurring amino acids. Exemplary amino acids include naturally-occurring amino acids; analogs, derivatives and congeners thereof; amino acid analogs having variant side chains; and all stereoisomers of any of any of the foregoing. As used herein the term "amino acid" includes both the D- or L- optical isomers and peptidomimetics.

A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues

having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine).

The terms "polypeptide", "peptide" and "protein" (if single chain) are used interchangeably herein to refer to polymers of amino acids of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation, such as conjugation with a labeling component. The polypeptide can be isolated from natural sources, can be produced by recombinant techniques from a eukaryotic or prokaryotic host, or can be a product of synthetic procedures.

The terms "nucleic acid," "nucleic acid sequence," "nucleotide sequence," or "polynucleotide sequence," and "polynucleotide" are used interchangeably. They refer to a polymeric form of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. The polynucleotide may be either single-stranded or double-stranded, and if single-stranded may be the coding strand or non-coding (antisense) strand. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. The nucleic acid may be a recombinant polynucleotide, or a polynucleotide of genomic, cDNA, semisynthetic, or synthetic origin which either does not occur in nature or is linked to another polynucleotide in a nonnatural arrangement.

The term "isolated," as used herein, refers to material that is removed from its original or native environment (*e.g.*, the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide, separated by human intervention from some or all of the co-existing materials in the natural system, is isolated. Such polynucleotides could be part of a vector and/or such polynucleotides or polypeptides could be part of a composition, and still be

isolated in that such vector or composition is not part of the environment in which it is found in nature.

Various aspects of the invention are described in further detail below. Additional definitions are set out throughout the specification.

Exemplary Combinations of Antigen-Presentation Combinations, Effector Cell Combinations and Anti-tumor Immunosuppression Combinations

Exemplary combinations of therapeutic agents from two or more of the antigen-presentation category (A), effector cell category (B), and anti-tumor immunosuppression category (C) are provided herein.

Table 8: Listing of Therapeutic Agents in Categories (A)-(C)

	<i>A = Antigen-Presentation</i>	<i>B = Effector Cell</i>	<i>C = Anti-tumor Immunosuppression</i>
1	STING agonist	GITR agonist	PD-1 inhibitor
2	TLR agonist	PD-1 inhibitor	PD-L1 inhibitor
3	TIM-3 modulator	PD-L1 inhibitor	LAG-3 inhibitor
4	VEGFR inhibitor	IAP inhibitor	TIM-3 inhibitor
5	c-MET inhibitor	EGFR inhibitor	GITR inhibitor
6	TGFb inhibitor	mTOR inhibitor	CSF-1/1R inhibitor
7	IDO/TDO inhibitor	IL-15 agonist	IL-17 inhibitor
8	A2AR antagonist	CTLA-4 inhibitor	IL-1 β inhibitor
9	Oncolytic viruses	Bispecific T-cell engagers	CXCR2 inhibitor
10	Scaffold vaccines	CD40 agonist	PI3K- γ , - δ inhibitor

11	Bispecific T-cell engagers	OX40 agonist	BAFF-R inhibitor
12		CD27 agonist	MALT-1/BTK inhibitor
13			JAK inhibitor
14			CRTH2 inhibitor
15			VEGFR inhibitor
16			IL-15 agonist
17			Anti-TGFb inhibitor
18			IDO/TDO inhibitor
19			A2AR antagonist
20			CTLA-4 inhibitor
21			PFKFB3 inhibitor

In some embodiments, the combinations of the present invention include one or more of the following:

A1B1, A1B2, A1B3, A1B4, A1B5, A1B6, A1B7, A1B8, A1B9, A1B10, A1B11, A1B12, A2B1, A2B2, A2B3, A2B4, A2B5, A2B6, A2B7, A2B8, A2B9, A2B10, A2B11, A2B12, A3B1, A3B2, A3B3, A3B4, A3B5, A3B6, A3B7, A3B8, A3B9, A3B10, A3B11, A3B12, A4B1, A4B2, A4B3, A4B4, A4B5, A4B6, A4B7, A4B8, A4B9, A4B10, A4B11, A4B12, A5B1, A5B2, A5B3, A5B4, A5B5, A5B6, A5B7, A5B8, A5B9, A5B10, A5B11, A5B12, A6B1, A6B2, A6B3, A6B4, A6B5, A6B6, A6B7, A6B8, A6B9, A6B10, A6B11, A6B12, A7B1, A7B2, A7B3, A7B4, A7B5, A7B6, A7B7, A7B8, A7B9, A7B10, A7B11, A7B12, A8B1, A8B2, A8B3, A8B4, A8B5, A8B6, A8B7, A8B8, A8B9, A8B10, A8B11, A8B12, A9B1, A9B2, A9B3, A9B4, A9B5, A9B6, A9B7, A9B8, A9B9, A9B10, A9B11, A9B12, A10B1, A10B2, A10B3, A10B4, A10B5, A10B6, A10B7, A10B8, A10B9, A10B10, A10B11, A10B12, A11B1, A11B2, A11B3, A11B4, A11B5, A11B6, A11B7, A11B8, A11B9, A11B10, A11B11, A11B12, A1C1, A1C2, A1C3, A1C4, A1C5, A1C6, A1C7, A1C8, A1C9, A1C10, A1C11, A1C12, A1C13, A1C14, A1C15, A1C16, A1C17, A1C18, A1C19, A1C20, A1C21, A2C1, A2C2, A2C3, A2C4, A2C5, A2C6, A2C7, A2C8, A2C9, A2C10, A2C11, A2C12, A2C13, A2C14, A2C15, A2C16, A2C17, A2C18, A2C19, A2C20, A2C21, A3C1, A3C2, A3C3, A3C4, A3C5, A3C6, A3C7, A3C8, A3C9, A3C10, A3C11, A3C12, A3C13, A3C14, A3C15, A3C16, A3C17, A3C18, A3C19, A3C20, A3C21, A4C1, A4C2, A4C3, A4C4, A4C5, A4C6, A4C7, A4C8, A4C9, A4C10, A4C11, A4C12, A4C13,

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5 A10B6C18, A10B6C19, A10B6C20, A10B6C21, A10B7C1, A10B7C2, A10B7C3, A10B7C4,
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5 A11B9C18, A11B9C19, A11B9C20, A11B9C21, A11B10C1, A11B10C2, A11B10C3, A11B10C4, A11B10C5, A11B10C6, A11B10C7, A11B10C8, A11B10C9, A11B10C10, A11B10C11, A11B10C12, A11B10C13, A11B10C14, A11B10C15, A11B10C16, A11B10C17, A11B10C18, A11B10C19, A11B10C20, A11B10C21, A11B11C1, A11B11C2, A11B11C3, A11B11C4, A11B11C5, A11B11C6, A11B11C7, A11B11C8, A11B11C9, A11B11C10, A11B11C11, A11B11C12, A11B11C13, A11B11C14, A11B11C15, A11B11C16, A11B11C17, A11B11C18, A11B11C19, A11B11C20, A11B11C21, A11B12C1, A11B12C2, A11B12C3, A11B12C4, A11B12C5, A11B12C6, A11B12C7, A11B12C8, A11B12C9, A11B12C10, A11B12C11, A11B12C12, A11B12C13, A11B12C14, A11B12C15, A11B12C16, A11B12C17, A11B12C18, A11B12C19, A11B12C20, or A11B12C21.

Antibody Molecules

In one embodiment, the antibody molecule binds to a mammalian, *e.g.*, human, LAG-3. For example, the antibody molecule binds specifically to an epitope, *e.g.*, linear or conformational epitope, (*e.g.*, an epitope as described herein) on LAG-3. In some embodiments, the antibody molecule binds to one or more extracellular Ig-like domains of LAG-3, *e.g.*, the first, second, third or fourth extracellular Ig-like domain of LAG-3.

As used herein, the term "antibody molecule" refers to a protein, *e.g.*, an immunoglobulin chain or fragment thereof, comprising at least one immunoglobulin variable domain sequence. The term "antibody molecule" includes, for example, a monoclonal antibody (including a full length antibody which has an immunoglobulin Fc region). In an embodiment, an antibody molecule comprises a full length antibody, or a full length immunoglobulin chain. In an embodiment, an antibody molecule comprises an antigen binding or functional fragment of a full length antibody, or a full length immunoglobulin chain.

In an embodiment, an antibody molecule is a monospecific antibody molecule and binds a single epitope. *E.g.*, a monospecific antibody molecule having a plurality of immunoglobulin variable domain sequences, each of which binds the same epitope.

In an embodiment an antibody molecule is a multispecific antibody molecule, *e.g.*, it comprises a plurality of immunoglobulin variable domains sequences, wherein a first immunoglobulin variable domain sequence of the plurality has binding specificity for a first epitope and a second immunoglobulin variable domain sequence of the plurality has binding specificity for a second epitope. In an embodiment the first and second epitopes are on the same antigen, *e.g.*, the same protein (or subunit of a multimeric protein). In an embodiment the first and second epitopes overlap. In an embodiment the first and second epitopes do not overlap. In

an embodiment the first and second epitopes are on different antigens, *e.g.*, the different proteins (or different subunits of a multimeric protein). In an embodiment a multispecific antibody molecule comprises a third, fourth or fifth immunoglobulin variable domain. In an embodiment, a multispecific antibody molecule is a bispecific antibody molecule, a trispecific antibody molecule, or tetraspecific antibody molecule,

In an embodiment a multispecific antibody molecule is a bispecific antibody molecule. A bispecific antibody has specificity for no more than two antigens. A bispecific antibody molecule is characterized by a first immunoglobulin variable domain sequence which has binding specificity for a first epitope and a second immunoglobulin variable domain sequence that has binding specificity for a second epitope. In an embodiment the first and second epitopes are on the same antigen, *e.g.*, the same protein (or subunit of a multimeric protein). In an embodiment the first and second epitopes overlap. In an embodiment the first and second epitopes do not overlap. In an embodiment the first and second epitopes are on different antigens, *e.g.*, the different proteins (or different subunits of a multimeric protein). In an embodiment a bispecific antibody molecule comprises a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a first epitope and a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a half antibody having binding specificity for a first epitope and a half antibody having binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a half antibody, or fragment thereof, having binding specificity for a first epitope and a half antibody, or fragment thereof, having binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a scFv, or fragment thereof, have binding specificity for a first epitope and a scFv, or fragment thereof, have binding specificity for a second epitope. In an embodiment, the first epitope is located on LAG-3 and the second epitope is located on a PD-1, TIM-3, CEACAM (*e.g.*, CEACAM-1, CEACAM-3 and/or CEACAM-5), PD-L1, or PD-L2.

In an embodiment, an antibody molecule comprises a diabody, and a single-chain molecule, as well as an antigen-binding fragment of an antibody (*e.g.*, Fab, F(ab')₂, and Fv). For example, an antibody molecule can include a heavy (H) chain variable domain sequence (abbreviated herein as VH), and a light (L) chain variable domain sequence (abbreviated herein

as VL). In an embodiment an antibody molecule comprises or consists of a heavy chain and a light chain (referred to herein as a half antibody). In another example, an antibody molecule includes two heavy (H) chain variable domain sequences and two light (L) chain variable domain sequence, thereby forming two antigen binding sites, such as Fab, Fab', F(ab')₂, Fc, Fd, Fd', Fv, single chain antibodies (scFv for example), single variable domain antibodies, diabodies (Dab) (bivalent and bispecific), and chimeric (*e.g.*, humanized) antibodies, which may be produced by the modification of whole antibodies or those synthesized *de novo* using recombinant DNA technologies. These functional antibody fragments retain the ability to selectively bind with their respective antigen or receptor. Antibodies and antibody fragments can be from any class of antibodies including, but not limited to, IgG, IgA, IgM, IgD, and IgE, and from any subclass (*e.g.*, IgG1, IgG2, IgG3, and IgG4) of antibodies. The a preparation of antibody molecules can be monoclonal or polyclonal. An antibody molecule can also be a human, humanized, CDR-grafted, or *in vitro* generated antibody. The antibody can have a heavy chain constant region chosen from, *e.g.*, IgG1, IgG2, IgG3, or IgG4. The antibody can also have a light chain chosen from, *e.g.*, kappa or lambda. The term "immunoglobulin" (Ig) is used interchangeably with the term "antibody" herein.

Examples of antigen-binding fragments of an antibody molecule include: (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) a F(ab')₂ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a diabody (dAb) fragment, which consists of a VH domain; (vi) a camelid or camelized variable domain; (vii) a single chain Fv (scFv), see *e.g.*, Bird *et al.* (1988) *Science* 242:423-426; and Huston *et al.* (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883); (viii) a single domain antibody. These antibody fragments are obtained using conventional techniques known to those with skill in the art, and the fragments are screened for utility in the same manner as are intact antibodies.

The term "antibody" includes intact molecules as well as functional fragments thereof. Constant regions of the antibodies can be altered, *e.g.*, mutated, to modify the properties of the antibody (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function).

Antibodies of the present invention can also be single domain antibodies. Single domain antibodies can include antibodies whose complementary determining regions are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain antibodies, antibodies naturally devoid of light chains, single domain antibodies derived from conventional 4-chain antibodies, engineered antibodies and single domain scaffolds other than those derived from antibodies. Single domain antibodies may be any of the art, or any future single domain antibodies. Single domain antibodies may be derived from any species including, but not limited to mouse, human, camel, llama, fish, shark, goat, rabbit, and bovine. According to another aspect of the invention, a single domain antibody is a naturally occurring single domain antibody known as heavy chain antibody devoid of light chains. Such single domain antibodies are disclosed in WO 94/04678, for example. For clarity reasons, this variable domain derived from a heavy chain antibody naturally devoid of light chain is known herein as a VHH or nanobody to distinguish it from the conventional VH of four chain immunoglobulins. Such a VHH molecule can be derived from antibodies raised in *Camelidae* species, for example in camel, llama, dromedary, alpaca and guanaco. Other species besides *Camelidae* may produce heavy chain antibodies naturally devoid of light chain; such VHHs are within the scope of the invention.

The VH and VL regions can be subdivided into regions of hypervariability, termed "complementarity determining regions" (CDR), interspersed with regions that are more conserved, termed "framework regions" (FR or FW). The extent of the framework region and CDRs has been precisely defined by a number of methods (see, Kabat, E. A., *et al.* (1991) *Sequences of Proteins of Immunological Interest*, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Chothia, C. *et al.* (1987) *J. Mol. Biol.* 196:901-917; and the AbM definition used by Oxford Molecular's AbM antibody modeling software. See, generally, *e.g.*, *Protein Sequence and Structure Analysis of Antibody Variable Domains*. In: *Antibody Engineering Lab Manual* (Ed.: Duebel, S. and Kontermann, R., Springer-Verlag, Heidelberg).

The terms "complementarity determining region," and "CDR," as used herein refer to the sequences of amino acids within antibody variable regions which confer antigen specificity and binding affinity. In general, there are three CDRs in each heavy chain variable region (HCDR1, HCDR2, HCDR3) and three CDRs in each light chain variable region (LCDR1, LCDR2, LCDR3).

The precise amino acid sequence boundaries of a given CDR can be determined using any of a number of well-known schemes, including those described by Kabat *et al.* (1991), "Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD ("Kabat" numbering scheme), Al-Lazikani *et al.*, (1997) JMB 273,927-948 ("Chothia" numbering scheme). As used herein, the CDRs defined according the "Chothia" number scheme are also sometimes referred to as "hypervariable loops."

For example, under Kabat, the CDR amino acid residues in the heavy chain variable domain (VH) are numbered 31-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3); and the CDR amino acid residues in the light chain variable domain (VL) are numbered 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3). Under Chothia the CDR amino acids in the VH are numbered 26-32 (HCDR1), 52-56 (HCDR2), and 95-102 (HCDR3); and the amino acid residues in VL are numbered 26-32 (LCDR1), 50-52 (LCDR2), and 91-96 (LCDR3). By combining the CDR definitions of both Kabat and Chothia, the CDRs consist of amino acid residues 26-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3) in human VH and amino acid residues 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3) in human VL.

Generally, unless specifically indicated, the anti-LAG-3 antibody molecules can include any combination of one or more Kabat CDRs and/or Chothia hypervariable loops, *e.g.*, described in Table 1. In one embodiment, the following definitions are used for the anti-LAG-3 antibody molecules described in Table 1: HCDR1 according to the combined CDR definitions of both Kabat and Chothia, and HCCDRs 2-3 and LCCDRs 1-3 according the CDR definition of Kabat. Under all definitions, each VH and VL typically includes three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4.

As used herein, an "immunoglobulin variable domain sequence" refers to an amino acid sequence which can form the structure of an immunoglobulin variable domain. For example, the sequence may include all or part of the amino acid sequence of a naturally-occurring variable domain. For example, the sequence may or may not include one, two, or more N- or C-terminal amino acids, or may include other alterations that are compatible with formation of the protein structure.

The term "antigen-binding site" refers to the part of an antibody molecule that comprises determinants that form an interface that binds to the LAG-3 polypeptide, or an epitope thereof.

With respect to proteins (or protein mimetics), the antigen-binding site typically includes one or more loops (of at least four amino acids or amino acid mimics) that form an interface that binds to the LAG-3 polypeptide. Typically, the antigen-binding site of an antibody molecule includes at least one or two CDRs and/or hypervariable loops, or more typically at least three, four, five or six CDRs and/or hypervariable loops.

The terms “compete” or “cross-compete” are used interchangeably herein to refer to the ability of an antibody molecule to interfere with binding of an anti-LAG-3 antibody molecule, *e.g.*, an anti-LAG-3 antibody molecule provided herein, to a target, *e.g.*, human LAG-3. The interference with binding can be direct or indirect (*e.g.*, through an allosteric modulation of the antibody molecule or the target). The extent to which an antibody molecule is able to interfere with the binding of another antibody molecule to the target, and therefore whether it can be said to compete, can be determined using a competition binding assay, for example, a FACS assay, an ELISA or BIACORE assay. In some embodiments, a competition binding assay is a quantitative competition assay. In some embodiments, a first anti-LAG-3 antibody molecule is said to compete for binding to the target with a second anti-LAG-3 antibody molecule when the binding of the first antibody molecule to the target is reduced by 10% or more, *e.g.*, 20% or more, 30% or more, 40% or more, 50% or more, 55% or more, 60% or more, 65% or more, 70% or more, 75% or more, 80% or more, 85% or more, 90% or more, 95% or more, 98% or more, 99% or more in a competition binding assay (*e.g.*, a competition assay described herein).

As used herein, the term “epitope” refers to the moieties of an antigen (*e.g.*, human LAG-3) that specifically interact with an antibody molecule. Such moieties, referred to herein as epitopic determinants, typically comprise, or are part of, elements such as amino acid side chains or sugar side chains. An epitopic determinant can be defined by methods known in the art or disclosed herein, *e.g.*, by crystallography or by hydrogen-deuterium exchange. At least one or some of the moieties on the antibody molecule, that specifically interact with an epitopic determinant, are typically located in a CDR(s). Typically an epitope has a specific three dimensional structural characteristics. Typically an epitope has specific charge characteristics. Some epitopes are linear epitopes while others are conformational epitopes.

The terms "monoclonal antibody" or "monoclonal antibody composition" as used herein refer to a preparation of antibody molecules of single molecular composition. A monoclonal antibody composition displays a single binding specificity and affinity for a particular epitope.

A monoclonal antibody can be made by hybridoma technology or by methods that do not use hybridoma technology (*e.g.*, recombinant methods).

An “effectively human” protein is a protein that does not evoke a neutralizing antibody response, *e.g.*, the human anti-murine antibody (HAMA) response. HAMA can be problematic in a number of circumstances, *e.g.*, if the antibody molecule is administered repeatedly, *e.g.*, in treatment of a chronic or recurrent disease condition. A HAMA response can make repeated antibody administration potentially ineffective because of an increased antibody clearance from the serum (*see, e.g.*, Saleh *et al.*, *Cancer Immunol. Immunother.*, 32:180-190 (1990)) and also because of potential allergic reactions (*see, e.g.*, LoBuglio *et al.*, *Hybridoma*, 5:5117-5123 (1986)).

The antibody molecule can be a polyclonal or a monoclonal antibody. In other embodiments, the antibody can be recombinantly produced, *e.g.*, produced by phage display or by combinatorial methods.

Phage display and combinatorial methods for generating antibodies are known in the art (as described in, *e.g.*, Ladner *et al.* U.S. Patent No. 5,223,409; Kang *et al.* International Publication No. WO 92/18619; Dower *et al.* International Publication No. WO 91/17271; Winter *et al.* International Publication WO 92/20791; Markland *et al.* International Publication No. WO 92/15679; Breitling *et al.* International Publication WO 93/01288; McCafferty *et al.* International Publication No. WO 92/01047; Garrard *et al.* International Publication No. WO 92/09690; Ladner *et al.* International Publication No. WO 90/02809; Fuchs *et al.* (1991) *Bio/Technology* 9:1370-1372; Hay *et al.* (1992) *Hum Antibod Hybridomas* 3:81-85; Huse *et al.* (1989) *Science* 246:1275-1281; Griffiths *et al.* (1993) *EMBO J* 12:725-734; Hawkins *et al.* (1992) *J Mol Biol* 226:889-896; Clackson *et al.* (1991) *Nature* 352:624-628; Gram *et al.* (1992) *PNAS* 89:3576-3580; Garrard *et al.* (1991) *Bio/Technology* 9:1373-1377; Hoogenboom *et al.* (1991) *Nuc Acid Res* 19:4133-4137; and Barbas *et al.* (1991) *PNAS* 88:7978-7982, the contents of all of which are incorporated by reference herein).

In one embodiment, the antibody is a fully human antibody (*e.g.*, an antibody made in a mouse which has been genetically engineered to produce an antibody from a human immunoglobulin sequence), or a non-human antibody, *e.g.*, a rodent (mouse or rat), goat, primate (*e.g.*, monkey), camel antibody. Preferably, the non-human antibody is a rodent (mouse or rat antibody). Methods of producing rodent antibodies are known in the art.

Human monoclonal antibodies can be generated using transgenic mice carrying the human immunoglobulin genes rather than the mouse system. Splenocytes from these transgenic mice immunized with the antigen of interest are used to produce hybridomas that secrete human mAbs with specific affinities for epitopes from a human protein (*see, e.g., Wood et al. International Application WO 91/00906, Kucherlapati et al. PCT publication WO 91/10741; Lonberg et al. International Application WO 92/03918; Kay et al. International Application 92/03917; Lonberg, N. et al. 1994 Nature 368:856-859; Green, L.L. et al. 1994 Nature Genet. 7:13-21; Morrison, S.L. et al. 1994 Proc. Natl. Acad. Sci. USA 81:6851-6855; Bruggeman et al. 1993 Year Immunol 7:33-40; Tuailon et al. 1993 PNAS 90:3720-3724; Bruggeman et al. 1991 Eur J Immunol 21:1323-1326*).

An antibody can be one in which the variable region, or a portion thereof, *e.g.,* the CDRs, are generated in a non-human organism, *e.g.,* a rat or mouse. Chimeric, CDR-grafted, and humanized antibodies are within the invention. Antibodies generated in a non-human organism, *e.g.,* a rat or mouse, and then modified, *e.g.,* in the variable framework or constant region, to decrease antigenicity in a human are within the invention.

Chimeric antibodies can be produced by recombinant DNA techniques known in the art (see Robinson *et al.*, International Patent Publication PCT/US86/02269; Akira, *et al.*, European Patent Application 184,187; Taniguchi, M., European Patent Application 171,496; Morrison *et al.*, European Patent Application 173,494; Neuberger *et al.*, International Application WO 86/01533; Cabilly *et al.* U.S. Patent No. 4,816,567; Cabilly *et al.*, European Patent Application 125,023; Better *et al.* (1988 *Science* 240:1041-1043); Liu *et al.* (1987) *PNAS* 84:3439-3443; Liu *et al.*, 1987, *J. Immunol.* 139:3521-3526; Sun *et al.* (1987) *PNAS* 84:214-218; Nishimura *et al.*, 1987, *Canc. Res.* 47:999-1005; Wood *et al.* (1985) *Nature* 314:446-449; and Shaw *et al.*, 1988, *J. Natl Cancer Inst.* 80:1553-1559).

A humanized or CDR-grafted antibody will have at least one or two but generally all three recipient CDRs (of heavy and or light immunoglobulin chains) replaced with a donor CDR. The antibody may be replaced with at least a portion of a non-human CDR or only some of the CDRs may be replaced with non-human CDRs. It is only necessary to replace the number of CDRs required for binding of the humanized antibody to LAG-3. Preferably, the donor will be a rodent antibody, *e.g.,* a rat or mouse antibody, and the recipient will be a human framework or a human consensus framework. Typically, the immunoglobulin providing the CDRs is called the

"donor" and the immunoglobulin providing the framework is called the "acceptor." In one embodiment, the donor immunoglobulin is a non-human (*e.g.*, rodent). The acceptor framework is a naturally-occurring (*e.g.*, a human) framework or a consensus framework, or a sequence about 85% or higher, preferably 90%, 95%, 99% or higher identical thereto.

As used herein, the term "consensus sequence" refers to the sequence formed from the most frequently occurring amino acids (or nucleotides) in a family of related sequences (*See e.g.*, Winnaker, *From Genes to Clones* (Verlagsgesellschaft, Weinheim, Germany 1987). In a family of proteins, each position in the consensus sequence is occupied by the amino acid occurring most frequently at that position in the family. If two amino acids occur equally frequently, either can be included in the consensus sequence. A "consensus framework" refers to the framework region in the consensus immunoglobulin sequence.

An antibody can be humanized by methods known in the art (see *e.g.*, Morrison, S. L., 1985, *Science* 229:1202-1207, by Oi *et al.*, 1986, *BioTechniques* 4:214, and by Queen *et al.* US 5,585,089, US 5,693,761 and US 5,693,762, the contents of all of which are hereby incorporated by reference).

Humanized or CDR-grafted antibodies can be produced by CDR-grafting or CDR substitution, wherein one, two, or all CDRs of an immunoglobulin chain can be replaced. *See e.g.*, U.S. Patent 5,225,539; Jones *et al.* 1986 *Nature* 321:552-525; Verhoeyan *et al.* 1988 *Science* 239:1534; Beidler *et al.* 1988 *J. Immunol.* 141:4053-4060; Winter US 5,225,539, the contents of all of which are hereby expressly incorporated by reference. Winter describes a CDR-grafting method which may be used to prepare the humanized antibodies of the present invention (UK Patent Application GB 2188638A, filed on March 26, 1987; Winter US 5,225,539), the contents of which is expressly incorporated by reference.

Also within the scope of the invention are humanized antibodies in which specific amino acids have been substituted, deleted or added. Criteria for selecting amino acids from the donor are described in US 5,585,089, *e.g.*, columns 12-16 of US 5,585,089, the *e.g.*, columns 12-16 of US 5,585,089, the contents of which are hereby incorporated by reference. Other techniques for humanizing antibodies are described in Padlan *et al.* EP 519596 A1, published on December 23, 1992.

The antibody molecule can be a single chain antibody. A single-chain antibody (scFV) may be engineered (see, for example, Colcher, D. *et al.* (1999) *Ann N Y Acad Sci* 880:263-80;

and Reiter, Y. (1996) *Clin Cancer Res* 2:245-52). The single chain antibody can be dimerized or multimerized to generate multivalent antibodies having specificities for different epitopes of the same target protein.

In yet other embodiments, the antibody molecule has a heavy chain constant region chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE; particularly, chosen from, *e.g.*, the (*e.g.*, human) heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4. In another embodiment, the antibody molecule has a light chain constant region chosen from, *e.g.*, the (*e.g.*, human) light chain constant regions of kappa or lambda. The constant region can be altered, *e.g.*, mutated, to modify the properties of the antibody (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, and/or complement function). In one embodiment the antibody has: effector function; and can fix complement. In other embodiments the antibody does not; recruit effector cells; or fix complement. In another embodiment, the antibody has reduced or no ability to bind an Fc receptor. For example, it is an isotype or subtype, fragment or other mutant, which does not support binding to an Fc receptor, *e.g.*, it has a mutagenized or deleted Fc receptor binding region.

Methods for altering an antibody constant region are known in the art. Antibodies with altered function, *e.g.*, altered affinity for an effector ligand, such as FcR on a cell, or the C1 component of complement can be produced by replacing at least one amino acid residue in the constant portion of the antibody with a different residue (*see e.g.*, EP 388,151 A1, U.S. Pat. No. 5,624,821 and U.S. Pat. No. 5,648,260, the contents of all of which are hereby incorporated by reference). Similar type of alterations could be described which if applied to the murine, or other species immunoglobulin would reduce or eliminate these functions.

An antibody molecule can be derivatized or linked to another functional molecule (*e.g.*, another peptide or protein). As used herein, a "derivatized" antibody molecule is one that has been modified. Methods of derivatization include but are not limited to the addition of a fluorescent moiety, a radionucleotide, a toxin, an enzyme or an affinity ligand such as biotin. Accordingly, the antibody molecules of the invention are intended to include derivatized and otherwise modified forms of the antibodies described herein, including immunoadhesion molecules. For example, an antibody molecule can be functionally linked (by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other molecular entities,

such as another antibody (*e.g.*, a bispecific antibody or a diabody), a detectable agent, a cytotoxic agent, a pharmaceutical agent, and/or a protein or peptide that can mediate association of the antibody or antibody portion with another molecule (such as a streptavidin core region or a polyhistidine tag).

One type of derivatized antibody molecule is produced by crosslinking two or more antibodies (of the same type or of different types, *e.g.*, to create bispecific antibodies). Suitable crosslinkers include those that are heterobifunctional, having two distinctly reactive groups separated by an appropriate spacer (*e.g.*, *m*-maleimidobenzoyl-*N*-hydroxysuccinimide ester) or homobifunctional (*e.g.*, disuccinimidyl suberate). Such linkers are available from Pierce Chemical Company, Rockford, Ill.

Useful detectable agents with which an antibody molecule of the invention may be derivatized (or labeled) to include fluorescent compounds, various enzymes, prosthetic groups, luminescent materials, bioluminescent materials, fluorescent emitting metal atoms, *e.g.*, europium (Eu), and other anthanides, and radioactive materials (described below). Exemplary fluorescent detectable agents include fluorescein, fluorescein isothiocyanate, rhodamine, 5dimethylamine-1-naphthalenesulfonyl chloride, phycoerythrin and the like. An antibody may also be derivatized with detectable enzymes, such as alkaline phosphatase, horseradish peroxidase, β -galactosidase, acetylcholinesterase, glucose oxidase and the like. When an antibody is derivatized with a detectable enzyme, it is detected by adding additional reagents that the enzyme uses to produce a detectable reaction product. For example, when the detectable agent horseradish peroxidase is present, the addition of hydrogen peroxide and diaminobenzidine leads to a colored reaction product, which is detectable. An antibody molecule may also be derivatized with a prosthetic group (*e.g.*, streptavidin/biotin and avidin/biotin). For example, an antibody may be derivatized with biotin, and detected through indirect measurement of avidin or streptavidin binding. Examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; and examples of bioluminescent materials include luciferase, luciferin, and aequorin.

Labeled antibody molecule can be used, for example, diagnostically and/or experimentally in a number of contexts, including (i) to isolate a predetermined antigen by standard techniques, such as affinity chromatography or immunoprecipitation; (ii) to detect a

predetermined antigen (*e.g.*, in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the protein; (iii) to monitor protein levels in tissue as part of a clinical testing procedure, *e.g.*, to determine the efficacy of a given treatment regimen.

An antibody molecules may be conjugated to another molecular entity, typically a label or a therapeutic (*e.g.*, a cytotoxic or cytostatic) agent or moiety. Radioactive isotopes can be used in diagnostic or therapeutic applications. Radioactive isotopes that can be coupled to the anti-PSMA antibodies include, but are not limited to α -, β -, or γ -emitters, or β -and γ -emitters. Such radioactive isotopes include, but are not limited to iodine (^{131}I or ^{125}I), yttrium (^{90}Y), lutetium (^{177}Lu), actinium (^{225}Ac), praseodymium, astatine (^{211}At), rhenium (^{186}Re), bismuth (^{212}Bi or ^{213}Bi), indium (^{111}In), technetium ($^{99\text{m}}\text{Tc}$), phosphorus (^{32}P), rhodium (^{188}Rh), sulfur (^{35}S), carbon (^{14}C), tritium (^3H), chromium (^{51}Cr), chlorine (^{36}Cl), cobalt (^{57}Co or ^{58}Co), iron (^{59}Fe), selenium (^{75}Se), or gallium (^{67}Ga). Radioisotopes useful as therapeutic agents include yttrium (^{90}Y), lutetium (^{177}Lu), actinium (^{225}Ac), praseodymium, astatine (^{211}At), rhenium (^{186}Re), bismuth (^{212}Bi or ^{213}Bi), and rhodium (^{188}Rh). Radioisotopes useful as labels, *e.g.*, for use in diagnostics, include iodine (^{131}I or ^{125}I), indium (^{111}In), technetium ($^{99\text{m}}\text{Tc}$), phosphorus (^{32}P), carbon (^{14}C), and tritium (^3H), or one or more of the therapeutic isotopes listed above.

The invention provides radiolabeled antibody molecules and methods of labeling the same. In one embodiment, a method of labeling an antibody molecule is disclosed. The method includes contacting an antibody molecule, with a chelating agent, to thereby produce a conjugated antibody. The conjugated antibody is radiolabeled with a radioisotope, *e.g.*, $^{111}\text{Indium}$, $^{90}\text{Yttrium}$ and $^{177}\text{Lutetium}$, to thereby produce a labeled antibody molecule.

As is discussed above, the antibody molecule can be conjugated to a therapeutic agent. Therapeutically active radioisotopes have already been mentioned. Examples of other therapeutic agents include taxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, puromycin, maytansinoids, *e.g.*, maytansinol (*see* U.S. Pat. No. 5,208,020), CC-1065 (*see* U.S. Pat. Nos. 5,475,092, 5,585,499, 5,846, 545) and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (*e.g.*, methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (*e.g.*, mechlorethamine, thioepa

chlorambucil, CC-1065, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (*e.g.*, daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (*e.g.*, dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (*e.g.*, vincristine, vinblastine, taxol and maytansinoids).

In one aspect, the invention features a method of providing a target binding molecule that specifically binds to a LAG-3 receptor. For example, the target binding molecule is an antibody molecule. The method includes: providing a target protein that comprises at least a portion of non-human protein, the portion being homologous to (at least 70, 75, 80, 85, 87, 90, 92, 94, 95, 96, 97, 98% identical to) a corresponding portion of a human target protein, but differing by at least one amino acid (*e.g.*, at least one, two, three, four, five, six, seven, eight, or nine amino acids); obtaining an antibody molecule that specifically binds to the antigen; and evaluating efficacy of the binding agent in modulating activity of the target protein. The method can further include administering the binding agent (*e.g.*, antibody molecule) or a derivative (*e.g.*, a humanized antibody molecule) to a human subject.

This invention provides an isolated nucleic acid molecule encoding the above antibody molecule, vectors and host cells thereof. The nucleic acid molecule includes but is not limited to RNA, genomic DNA and cDNA.

Multisppecific Antibody Molecules

In certain embodiments, the antibody molecule is a multi-specific (*e.g.*, a bispecific or a trisppecific) antibody molecule. Protocols for generating bispecific or heterodimeric antibody molecules are known in the art; including but not limited to, for example, the “knob in a hole” approach described in, *e.g.*, US 5731168; the electrostatic steering Fc pairing as described in, *e.g.*, WO 09/089004, WO 06/106905 and WO 2010/129304; Strand Exchange Engineered Domains (SEED) heterodimer formation as described in, *e.g.*, WO 07/110205; Fab arm exchange as described in, *e.g.*, WO 08/119353, WO 2011/131746, and WO 2013/060867; double antibody conjugate, *e.g.*, by antibody cross-linking to generate a bi-specific structure using a heterobifunctional reagent having an amine-reactive group and a sulfhydryl reactive group as described in, *e.g.*, US 4433059; bispecific antibody determinants generated by recombining half

antibodies (heavy-light chain pairs or Fabs) from different antibodies through cycle of reduction and oxidation of disulfide bonds between the two heavy chains, as described in, *e.g.*, US 4444878; trifunctional antibodies, *e.g.*, three Fab' fragments cross-linked through sulfhydryl reactive groups, as described in, *e.g.*, US5273743; biosynthetic binding proteins, *e.g.*, pair of scFvs cross-linked through C-terminal tails preferably through disulfide or amine-reactive chemical cross-linking, as described in, *e.g.*, US5534254; bifunctional antibodies, *e.g.*, Fab fragments with different binding specificities dimerized through leucine zippers (*e.g.*, c-fos and c-jun) that have replaced the constant domain, as described in, *e.g.*, US5582996; bispecific and oligospecific mono- and oligovalent receptors, *e.g.*, VH-CH1 regions of two antibodies (two Fab fragments) linked through a polypeptide spacer between the CH1 region of one antibody and the VH region of the other antibody typically with associated light chains, as described in, *e.g.*, US5591828; bispecific DNA-antibody conjugates, *e.g.*, crosslinking of antibodies or Fab fragments through a double stranded piece of DNA, as described in, *e.g.*, US5635602; bispecific fusion proteins, *e.g.*, an expression construct containing two scFvs with a hydrophilic helical peptide linker between them and a full constant region, as described in, *e.g.*, US5637481; multivalent and multispecific binding proteins, *e.g.*, dimer of polypeptides having first domain with binding region of Ig heavy chain variable region, and second domain with binding region of Ig light chain variable region, generally termed diabodies (higher order structures are also encompassed creating for bispecific, trispecific, or tetraspecific molecules, as described in, *e.g.*, US5837242; minibody constructs with linked VL and VH chains further connected with peptide spacers to an antibody hinge region and CH3 region, which can be dimerized to form bispecific/multivalent molecules, as described in, *e.g.*, US5837821; VH and VL domains linked with a short peptide linker (*e.g.*, 5 or 10 amino acids) or no linker at all in either orientation, which can form dimers to form bispecific diabodies; trimers and tetramers, as described in, *e.g.*, US5844094; String of VH domains (or VL domains in family members) connected by peptide linkages with crosslinkable groups at the C-terminus further associated with VL domains to form a series of FVs (or scFvs), as described in, *e.g.*, US5864019; and single chain binding polypeptides with both a VH and a VL domain linked through a peptide linker are combined into multivalent structures through non-covalent or chemical crosslinking to form, *e.g.*, homobivalent, heterobivalent, trivalent, and tetravalent structures using both scFV or diabody type format, as described in, *e.g.*, US5869620. Additional exemplary multispecific and bispecific

molecules and methods of making the same are found, for example, in US5910573, US5932448, US5959083, US5989830, US6005079, US6239259, US6294353, US6333396, US6476198, US6511663, US6670453, US6743896, US6809185, US6833441, US7129330, US7183076, US7521056, US7527787, US7534866, US7612181, US2002004587A1, US2002076406A1, US2002103345A1, US2003207346A1, US2003211078A1, US2004219643A1, US2004220388A1, US2004242847A1, US2005003403A1, US2005004352A1, US2005069552A1, US2005079170A1, US2005100543A1, US2005136049A1, US2005136051A1, US2005163782A1, US2005266425A1, US2006083747A1, US2006120960A1, US2006204493A1, US2006263367A1, US2007004909A1, US2007087381A1, US2007128150A1, US2007141049A1, US2007154901A1, US2007274985A1, US2008050370A1, US2008069820A1, US2008152645A1, US2008171855A1, US2008241884A1, US2008254512A1, US2008260738A1, US2009130106A1, US2009148905A1, US2009155275A1, US2009162359A1, US2009162360A1, US2009175851A1, US2009175867A1, US2009232811A1, US2009234105A1, US2009263392A1, US2009274649A1, EP346087A2, WO0006605A2, WO02072635A2, WO04081051A1, WO06020258A2, WO2007044887A2, WO2007095338A2, WO2007137760A2, WO2008119353A1, WO2009021754A2, WO2009068630A1, WO9103493A1, WO9323537A1, WO9409131A1, WO9412625A2, WO9509917A1, WO9637621A2, WO9964460A1. The contents of the above-referenced applications are incorporated herein by reference in their entireties.

In other embodiments, the anti-LAG-3 antibody molecule (*e.g.*, a monospecific, bispecific, or multispecific antibody molecule) is covalently linked, *e.g.*, fused, to another partner *e.g.*, a protein *e.g.*, one, two or more cytokines, *e.g.*, as a fusion molecule for example a fusion protein. In other embodiments, the fusion molecule comprises one or more proteins, *e.g.*, one, two or more cytokines. In one embodiment, the cytokine is an interleukin (IL) chosen from one, two, three or more of IL-1, IL-2, IL-12, IL-15 or IL-21. In one embodiment, a bispecific antibody molecule has a first binding specificity to a first target (*e.g.*, to LAG-3), a second binding specificity to a second target (*e.g.*, PD-1, TIM-3, or PD-L1), and is optionally linked to an interleukin (*e.g.*, IL-12) domain *e.g.*, full length IL-12 or a portion thereof.

A “fusion protein” and a “fusion polypeptide” refer to a polypeptide having at least two portions covalently linked together, where each of the portions is a polypeptide having a

different property. The property may be a biological property, such as activity *in vitro* or *in vivo*. The property can also be simple chemical or physical property, such as binding to a target molecule, catalysis of a reaction, etc. The two portions can be linked directly by a single peptide bond or through a peptide linker, but are in reading frame with each other.

This invention provides an isolated nucleic acid molecule encoding the above antibody molecules, vectors and host cells thereof. The nucleic acid molecule includes but is not limited to RNA, genomic DNA and cDNA.

Exemplary Agents used in the Combinations

Described herein are methods and compositions that include a combination of one or more of: (i) an agent that enhances antigen (*e.g.*, tumor antigen) presentation; (ii) an agent that enhances an effector cell response (*e.g.*, B cell and/or T cell activation and/or mobilization); or (iii) an agent that decreases tumor immunosuppression, thereby treating the disorder, *e.g.*, the hyperproliferative condition or disorder (*e.g.*, the cancer). In some embodiments, the combination includes a LAG-3 inhibitor (*e.g.*, an anti-LAG-3 antibody molecule as described herein). Exemplary agents that can be used in these combinations are provided herein.

Exemplary STING Agonists

In an embodiment, the combination includes a STING agonist. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein *e.g.*, a solid tumor (*e.g.*, a breast cancer, a squamous cell carcinoma, a melanoma, an ovarian cancer, a fallopian tube carcinoma, a peritoneal carcinoma, a soft tissue sarcoma, a melanoma, a lung cancer (*e.g.*, a non-small cell lung cancer), a breast cancer, an esophageal cancer, a head and neck cancer, an endometrial cancer, a cervical cancer, or a basal cell carcinoma), *e.g.*, a hematologic malignancy (*e.g.*, a leukemia (*e.g.*, a chronic lymphocytic leukemia (CLL), or a lymphoma (*e.g.*, a marginal zone B-cell lymphoma, a small lymphocytic lymphoma, a follicular lymphoma, Hodgkin lymphoma, non-Hodgkin lymphoma)).

In some embodiments, the STING agonist is cyclic dinucleotide, *e.g.*, a cyclic dinucleotide comprising purine or pyrimidine nucleobases (*e.g.*, adenosine, guanine, uracil, thymine, or cytosine nucleobases). In some embodiments, the nucleobases of the cyclic dinucleotide comprise the same nucleobase or different nucleobases.

In some embodiments, the STING agonist comprises an adenosine or a guanosine nucleobase. In some embodiments, the STING agonist comprises one adenosine nucleobase and one guanosine nucleobase. In some embodiments, the STING agonist comprises two adenosine nucleobases or two guanosine nucleobases.

In some embodiments, the STING agonist comprises a modified cyclic dinucleotide, *e.g.*, comprising a modified nucleobase, a modified ribose, or a modified phosphate linkage. In some embodiments, the modified cyclic dinucleotide comprises a modified phosphate linkage, *e.g.*, a thiophosphate.

In some embodiments, the STING agonist comprises a cyclic dinucleotide (*e.g.*, a modified cyclic dinucleotide) with 2',5' or 3',5' phosphate linkages. In some embodiments, the STING agonist comprises a cyclic dinucleotide (*e.g.*, a modified cyclic dinucleotide) with Rp or Sp stereochemistry around the phosphate linkages.

In some embodiments, the STING agonist is Rp,Rp dithio 2',3' c-di-AMP (*e.g.*, Rp,Rp-dithio c-[A(2',5')pA(3',5')p]), or a cyclic dinucleotide analog thereof. In some embodiments, the STING agonist is a compound depicted in U.S. Patent Publication No. US2015/0056224 (*e.g.*, a compound in Figure 2c, *e.g.*, compound 21 or compound 22). In some embodiments, the STING agonist is c-[G(2',5')pG(3',5')p], a dithio ribose O-substituted derivative thereof, or a compound depicted in Fig. 4 of PCT Publication Nos. WO 2014/189805 and WO 2014/189806. In some embodiments, the STING agonist is c-[A(2',5')pA(3',5')p] or a dithio ribose O-substituted derivative thereof, or is a compound depicted in Fig. 5 of PCT Publication Nos. WO 2014/189805 and WO 2014/189806. In some embodiments, the STING agonist is c-[G(2',5')pA(3',5')p], or a dithio ribose O-substituted derivative thereof, or is a compound depicted in Fig. 5 of PCT Publication Nos. WO 2014/189805 and WO 2014/189806. In some embodiments, the STING agonist is 2'-O-propargyl-cyclic-[A(2',5')pA(3',5')p] (2'-O-propargyl-ML-CDA) or a compound depicted in Fig. 7 of PCT Publication No. WO 2014/189806.

Other exemplary STING agonists are disclosed, *e.g.*, in PCT Publication Nos. WO 2014/189805 and WO 2014/189806, and U.S. Publication No. 2015/0056225.

Exemplary TLR Agonists

In an embodiment, a combination described herein includes a Toll-like receptor (TLR) agonist. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described

herein, *e.g.*, a solid tumor (*e.g.*, a breast cancer, a squamous cell carcinoma, a melanoma, an ovarian cancer, a fallopian tube carcinoma, a peritoneal carcinoma, a soft tissue sarcoma, a melanoma, a breast cancer, an esophageal cancer, a head and neck cancer, an endometrial cancer, a cervical cancer, a colon cancer (*e.g.*, a metastatic mismatch repair-proficient (MRP) colon cancer), a kidney cancer (*e.g.*, a renal cell carcinoma), or a basal cell carcinoma), *e.g.*, a hematologic malignancy (*e.g.*, a leukemia (*e.g.*, a chronic lymphocytic leukemia (CLL)), or a lymphoma (*e.g.*, a marginal zone B-cell lymphoma, a small lymphocytic lymphoma, a follicular lymphoma, Hodgkin lymphoma, non-Hodgkin lymphoma)).

TLRs are a family of pattern recognition receptors that were initially identified as sensors of the innate immune system that recognize microbial pathogens. In humans, the TLRs include TLR-1, TLR-2, TLR-3, TLR-4, TLR-5, TLR-6, TLR-7, TLR-8, TLR-9, and TLR-10. TLR-1, -2, -4, -5, and -6, are expressed on the surface of cells and TLR-3, -7/8, and -9 are expressed with the ER compartment. Human dendritic cell subsets can be identified on the basis of distinct TLR expression patterns. The myeloid or “conventional” subset of human dendritic cells express TLRs 1-8 and the plasmacytoid subset of dendritic cells express only TLR-7 and TLR-9. Ligand binding to TLRs invokes a cascade of intra-cellular signaling pathways that induce the production of factors involved in inflammation and immunity. Upon stimulation, the myeloid subset and the plasmacytoid subset of human dendritic cells result in antigen-specific CD4+ and CD8+ T cell priming and activation of NK cells and T-cells, respectively.

In some embodiments, the TLR agonist is chosen from one or more of a TLR-1 agonist, a TLR-2 agonist, a TLR-3 agonist, a TLR-4 agonist, a TLR-5 agonist, a TLR-6 agonist, a TLR-7 agonist, a TLR-8 agonist, a TLR-9 agonist, a TLR-10 agonist, a TLR-1/2 agonist, a TLR-2/6 agonist, or a TLR-7/8 agonist. In one embodiment, the TLR agonist is a TLR7 agonist.

In some embodiments, the TLR agonist is imiquimod or 3-(2-Methylpropyl)-3,5,8-triazatricyclo[7.4.0.0^{2,6}]trideca-1(9),2(6),4,7,10,12-hexaen-7-amine. Imiquimod or 3-(2-Methylpropyl)-3,5,8-triazatricyclo[7.4.0.0^{2,6}]trideca-1(9),2(6),4,7,10,12-hexaen-7-amine can bind to and activate TLR-7 and/or TLR-8.

In some embodiments, the TLR agonist is 852A. 852A is disclosed, *e.g.*, in Inglefield *et al. J Interferon Cytokine Res.* 2008; 28(4):253-63. 852A can bind to and activate TLR-7 and/or TLR-8.

In some embodiments, the TLR agonist is Bacille Calmette-Guérin (BCG). BCG can bind to and activate TLR-9.

In some embodiments, the TLR agonist is EMD 120108. EMD 120108 is a synthetic oligonucleotide containing phosphorothioate oligodeoxynucleotide. EMD 1201081 can bind to and activate TLR-9, e.g. in monocytes/macrophages, plasmacytoid dendritic cells (DCs) and B cells, initiating immune signaling pathways, activating B cells and inducing T-helper cell cytokine production.

In some embodiments, the TLR agonist is IMO-2055. IMO-2055 is a synthetic oligonucleotide containing unmethylated CpG dinucleotides. Mimicking unmethylated CpG sequences in bacterial DNA, IMO-2055 can bind to and activate TLR-9, e.g., in monocytes/macrophages, plasmacytoid dendritic cells (DCs) and B cells, initiating immune signaling pathways and activating B cells and DCs and inducing T-helper cell cytokine production.

Other exemplary TLR agonists that can be used in the combination include, e.g., TLR-1/2 agonists (e.g., Pam3Cys), TLR-2 agonists (e.g., CFA, MALP2, Pam2Cys, FSL-1, or Hib-OMPC), TLR-3 agonists (e.g., polyribosinic:polyribocytidic acid (Poly I:C), polyadenosine-polyuridylic acid (poly AU), polyinosinic-polycytidylic acid stabilized with poly-L-lysine and carboxymethylcellulose (Hiltonol®)), TLR-4 agonists (e.g., monophosphoryl lipid A (MPL), LPS, sialyl-Tn (STn)), TLR-5 agonists (e.g., bacterial flagellin), TLR-7 agonists (e.g., imiquimod), TLR-7/8 agonists (e.g., resiquimod or loxoribine), and TLR-9 agonists (e.g., unmethylated CpG dinucleotide (CpG-ODN)).

In another embodiment, the TLR agonist is used in combination with a GITR agonist, e.g., as described in WO2004/060319, and International Publication No.: WO2014/012479.

Exemplary VEGFR Inhibitors

In one embodiment, a combination described herein includes a vascular endothelial growth factor (VEGF) receptor inhibitor (e.g., an inhibitor of one or more of VEGFR (e.g., VEGFR-1, VEGFR-2, VEGFR-3) or VEGF). In some embodiments, the combination is used to treat a cancer, e.g., a cancer described herein, e.g., a solid tumor (e.g., a melanoma, a breast cancer, a colon cancer, an esophageal cancer, a gastrointestinal stromal tumor (GIST), a kidney cancer (e.g., a renal cell cancer), a liver cancer, a non-small cell lung cancer (NSCLC), an

ovarian cancer, a pancreatic cancer, a prostate cancer, or a stomach cancer), *e.g.*, a hematologic malignancy (*e.g.*, a lymphoma).

In some embodiments, the VEGFR inhibitor is vatalanib succinate (Compound A47) or a compound disclosed in EP 296122.

In some embodiment, the VEGFR inhibitor is an inhibitor of one or more of VEGFR-2, PDGFRbeta, KIT or Raf kinase C, 1-methyl-5-((2-(5-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-4-yl)oxy)-N-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazol-2-amine (Compound A37) or a compound disclosed in PCT Publication No. WO 2007/030377.

Other exemplary VEGFR pathway inhibitors that can be used in the combinations disclosed herein include, *e.g.*, bevacizumab (AVASTIN®), axitinib (INLYTA®); brivanib alaninate (BMS-582664, (S)-((R)-1-(4-(4-Fluoro-2-methyl-1H-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy)propan-2-yl)2-aminopropanoate); sorafenib (NEXAVAR®); pazopanib (VOTRIENT®); sunitinib malate (SUTENT®); cediranib (AZD2171, CAS 288383-20-1); vargatef (BIBF1120, CAS 928326-83-4); Foretinib (GSK1363089); telatinib (BAY57-9352, CAS 332012-40-5); apatinib (YN968D1, CAS 811803-05-1); imatinib (GLEEVEC®); ponatinib (AP24534, CAS 943319-70-8); tivozanib (AV951, CAS 475108-18-0); regorafenib (BAY73-4506, CAS 755037-03-7); vatalanib dihydrochloride (PTK787, CAS 212141-51-0); brivanib (BMS-540215, CAS 649735-46-6); vandetanib (CAPRELSA® or AZD6474); motesanib diphosphate (AMG706, CAS 857876-30-3, N-(2,3-dihydro-3,3-dimethyl-1H-indol-6-yl)-2-[(4-pyridinylmethyl)amino]-3-pyridinecarboxamide, described in PCT Publication No. WO 02/066470); dovitinib dilactic acid (TKI258, CAS 852433-84-2); linafanib (ABT869, CAS 796967-16-3); cabozantinib (XL184, CAS 849217-68-1); lestaurtinib (CAS 111358-88-4); N-[5-[[[5-(1,1-dimethylethyl)-2-oxazolyl]methyl]thio]-2-thiazolyl]-4-piperidinecarboxamide (BMS38703, CAS 345627-80-7); (3R,4R)-4-amino-1-((4-((3-methoxyphenyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)methyl)piperidin-3-ol (BMS690514); N-(3,4-Dichloro-2-fluorophenyl)-6-methoxy-7-[(3 α ,5 β ,6 α)-octahydro-2-methylcyclopenta[c]pyrrol-5-yl]methoxy]-4-quinazolinamine (XL647, CAS 781613-23-8); 4-methyl-3-[[1-methyl-6-(3-pyridinyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]amino]-N-[3-(trifluoromethyl)phenyl]-benzamide (BHG712, CAS 940310-85-0); aflibercept (EYLEA®), and endostatin (ENDOSTAR®).

Exemplary anti-VEGF antibodies that can be used in the combinations disclosed herein include, *e.g.*, a monoclonal antibody that binds to the same epitope as the monoclonal anti-VEGF antibody A4.6.1 produced by hybridoma ATCC HB 10709; a recombinant humanized anti-VEGF monoclonal antibody generated according to Presta *et al.* (1997) *Cancer Res.* 57:4593-4599. In one embodiment, the anti-VEGF antibody is Bevacizumab (BV), also known as rhuMAb VEGF or AVASTIN®. It comprises mutated human IgG1 framework regions and antigen-binding complementarity- determining regions from the murine anti-hVEGF monoclonal antibody A.4.6.1 that blocks binding of human VEGF to its receptors. Bevacizumab and other humanized anti-VEGF antibodies are further described in U.S. Pat. No. 6,884,879 issued Feb. 26, 2005. Additional antibodies include the G6 or B20 series antibodies (*e.g.*, G6-31, B20-4.1), as described in PCT Publication No. WO2005/012359, PCT Publication No. WO2005/044853, the contents of these patent applications are expressly incorporated herein by reference. For additional antibodies see U.S. Pat. Nos. 7,060,269, 6,582,959, 6,703,020, 6,054,297, WO98/45332, WO 96/30046, WO94/10202, EP 0666868B1, U.S. Patent Application Publication Nos. 2006/009360, 2005/0186208, 2003/0206899, 2003/0190317, 2003/0203409, and 2005/0112126; and Popkov *et al.*, *Journal of Immunological Methods* 288: 149-164 (2004). Other antibodies include those that bind to a functional epitope on human VEGF comprising of residues F17, M18, D19, Y21, Y25, Q89, 191, K101, E103, and C104 or, alternatively, comprising residues F17, Y21, Q22, Y25, D63, 183 and Q89.

Exemplary c-MET Inhibitors

In one embodiment, a combination described herein includes an inhibitor of c-MET. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a non-small cell lung cancer, a pancreatic cancer, a liver cancer (*e.g.*, a hepatocellular carcinoma, *e.g.*, a c-MET overexpressing hepatocellular carcinoma), a thyroid cancer, a brain tumor (*e.g.*, a glioblastoma), a kidney cancer (*e.g.*, a renal cell carcinoma), a head and neck cancer (*e.g.*, a head and neck squamous cell carcinoma).

In some embodiments, the c-MET inhibitor is Compound A17 or a compound described in U.S. Patent Nos. 7,767,675 and 8,420,645). c-MET, a receptor tyrosine kinase overexpressed or mutated in many tumor cell types, plays key roles in tumor cell proliferation, survival,

invasion, metastasis, and tumor angiogenesis. Inhibition of c-MET may induce cell death in tumor cells overexpressing c-MET protein or expressing constitutively activated c-MET protein.

In some embodiments, the c-MET inhibitor is JNJ-38877605. JNJ-38877605 is an orally available, small molecule inhibitor of c-Met. JNJ-38877605 selectively binds to c-MET, thereby inhibiting c-MET phosphorylation and disrupting c-Met signal transduction pathways.

In some embodiments, the c-Met inhibitor is AMG 208. AMG 208 is a selective small-molecule inhibitor of c-MET. AMG 208 inhibits the ligand-dependent and ligand-independent activation of c-MET, inhibiting its tyrosine kinase activity, which may result in cell growth inhibition in tumors that overexpress c-Met.

In some embodiments, the c-Met inhibitor is AMG 337. AMG 337 is an orally bioavailable inhibitor of c-Met. AMG 337 selectively binds to c-MET, thereby disrupting c-MET signal transduction pathways.

In some embodiments, the c-Met inhibitor is LY2801653. LY2801653 is an orally available, small molecule inhibitor of c-Met. LY2801653 selectively binds to c-MET, thereby inhibiting c-MET phosphorylation and disrupting c-Met signal transduction pathways.

In some embodiments, c-Met inhibitor is MSC2156119J. MSC2156119J is an orally bioavailable inhibitor of c-Met. MSC2156119J selectively binds to c-MET, which inhibits c-MET phosphorylation and disrupts c-Met-mediated signal transduction pathways.

In some embodiments, the c-MET inhibitor is capmatinib. Capmatinib is also known as INCB028060. Capmatinib is an orally bioavailable inhibitor of c-MET. Capmatinib selectively binds to c-Met, thereby inhibiting c-Met phosphorylation and disrupting c-Met signal transduction pathways.

In some embodiments, the c-MET inhibitor is crizotinib. Crizotinib is also known as PF-02341066. Crizotinib is an orally available aminopyridine-based inhibitor of the receptor tyrosine kinase anaplastic lymphoma kinase (ALK) and the c-Met/hepatocyte growth factor receptor (HGFR). Crizotinib, in an ATP-competitive manner, binds to and inhibits ALK kinase and ALK fusion proteins. In addition, crizotinib inhibits c-Met kinase, and disrupts the c-Met signaling pathway. Altogether, this agent inhibits tumor cell growth.

In some embodiments, the c-MET inhibitor is golvatinib. Golvatinib is an orally bioavailable dual kinase inhibitor of c-MET and VEGFR-2 with potential antineoplastic activity.

Golvatinib binds to and inhibits the activities of both c-MET and VEGFR-2, which may inhibit tumor cell growth and survival of tumor cells that overexpress these receptor tyrosine kinases.

In some embodiments, the c-MET inhibitor is tivantinib. Tivantinib is also known as ARQ 197. Tivantinib is an orally bioavailable small molecule inhibitor of c-MET. Tivantinib binds to the c-MET protein and disrupts c-Met signal transduction pathways, which may induce cell death in tumor cells overexpressing c-MET protein or expressing constitutively activated c-Met protein.

Exemplary TGF β Inhibitors

In one embodiment, a combination described herein includes a transforming growth factor beta (TGF- β) inhibitor. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a brain cancer (*e.g.*, a glioma), a melanoma, a kidney cancer (*e.g.*, a renal cell carcinoma), a pleural malignant mesothelioma (*e.g.*, a relapsed pleural malignant mesothelioma), or a breast cancer (*e.g.*, a metastatic breast cancer)).

In some embodiments, the TGF- β inhibitor is fresolimumab (CAS Registry Number: 948564-73-6). Fresolimumab is also known as GC1008. Fresolimumab is a human monoclonal antibody that binds to and inhibits TGF-beta isoforms 1, 2 and 3.

The heavy chain of fresolimumab has the amino acid sequence of:

QVQLVQSGAEVKKPGSSVKVSCASGYTFSSNVISWVRQAPGQGLEWMGGVPIVDIA
 NYAQRFKGRVTITADESTSTTYMELSSLRSEDVAVYYCASTLGLVLDAMDYWGQGLTLV
 TVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV
 LQSSGLYSLSSVTVPSSSLGKTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLG
 GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQ
 FNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPS
 QEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVD
 KSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLGK (SEQ ID NO: 294). The light chain of

fresolimumab has the amino acid sequence of:

ETVLTQSPGTLSLSPGERATLSCRASQSLGSSYLAWYQQKPGQAPRLLIYGASSRAPGIP
 DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYADSPITFGQGRLEIKRTVAAPSVFIFPPS
 DEQLKSGTASVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTL
 TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 295).

Fresolimumab is disclosed, *e.g.*, in WO 2006/086469, US 8,383,780, and US 8,591,901.

In some embodiments, the TGF- β inhibitor is XOMA 089. XOMA 089 is also known as XPA.42.089. XOMA 089 is a fully human monoclonal antibody that specifically binds and neutralizes TGF-beta 1 and 2 ligands.

The heavy chain variable region of XOMA 089 has the amino acid sequence of:
QVQLVQSGAEVKKPGSSVKVSCASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGTAN
YAQKFQGRVTITADESTSTAYMELSSLRSEDVAVYYCARGLWEVRALPSVYWGQGLTLV
TVSS (SEQ ID NO: 296) (disclosed as SEQ ID NO: 6 in WO 2012/167143). The light chain
variable region of XOMA 089 has the amino acid sequence of:
SYELTQPPSVSVAPGQTARITCGANDIGSKSVHWYQQKAGQAPVLVSEDIIRPSGIPERI
SGSNSGNTATLTISRVEAGDEADYYCQVWDRDSDQYVFGTGTKVTVLG (SEQ ID NO:
297) (disclosed as SEQ ID NO: 8 in WO 2012/167143).

Exemplary IDO/TDO Inhibitors

In one embodiment, a combination described herein includes an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO). In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, melanoma, non-small cell lung cancer, colon cancer, squamous cell head and neck cancer, ovarian cancer, peritoneal cancer, fallopian tube cancer, breast cancer (*e.g.*, metastatic or HER2-negative breast cancer)), *e.g.*, a hematologic malignancy (*e.g.*, a lymphoma, *e.g.*, a non-Hodgkin's lymphoma or a Hodgkin's lymphoma (*e.g.*, a diffuse large B-cell lymphoma (DLBCL))).

In some embodiments, the IDO/TDO inhibitor is chosen from (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine (also known as INCB24360), indoximod (1-methyl-D-tryptophan), or α -cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol (also known as NLG919).

In some embodiments, the IDO/TDO inhibitor is epacadostat (CAS Registry Number: 1204669-58-8). Epacadostat is also known as INCB24360 or INCB024360 (Incyte). Epacadostat is a potent and selective indoleamine 2,3-dioxygenase (IDO1) inhibitor with IC₅₀ of 10 nM, highly selective over other related enzymes such as IDO2 or tryptophan 2,3-dioxygenase (TDO).

In some embodiments, the IDO/TDO inhibitor is indoximod (New Link Genetics). Indoximod, the D isomer of 1-methyl-tryptophan, is an orally administered small-molecule indoleamine 2,3-dioxygenase (IDO) pathway inhibitor that disrupts the mechanisms by which tumors evade immune-mediated destruction.

In some embodiments, the IDO/TDO inhibitor is NLG919 (New Link Genetics). NLG919 is a potent IDO (indoleamine-(2,3)-dioxygenase) pathway inhibitor with K_i/EC_{50} of 7 nM/75 nM in cell-free assays.

In some embodiments, the IDO/TDO inhibitor is F001287 (Flexus/BMS). F001287 is a small molecule inhibitor of indoleamine 2,3-dioxygenase 1 (IDO1).

Exemplary A2AR Antagonists

In one embodiment, a combination described herein includes an adenosine A2a receptor (A2aR) antagonist (*e.g.*, an inhibitor of A2aR pathway, *e.g.*, an adenosine inhibitor, *e.g.*, an inhibitor of A2aR or CD-73). In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein. In certain embodiments, the cancer is a lung cancer, *e.g.*, a non-small cell lung cancer.

In some embodiments, the A2aR antagonist is istradefylline (CAS Registry Number: 155270-99-8). Istradefylline is also known as KW-6002 or 8-[(E)-2-(3,4-dimethoxyphenyl)vinyl]-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione. Istradefylline is disclosed, *e.g.*, in LeWitt *et al.* (2008) *Annals of Neurology* 63 (3): 295–302).

In some embodiments, the A2aR antagonist is tozadenant (Biotie). Tozadenant is also known as SYN115 or 4-hydroxy-N-(4-methoxy-7-morpholin-4-yl-1,3-benzothiazol-2-yl)-4-methylpiperidine-1-carboxamide. Tozadenant blocks the effect of endogenous adenosine at the A2a receptors, resulting in the potentiation of the effect of dopamine at the D2 receptor and inhibition of the effect of glutamate at the mGluR5 receptor. In some embodiments, the A2aR antagonist is preladenant (CAS Registry Number: 377727-87-2). Preladenant is also known as SCH 420814 or 2-(2-Furanyl)-7-[2-[4-[4-(2-methoxyethoxy)phenyl]-1-piperazinyl]ethyl]7H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidine-5-amine. Preladenant was developed as a drug that acted as a potent and selective antagonist at the adenosine A2A receptor.

In some embodiments, the A2aR antagonist is vipadenan. Vipadenan is also known as BIIB014, V2006, or 3-[(4-amino-3-methylphenyl)methyl]-7-(furan-2-yl)triazolo[4,5-

d]pyrimidin-5-amine. *e.g.*, In some embodiments, the A2aR antagonist is PBF-509 (Palobiofarma). *e.g.*, In some embodiments, the A2aR antagonist, *e.g.*, PBF-509 is administered at a daily dose of about 80 mg, 160 mg, or 240 mg.

Other exemplary A2aR antagonists include, *e.g.*, ATL-444, MSX-3, SCH-58261, SCH-412,348, SCH-442,416, VER-6623, VER-6947, VER-7835, CGS-15943, or ZM-241,385.

In some embodiments, the A2aR antagonist is an A2aR pathway antagonist (*e.g.*, a CD-73 inhibitor, *e.g.*, an anti-CD73 antibody) is MEDI9447. MEDI9447 is a monoclonal antibody specific for CD73. Targeting the extracellular production of adenosine by CD73 may reduce the immunosuppressive effects of adenosine. MEDI9447 was reported to have a range of activities, *e.g.*, inhibition of CD73 ectonucleotidase activity, relief from AMP-mediated lymphocyte suppression, and inhibition of syngeneic tumor growth. MEDI9447 can drive changes in both myeloid and lymphoid infiltrating leukocyte populations within the tumor microenvironment. These changes include, *e.g.*, increases in CD8 effector cells and activated macrophages, as well as a reduction in the proportions of myeloid-derived suppressor cells (MDSC) and regulatory T lymphocytes.

Exemplary Oncolytic Viruses

In some embodiments, a combination as described herein includes an oncolytic virus. In embodiments, oncolytic viruses are capable of selectively replicating in and triggering the death of or slowing the growth of a cancer cell. In some cases, oncolytic viruses have no effect or a minimal effect on non-cancer cells. An oncolytic virus includes but is not limited to an oncolytic adenovirus, oncolytic Herpes Simplex Viruses, oncolytic retrovirus, oncolytic parvovirus, oncolytic vaccinia virus, oncolytic Sindbis virus, oncolytic influenza virus, or oncolytic RNA virus (*e.g.*, oncolytic reovirus, oncolytic Newcastle Disease Virus (NDV), oncolytic measles virus, or oncolytic vesicular stomatitis virus (VSV)). In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein. In some embodiments, the cancer is a brain cancer, *e.g.*, a glioblastoma.

In some embodiments, the oncolytic virus is a virus, *e.g.*, recombinant oncolytic virus, described in US2010/0178684 A1, which is incorporated herein by reference in its entirety. In some embodiments, a recombinant oncolytic virus comprises, or comprises a nucleic acid sequence (*e.g.*, heterologous nucleic acid sequence) encoding, an inhibitor of an immune or

inflammatory response, *e.g.*, as described in US2010/0178684 A1, incorporated herein by reference in its entirety. In embodiments, the recombinant oncolytic virus, *e.g.*, oncolytic NDV, comprises, or comprises a nucleic acid sequence encoding, a pro-apoptotic protein (*e.g.*, apoptin), a cytokine (*e.g.*, GM-CSF, CSF, interferon-gamma, interleukin-2 (IL-2), tumor necrosis factor-alpha), an immunoglobulin (*e.g.*, an antibody against ED-B fibronectin), a tumor associated antigen, a bispecific adapter protein (*e.g.*, bispecific antibody or antibody fragment directed against NDV HN protein and a T cell co-stimulatory receptor, such as CD3 or CD28; or a fusion protein between human IL-2 and single chain antibody directed against NDV HN protein). *See, e.g.*, Zamarin *et al.* Future Microbiol. 7.3(2012):347-67, incorporated herein by reference in its entirety. In some embodiments, the oncolytic virus is a chimeric oncolytic NDV described in US 8591881 B2, US 2012/0122185 A1, or US 2014/0271677 A1, each of which is incorporated herein by reference in their entireties.

In some embodiments, the oncolytic virus comprises a conditionally replicative adenovirus (CRAd), which is designed to replicate exclusively in cancer cells. *See, e.g.*, Alemany *et al.* Nature Biotechnol. 18(2000):723-27. In some embodiments, an oncolytic adenovirus comprises one described in Table 1 on page 725 of Alemany *et al.*, incorporated herein by reference in its entirety.

Exemplary oncolytic viruses include but are not limited to the following:

Group B Oncolytic Adenovirus (ColoAd1) (PsiOxus Therapeutics Ltd.) (*see, e.g.*, Clinical Trial Identifier: NCT02053220);

ONCOS-102 (previously called CGTG-102), which is an adenovirus comprising granulocyte-macrophage colony stimulating factor (GM-CSF) (Oncos Therapeutics) (*see, e.g.*, Clinical Trial Identifier: NCT01598129);

VCN-01, which is a genetically modified oncolytic human adenovirus encoding human PH20 hyaluronidase (VCN Biosciences, S.L.) (*see, e.g.*, Clinical Trial Identifiers: NCT02045602 and NCT02045589);

Conditionally Replicative Adenovirus ICOVIR-5, which is a virus derived from wild-type human adenovirus serotype 5 (Had5) that has been modified to selectively replicate in cancer cells with a deregulated retinoblastoma/E2F pathway (Institut Català d'Oncologia) (*see, e.g.*, Clinical Trial Identifier: NCT01864759);

Celyvir, which comprises bone marrow-derived autologous mesenchymal stem cells (MSCs) infected with ICOVIR5, an oncolytic adenovirus (Hospital Infantil Universitario Niño Jesús, Madrid, Spain/ Ramon Alemany) (see, *e.g.*, Clinical Trial Identifier: NCT01844661);

CG0070, which is a conditionally replicating oncolytic serotype 5 adenovirus (Ad5) in which human E2F-1 promoter drives expression of the essential E1a viral genes, thereby restricting viral replication and cytotoxicity to Rb pathway-defective tumor cells (Cold Genesys, Inc.) (see, *e.g.*, Clinical Trial Identifier: NCT02143804); or

DNX-2401 (formerly named Delta-24-RGD), which is an adenovirus that has been engineered to replicate selectively in retinoblastoma (Rb)-pathway deficient cells and to infect cells that express certain RGD-binding integrins more efficiently (Clinica Universidad de Navarra, Universidad de Navarra/ DNATRIX, Inc.) (see, *e.g.*, Clinical Trial Identifier: NCT01956734).

In some embodiments, an oncolytic virus described herein is administered by injection, *e.g.*, subcutaneous, intra-arterial, intravenous, intramuscular, intrathecal, or intraperitoneal injection. In other embodiments, an oncolytic virus described herein is administered intratumorally, transdermally, transmucosally, orally, intranasally, or via pulmonary administration.

Exemplary vaccines, e.g., Scaffold vaccines

In one embodiment, a combination described herein includes a vaccine, *e.g.*, a scaffold vaccine. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein.

Cancer vaccines are disclosed, *e.g.*, in PCT Publication Nos. WO 2007/070660 and WO 2012/167230, EP 1960009 B1, U.S. Patent Nos. US 8,067,237 and US 8,932,583, and U.S. Publication No. US 2011/0020216. The components that can be used within cancer vaccines (*e.g.*, implantable scaffold materials) are disclosed, *e.g.*, in PCT Publication Nos. WO 2009/102465 and WO 2013/106852. Methods that can be used for administration of cancer vaccines are disclosed, *e.g.*, in PCT Publication Nos. WO 2013/158673, WO 2012/048165, and WO 2012/149358.

In some embodiments, the cancer vaccine includes a macroporous scaffold comprising (i) cells or a cell recruitment composition, and (ii) a deployment signal capable of inducing or promoting migration of cells, and (iii) a bioactive composition coated or seeded onto/into the

scaffold, which causes cells recruited into the scaffold be modified. Migration of the modified cells can be promoted by the open, interconnected macropores and the deployment signal.

In some embodiments, the cancer vaccine induces an endogenous immune response to a cancer target via administration of a porous scaffold bearing a recruitment composition and a target antigen composition, wherein an endogenous antigen presenting cell is recruited into the scaffold to encounter antigen and where said cell resides until a deployment signal induces egress to a lymph node tissue outside the scaffold, thereby stimulating an endogenous immune response to said cancer target.

In some embodiments, the cancer vaccine is used to remove a target cell from a mammal using a scaffold composition.

In some embodiments, an *in situ* cancer vaccine is generated via recruitment of cancer cells to an implanted scaffold and destruction of the cells using a cytotoxic agent.

In some embodiments, a cytosine-guanosine oligonucleotide (CpG-ODN) is used as a component of a scaffold, which can effectively reprogram and deploy dendritic cells recruited to the scaffold, and generate an effective anti-tumor response.

In some embodiments, polyinosine-polycytidylic acid (poly I:C) and/or CpG ODN are used to exert a synergistic effect on tumor inhibition.

In some embodiments, porous rods comprising an immune cell recruitment compound (*e.g.* GM-CSF) and an immune cell activation compound (*e.g.* CpG ODN), and optionally comprising an antigen such as a tumor lysate, are used, *e.g.*, to elicit an immune response to a vaccine antigen. In some embodiments, pores that facilitate recruitment or release of cells are formed *in situ* within hydrogels following hydrogel injection. In some embodiments, injectable shape memory porous hydrogel polymer is used for administration.

In other embodiments, the combinations disclosed herein include a cancer or tumor vaccine. Non-limiting examples of tumor vaccines that can be used include peptides of melanoma antigens, such as peptides of gp100, MAGE antigens, Trp-2, MART1 and/or tyrosinase, tumor cells transfected to express the cytokine GM-CSF, DNA-based vaccines, RNA-based vaccines, and viral transduction-based vaccines. The cancer vaccine may be prophylactic or therapeutic.

Many experimental strategies for vaccination against tumors have been devised (*see* Rosenberg, S., 2000, Development of Cancer Vaccines, ASCO Educational Book Spring: 60-62;

Logothetis, C., 2000, ASCO Educational Book Spring: 300-302; Khayat, D. 2000, ASCO Educational Book Spring: 414-428; Foon, K. 2000, ASCO Educational Book Spring: 730-738; *see also* Restifo, N. and Sznol, M., *Cancer Vaccines*, Ch. 61, pp. 3023-3043 in DeVita, V. *et al.* (eds.), 1997, *Cancer: Principles and Practice of Oncology*. Fifth Edition). In one of these strategies, a vaccine is prepared using autologous or allogeneic tumor cells. These cellular vaccines have been shown to be most effective when the tumor cells are transduced to express GM-CSF. GM-CSF has been shown to be a potent activator of antigen presentation for tumor vaccination (Dranoff *et al.* (1993) *Proc. Natl. Acad. Sci. U.S.A.* 90: 3539-43).

The combinations disclosed herein, *e.g.*, LAG-3 blockade, can be used in conjunction with a collection of recombinant proteins and/or peptides expressed in a tumor in order to generate an immune response to these proteins. These proteins are normally viewed by the immune system as self antigens and are therefore tolerant to them. The tumor antigen may also include the protein telomerase, which is required for the synthesis of telomeres of chromosomes and which is expressed in more than 85% of human cancers and in only a limited number of somatic tissues (Kim, N *et al.* (1994) *Science* 266: 2011-2013). (These somatic tissues may be protected from immune attack by various means). Tumor antigen may also be "neo-antigens" expressed in cancer cells because of somatic mutations that alter protein sequence or create fusion proteins between two unrelated sequences (*ie.* bcr-abl in the Philadelphia chromosome), or idiotype from B cell tumors.

Other tumor vaccines may include the proteins from viruses implicated in human cancers such a Human Papilloma Viruses (HPV), Hepatitis Viruses (HBV and HCV), Kaposi's Herpes Sarcoma Virus (KHSV), and Epstein-Barr virus (EBV). Another form of tumor specific antigen which may be used in conjunction with PD-1 blockade is purified heat shock proteins (HSP) isolated from the tumor tissue itself. These heat shock proteins contain fragments of proteins from the tumor cells and these HSPs are highly efficient at delivery to antigen presenting cells for eliciting tumor immunity (Suot, R & Srivastava, P (1995) *Science* 269:1585-1588; Tamura, Y. *et al.* (1997) *Science* 278:117-120).

Dendritic cells (DC) are potent antigen presenting cells that can be used to prime antigen-specific responses. DC's can be produced *ex vivo* and loaded with various protein and peptide antigens as well as tumor cell extracts (Nestle, F. *et al.* (1998) *Nature Medicine* 4: 328-332). DCs may also be transduced by genetic means to express these tumor antigens as well. DCs have also

been fused directly to tumor cells for the purposes of immunization (Kugler, A. *et al.* (2000) *Nature Medicine* 6:332-336). As a method of vaccination, DC immunization may be effectively combined with other agent, *e.g.*, PD-1 blockade, to activate more potent anti-tumor responses.

Exemplary Bispecific T-cell engagers

In one embodiment, a combination described herein includes a bispecific T-cell engager. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a gastrointestinal cancer, a melanoma, or a lung cancer) or a hematologic malignancy (*e.g.*, a lymphoma (*e.g.*, non-Hodgkin's lymphoma) or a leukemia (*e.g.*, an acute lymphoblastic leukemia).

Bi-specific T-cell engagers (BiTE®) are a class of artificial bispecific monoclonal antibodies that can direct a host's immune system, *e.g.*, the T cells' cytotoxic activity, against cancer cells. Bi-specific T-cell engagers can form a link between T cells and tumor cells, which causes T cells to exert cytotoxic activity on tumor cells by producing proteins like perforin and granzymes, independently of the presence of MHC I or co-stimulatory molecules. These proteins enter tumor cells and initiate the cell's apoptosis. This action mimics physiological processes observed during T cell attacks against tumor cells.

In some embodiments, the bi-specific T-cell engager is a fusion protein comprising two single-chain variable fragments (scFvs) of different antibodies. In some embodiments, one of the scFvs binds to T cells, *e.g.*, via the CD3 receptor, and the other to a tumor cell, *e.g.*, via a tumor specific molecule.

In some embodiments, the bi-specific T-cell engager is a bispecific antibody molecule of NKG2A and CD138, or a bispecific antibody molecule of CD3 and TCR. In some embodiments, the bispecific T-cell engager is a bispecific antibody molecule that binds to CD3 and a tumor antigen (*e.g.*, EGFR, PSCA, PSMA, EpCAM, HER2 among others).

In some embodiments, the bi-specific T-cell engager is blinatumomab (CAS Registry Number: 853426-35-4). Blinatumomab is also known as MT103. Blinatumomab specifically targets a CD3 site for T cells and a CD19 site for B cells.

In some embodiments, the bi-specific T-cell engager is MT110. MT110 is a single-chain antibody that targets EpCAM and CD3. MT110 is disclosed, *e.g.*, in Amann *et al.* *J Immunother.* 2009;32(5):452-64.

In some embodiments, the bi-specific T-cell engager targets melanoma-associated chondroitin sulfate proteoglycan (MCSP). In some embodiments, the bi-specific T-cell engager targets CD33. In some embodiments the bi-specific T-cell engager comprises trastuzumab (targeting HER2/neu), cetuximab, or panitumumab (both targeting the EGF receptor), a functional fragment thereof. In some embodiments, the bi-specific T-cell engager targets CD66e and EphA2.

Exemplary GITR agonist

In one embodiment, a combination described herein includes a GITR agonist. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor or a hematologic malignancy. In some embodiments, the cancer is a lung cancer (*e.g.*, a non-small cell lung cancer), a head and neck cancer, or a FoxP3-expressing cancer.

Exemplary GITR agonists include, *e.g.*, GITR fusion proteins and anti-GITR antibodies (*e.g.*, bivalent anti-GITR antibodies), such as, a GITR fusion protein described in U.S. Patent No.: 6,111,090, European Patent No.: 0920505B1, U.S Patent No.: 8,586,023, PCT Publication Nos.: WO 2010/003118 and 2011/090754, or an anti-GITR antibody described, *e.g.*, in U.S. Patent No.: 7,025,962, European Patent No.: 1947183B1, U.S. Patent No.: 7,812,135, U.S. Patent No.: 8,388,967, U.S. Patent No.: 8,591,886, European Patent No.: EP 1866339, PCT Publication No.: WO 2011/028683, U.S. Patent No.: 8,709,424, PCT Publication No.: WO 2013/039954, International Publication No.: WO2013/039954, U.S. Publication No.: US2014/0072566, International Publication No.: WO2015/026684, PCT Publication No.: WO2005/007190, PCT Publication No.: WO 2007/133822, PCT Publication No.: WO2005/055808, PCT Publication No.: WO 99/40196, PCT Publication No.: WO 2001/03720, PCT Publication No.: WO99/20758, U.S. Patent No.: 6,689,607, PCT Publication No.: WO2006/083289, PCT Publication No.: WO 2005/115451, U.S. Patent No.: 7,618,632, PCT Publication No.: WO 2011/051726, International Publication No.: WO2004060319, and International Publication No.: WO2014/012479.

In one embodiment, the GITR agonist is used in combination with a PD-1 inhibitor, *e.g.*, as described in WO2015/026684.

In another embodiment, the GITR agonist is used in combination with a TLR agonist, *e.g.*, as described in WO2004/060319, and International Publication No.: WO2014/012479.

Exemplary PD-1 Inhibitors

PD-1 is a CD28/CTLA-4 family member expressed, *e.g.*, on activated CD4⁺ and CD8⁺ T cells, T_{regs}, and B cells. It negatively regulates effector T cell signaling and function. PD-1 is induced on tumor-infiltrating T cells, and can result in functional exhaustion or dysfunction (Keir *et al.* (2008) *Annu. Rev. Immunol.* 26:677-704; Pardoll *et al.* (2012) *Nat Rev Cancer* 12(4):252-64). PD-1 delivers a coinhibitory signal upon binding to either of its two ligands, Programmed Death-Ligand 1 (PD-L1) or Programmed Death-Ligand 2 (PD-L2). PD-L1 is expressed on a number of cell types, including T cells, natural killer (NK) cells, macrophages, dendritic cells (DCs), B cells, epithelial cells, vascular endothelial cells, as well as many types of tumors. High expression of PD-L1 on murine and human tumors has been linked to poor clinical outcomes in a variety of cancers (Keir *et al.* (2008) *Annu. Rev. Immunol.* 26:677-704; Pardoll *et al.* (2012) *Nat Rev Cancer* 12(4):252-64). PD-L2 is expressed on dendritic cells, macrophages, and some tumors. Blockade of the PD-1 pathway has been pre-clinically and clinically validated for cancer immunotherapy. Both preclinical and clinical studies have demonstrated that anti-PD-1 blockade can restore activity of effector T cells and results in robust anti-tumor response. For example, blockade of PD-1 pathway can restore exhausted/dysfunctional effector T cell function (*e.g.*, proliferation, IFN- γ secretion, or cytolytic function) and/or inhibit T_{reg} cell function (Keir *et al.* (2008) *Annu. Rev. Immunol.* 26:677-704; Pardoll *et al.* (2012) *Nat Rev Cancer* 12(4):252-64). Blockade of the PD-1 pathway can be effected with an antibody, an antigen binding fragment thereof, an immunoadhesin, a fusion protein, or oligopeptide of PD-1, PD-L1 and/or PD-L2.

As used herein, the term “Programmed Death 1” or “PD-1” include isoforms, mammalian, *e.g.*, human PD-1, species homologs of human PD-1, and analogs comprising at least one common epitope with PD-1. The amino acid sequence of PD-1, *e.g.*, human PD-1, is known in the art, *e.g.*, Shinohara T *et al.* (1994) *Genomics* 23(3):704-6; Finger LR, *et al.* *Gene* (1997) 197(1-2):177-87.

In one embodiment, a combination described herein includes a PD-1 inhibitor. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor or a hematologic malignancy. In some embodiments, the cancer is chosen from a thyroid cancer (*e.g.*, an anaplastic thyroid cancer), a renal cancer (*e.g.*, a renal cell carcinoma), a

skin cancer (*e.g.*, a melanoma), a head and neck cancer, a brain cancer (*e.g.*, a glioblastoma), a pancreatic cancer, a nasopharyngeal cancer, a colorectal cancer, a lung cancer (*e.g.*, a non-small cell lung cancer), a breast cancer (*e.g.*, a triple negative breast cancer), an endometrial cancer, a liver cancer (*e.g.*, a hepatocellular carcinoma), a bladder cancer, an ovarian cancer, an MSI-high cancer, a FoxP3-expressing cancer, or a lymphoma.

Exemplary non-limiting combinations and uses of the anti-PD-1 antibody molecules are disclosed in U.S. Patent Application Publication No. 2015/0210769 (USSN 14/604415), entitled “Antibody Molecules to PD-1 and Uses Thereof,” incorporated by reference in its entirety.

In one embodiment, the anti-PD-1 antibody molecule includes at least one or two heavy chain variable domain (optionally including a constant region), at least one or two light chain variable domain (optionally including a constant region), or both, comprising the amino acid sequence of BAP049-Clone-A, BAP049-Clone-B, BAP049-Clone-C, BAP049-Clone-D, or BAP049-Clone-E; or as described in Table 1 of US 2015/0210769, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences. The anti-PD-1 antibody molecule, optionally, comprises a leader sequence from a heavy chain, a light chain, or both, as shown in Table 4 of US 2015/0210769; or a sequence substantially identical thereto.

In yet another embodiment, the anti-PD-1 antibody molecule includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region and/or a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP049-hum01, BAP049-hum02, BAP049-hum03, BAP049-hum04, BAP049-hum05, BAP049-hum06, BAP049-hum07, BAP049-hum08, BAP049-hum09, BAP049-hum10, BAP049-hum11, BAP049-hum12, BAP049-hum13, BAP049-hum14, BAP049-hum15, BAP049-hum16, BAP049-Clone-A, BAP049-Clone-B, BAP049-Clone-C, BAP049-Clone-D, or BAP049-Clone-E; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In yet another embodiment, the anti-PD-1 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in Table 1 of US 2015/0210769, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of

the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

In yet another embodiment, the anti-PD-1 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in Table 1 of US 2015/0210769, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In certain embodiments, the anti-PD-1 antibody molecule includes a substitution in a light chain CDR, *e.g.*, one or more substitutions in a CDR1, CDR2 and/or CDR3 of the light chain. In one embodiment, the anti-PD-1 antibody molecule includes a substitution in the light chain CDR3 at position 102 of the light variable region, *e.g.*, a substitution of a cysteine to tyrosine, or a cysteine to serine residue, at position 102 of the light variable region according to Table 1 (*e.g.*, SEQ ID NO: 16 or 24 for murine or chimeric, unmodified; or any of SEQ ID NOs: 34, 42, 46, 54, 58, 62, 66, 70, 74, or 78 for a modified sequence).

In another embodiment, the anti-PD-1 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 1 of US 2015/0210769, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

In one embodiment, the anti-PD-1 antibody molecule includes:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 33, each disclosed in Table 1 of US 2015/0210769;

(b) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 32, each disclosed in Table 1 of US 2015/0210769;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 224, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 33, each disclosed in Table 1 of US 2015/0210769; or

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 224; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 32, each disclosed in Table 1 of US 2015/0210769.

In the combinations herein below, in another embodiment, the anti-PD-1 antibody molecule comprises (i) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4, or SEQ ID NO: 224; a VHCDR2 amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 5; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and (ii) a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10 or SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 11 or SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 32 or SEQ ID NO: 33, each disclosed in Table 1 of US 2015/0210769.

In other embodiments, the PD-1 inhibitor is an anti-PD-1 antibody chosen from Nivolumab, Pembrolizumab or Pidilizumab.

In some embodiments, the anti-PD-1 antibody is Nivolumab. Alternative names for Nivolumab include MDX- 1106, MDX-1106-04, ONO-4538, or BMS-936558. In some embodiments, the anti-PD- 1 antibody is Nivolumab (CAS Registry Number: 946414-94-4). Nivolumab is a fully human IgG4 monoclonal antibody which specifically blocks PD1. Nivolumab (clone 5C4) and other human monoclonal antibodies that specifically bind to PD1 are disclosed in US 8,008,449 and WO2006/121168. In one embodiment, the inhibitor of

PD-1 is Nivolumab, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, *e.g.*, a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

The heavy and light chain amino acid sequences of Nivolumab are as follows:

Heavy chain

QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWIYDGSKRYIYADSV
 KGRFTISRDN SKNTLFLQMNSLRAEDTAVYYCATNDDYWGQGLVTVSSASTKGPSVFPLAPCS
 RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGK
 TYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV
 VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP
 PSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
 KTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLGLK (SEQ ID
 NO: 298)

Light chain

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASN RATGIPARFSG
 SSGTDFTLTISSLEPEDFAVYYCQQSSNWPRTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSG
 TASVVCLLNNFYFPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKVY
 ACEVTHQGLSPVTKSFNRGEC (SEQ ID NO: 299)

In some embodiments, the anti-PD-1 antibody is Pembrolizumab. Pembrolizumab (also referred to as Lambrolizumab, MK-3475, MK03475, SCH-900475 or KEYTRUDA®; Merck) is a humanized IgG4 monoclonal antibody that binds to PD-1. Pembrolizumab and other humanized anti-PD-1 antibodies are disclosed in Hamid, O. *et al.* (2013) *New England Journal of Medicine* 369 (2): 134–44, US 8,354,509 and WO2009/114335. The heavy and light chain amino acid sequences of Pembrolizumab are as follows:

Heavy chain (SEQ ID NO: 300)

QVQLVQSGVE VKKPGASVKV SCKASGYTFT NYMYWVRQA PGQGLEWMGG 50
 INPSNGGTNF NEKFKNRVTL TTDSSTTTAY MELKSLQFDD TAVYYCARRD 100
 YRFDMGFDYW GQGTITVTVSS ASTKGPSVFP LAPCSRSTSE STAALGCLVK 150
 DYFPEPVTVS WNSGALTSGV HTFPAVLQSS GLYSLSSVVT VPSSSLGKTK 200
 YTCNVDPKPS NTKVDKRVES KYGPPCPPCP APEFLGGPSV FLFPPKPKDT 250
 LMISRTPEVT CVVVDVSQED PEVQFNWYVD GVEVHNAKTK PREEQFNSTY 300
 RVVSVLTVLH QDWLNGKEYK CKVSNKGLPS SIEKTI SKAK GQPREPQVYT 350
 LPPSQEEMTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDSD 400
 DGSFFLYSRL TVDKSRWQEG NVFSCSVMHE ALHNHYTQKS LSLSLGLK 447

Ligh chain (SEQ ID NO: 301)

EIVLTQSPAT LSLSPGERAT LSCRASKGVS TSGYSYLHWY QOKPGQAPRL 50
 LIYLYSYLES GVPARFSGSG SGTDFTLTIS SLEPEDFAVY YCQHSRDLPL 100
 TFGGGTKVEI KRTVAAPSVF IFPPSDEQLK SGTASVVCLL NNFYPREAKV 150
 QWKVDNALQS GNSQESVTEQ DSKDSTYSLS STLTLKADY EKHKVYACEV 200
 THQGLSSPVT KSFNRGEC 218'

In one embodiment, the inhibitor of PD-1 is Pembrolizumab disclosed in, *e.g.*, US 8,354,509 and WO 2009/114335, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, *e.g.*, a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

In some embodiments, the anti-PD-1 antibody is Pidilizumab. Pidilizumab (CT-011; Cure Tech) is a humanized IgG1k monoclonal antibody that binds to PD1. Pidilizumab and other humanized anti-PD-1 monoclonal antibodies are disclosed in WO2009/101611.

Other anti-PD1 antibodies include AMP 514 (Amplimmune), among others, *e.g.*, anti-PD1 antibodies disclosed in US 8,609,089, US 2010028330, and/or US 20120114649.

In some embodiments, the PD-1 inhibitor is an immunoadhesin (*e.g.*, an immunoadhesin comprising an extracellular or PD-1 binding portion of PD-L1 or PD-L2 fused to a constant region (*e.g.*, an Fc region of an immunoglobulin sequence). In some embodiments, the PD-1 inhibitor is AMP-224 (B7-DCIg; Amplimmune; *e.g.*, disclosed in WO2010/027827 and WO2011/066342), is a PD-L2 Fc fusion soluble receptor that blocks the interaction between PD-1 and B7-H1. .

Exemplary PD-L1 or PD-L2 Inhibitors

In one embodiment, a combination described herein includes a PD-L1 or PD-L2 inhibitor. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor or a hematologic malignancy. In some embodiments, the cancer is a thyroid cancer (*e.g.*, an anaplastic thyroid cancer), a lung cancer (*e.g.*, a non-small cell lung cancer), a breast cancer (*e.g.*, a triple negative breast cancer), an endometrial cancer, an MSI-high cancer, or a lymphoma.

Exemplary non-limiting combinations and uses of the anti-PD-L1 antibody molecules are disclosed in U.S. Patent Application Publication No. 2016/0108123 (USSN 14/881,888), entitled "Antibody Molecules to PD-L1 and Uses Thereof," incorporated by reference in its entirety.

In one embodiment, the anti-PD-L1 antibody molecule includes at least one or two heavy chain variable domain (optionally including a constant region), at least one or two light chain variable domain (optionally including a constant region), or both, comprising the amino acid sequence of any of BAP058-hum01, BAP058-hum02, BAP058-hum03, BAP058-hum04, BAP058-hum05, BAP058-hum06, BAP058-hum07, BAP058-hum08, BAP058-hum09, BAP058-hum10, BAP058-hum11, BAP058-hum12, BAP058-hum13, BAP058-hum14, BAP058-hum15, BAP058-hum16, BAP058-hum17, BAP058-Clone-K, BAP058-Clone-L, BAP058-Clone-M, BAP058-Clone-N, or BAP058-Clone-O; or as described in Table 1 of US 2016/0108123, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In yet another embodiment, the anti-PD-L1 antibody molecule includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region and/or a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP058-hum01, BAP058-hum02, BAP058-hum03, BAP058-hum04, BAP058-hum05, BAP058-hum06, BAP058-hum07, BAP058-hum08, BAP058-hum09, BAP058-hum10, BAP058-hum11, BAP058-hum12, BAP058-hum13, BAP058-hum14, BAP058-hum15, BAP058-hum16, BAP058-hum17, BAP058-Clone-K, BAP058-Clone-L, BAP058-Clone-M, BAP058-Clone-N, or BAP058-Clone-O; or as described in Table 1 of US 2016/0108123, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In yet another embodiment, the anti-PD-L1 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in Table 1 of US 2016/0108123, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

In yet another embodiment, the anti-PD-L1 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an

amino acid sequence shown in Table 1 of US 2016/0108123, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In certain embodiments, the anti-PD-L1 antibody molecule includes a substitution in a light chain CDR, *e.g.*, one or more substitutions in a CDR1, CDR2 and/or CDR3 of the light chain.

In another embodiment, the anti-PD-L1 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1 of US 2016/0108123. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

In one embodiment, the anti-PD-L1 antibody molecule includes:

(i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 195; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3, each disclosed in Table 1 of US 2016/0108123; and

(ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 9, a VLCDR2 amino acid sequence of SEQ ID NO: 10, and a VLCDR3 amino acid sequence of SEQ ID NO: 11, each disclosed in Table 1 of US 2016/0108123.

In another embodiment, the anti-PD-L1 antibody molecule includes:

(i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 195; a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3, each disclosed in Table 1 of US 2016/0108123; and

(ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14, each disclosed in Table 1 of US 2016/0108123.

In one embodiment, the anti-PD-L1 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 1. In another embodiment, the anti-PD-L1 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 4. In yet another embodiment, the anti-PD-L1 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 195, each disclosed in Table 1 of US 2016/0108123.

In some embodiments, the PD-L1 inhibitor is an antibody molecule. In some embodiments, the anti-PD-L1 inhibitor is chosen from YW243.55.S70, MPDL3280A, MEDI-4736, MSB-0010718C, or MDX-1105.

In some embodiments, the anti-PD-L1 antibody is MSB0010718C. MSB0010718C (also referred to as A09-246-2; Merck Serono) is a monoclonal antibody that binds to PD-L1. Pembrolizumab and other humanized anti-PD-L1 antibodies are disclosed in WO2013/079174, and having a sequence disclosed herein (or a sequence substantially identical or similar thereto, *e.g.*, a sequence at least 85%, 90%, 95% identical or higher to the sequence specified). The heavy and light chain amino acid sequences of MSB0010718C include at least the following:

Heavy chain (SEQ ID NO: 302) (SEQ ID NO: 24 as disclosed in WO2013/079174)

EVQLLES^{GG}GLVQ^{PGG}SLRLSCAASGFT^{FSS}YIMMWVRQAPGKGLEWVSSIYPSGGITFYADKGRFTISRDN^{SKNT}LYLQMN^{SLRA}EDTAVYYCARIKLGTVTTVDYWGQGT^{LV}TVSS

Light chain (SEQ ID NO: 303) (SEQ ID NO: 25 as disclosed in WO2013/079174)

QSALTQ^{PASV}SGSPGQSITISCTGTSSDVG^{GYNY}VSWYQQHPGKAPKLM^{IYD}VSNRPSG^{VSNRF}SGSKSGNTASLTISGLQAEDEADY^{YC}SSYTSSSTRV^{FGT}GTKVTVL

In one embodiment, the PD-L1 inhibitor is YW243.55.S70. The YW243.55.S70 antibody is an anti-PD-L1 described in WO 2010/077634 (heavy and light chain variable region sequences shown in SEQ ID Nos. 20 and 21, respectively), and having a sequence disclosed therein (or a sequence substantially identical or similar thereto, *e.g.*, a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

In one embodiment, the PD-L1 inhibitor is MDX-1105. MDX-1105, also known as BMS-936559, is an anti-PD-L1 antibody described in WO2007/005874, and having a sequence disclosed therein (or a sequence substantially identical or similar thereto, *e.g.*, a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

In one embodiment, the PD-L1 inhibitor is MDPL3280A (Genentech / Roche). MDPL3280A is a human Fc optimized IgG1 monoclonal antibody that binds to PD-L1. MDPL3280A and other human monoclonal antibodies to PD-L1 are disclosed in U.S. Patent No.: 7,943,743, PCT Publication No. WO 2013/019906, and U.S Publication No.: 20120039906. For example, MDPL3280A can include a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:24, as disclosed in WO 2013/019906, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 21, as disclosed in WO 2013/019906 (or a sequence substantially identical or similar thereto, *e.g.*, a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

In one embodiment, the PD-L1 inhibitor is MEDI-4736 (also known as durvalumab). MEDI-4736 is described in WO 2011/066389 and WO 2015/036499. For example, MEDI-4736 can include a light chain variable region comprising the amino acid sequence of SEQ ID NO: 1, as disclosed in WO 2015/036499, and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:2, as disclosed in WO 2015/036499 (or a sequence substantially identical or similar thereto, *e.g.*, a sequence at least 85%, 90%, 95% identical or higher to the sequence specified).

In other embodiments, the PD-L2 inhibitor is AMP-224. AMP-224 is a PD-L2 Fc fusion soluble receptor that blocks the interaction between PD1 and B7-H1 (B7-DCIg; Amplimmune; *e.g.*, disclosed in WO2010/027827 and WO2011/066342).

Exemplary TIM-3 Inhibitors

In one embodiment, a combination described herein includes a TIM-3 inhibitor. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor or a hematologic malignancy. In some embodiments, the cancer is a lung cancer (*e.g.*, a non-small cell lung cancer), a skin cancer (*e.g.*, a melanoma), or a renal cancer (*e.g.*, a renal cell carcinoma).

In one embodiment, the anti-TIM-3 antibody or fragment thereof is an anti-TIM3 antibody molecule as described in U.S. Patent Application Publication No. 2015/0218274 (USSN 14/610837), entitled "Antibody Molecules to TIM-3 and Uses Thereof," incorporated by reference in its entirety.

In one embodiment, the anti-TIM-3 antibody molecule includes at least one or two heavy chain variable domain (optionally including a constant region), at least one or two light chain variable domain (optionally including a constant region), or both, comprising the amino acid sequence of ABTIM3, ABTIM3-hum01, ABTIM3-hum02, ABTIM3-hum03, ABTIM3-hum04, ABTIM3-hum05, ABTIM3-hum06, ABTIM3-hum07, ABTIM3-hum08, ABTIM3-hum09, ABTIM3-hum10, ABTIM3-hum11, ABTIM3-hum12, ABTIM3-hum13, ABTIM3-hum14, ABTIM3-hum15, ABTIM3-hum16, ABTIM3-hum17, ABTIM3-hum18, ABTIM3-hum19, ABTIM3-hum20, ABTIM3-hum21, ABTIM3-hum22, ABTIM3-hum23; or as described in Tables 1-4 of US 2015/0218274; or encoded by the nucleotide sequence in Tables 1-4; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences. The anti-TIM-3 antibody molecule, optionally, comprises a leader sequence from a heavy chain, a light chain, or both, as shown in US 2015/0218274; or a sequence substantially identical thereto.

In yet another embodiment, the anti-TIM-3 antibody molecule includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region and/or a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of ABTIM3, ABTIM3-hum01, ABTIM3-hum02, ABTIM3-hum03, ABTIM3-hum04, ABTIM3-hum05, ABTIM3-hum06, ABTIM3-hum07, ABTIM3-hum08, ABTIM3-hum09, ABTIM3-hum10, ABTIM3-hum11, ABTIM3-hum12, ABTIM3-hum13, ABTIM3-hum14, ABTIM3-hum15, ABTIM3-hum16, ABTIM3-hum17, ABTIM3-hum18, ABTIM3-hum19, ABTIM3-hum20, ABTIM3-hum21, ABTIM3-hum22, ABTIM3-hum23; or as described in Tables 1-4 of US 2015/0218274; or encoded by the nucleotide sequence in Tables 1-4; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In yet another embodiment, the anti-TIM-3 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in Tables 1-4 of US 2015/0218274, or encoded by a nucleotide sequence shown in Tables 1-4. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Tables 1-4, or encoded by a nucleotide sequence shown in Table 1-4.

In yet another embodiment, the anti-TIM-3 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in Tables 1-4 of US 2015/0218274, or encoded by a nucleotide sequence shown in Tables 1-4. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Tables 1-4, or encoded by a nucleotide sequence shown in Tables 1-4. In certain embodiments, the anti-TIM-3 antibody molecule includes a substitution in a light chain CDR, *e.g.*, one or more substitutions in a CDR1, CDR2 and/or CDR3 of the light chain.

In another embodiment, the anti-TIM-3 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Tables 1-4 of US 2015/0218274, or encoded by a nucleotide sequence shown in Tables 1-4. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Tables 1-4, or encoded by a nucleotide sequence shown in Tables 1-4.

In one embodiment, the anti-TIM-3 antibody molecule includes:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 10; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14, each disclosed in Tables 1-4 of US 2015/0218274;

(b) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 4; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8, each disclosed in Tables 1-4 of US 2015/0218274;

(c) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 25; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a

VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14, each disclosed in Tables 1-4 of US 2015/0218274;

(d) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 24; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8, each disclosed in Tables 1-4 of US 2015/0218274;

(e) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 9; a VHCDR2 amino acid sequence of SEQ ID NO: 31; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 12, a VLCDR2 amino acid sequence of SEQ ID NO: 13, and a VLCDR3 amino acid sequence of SEQ ID NO: 14, each disclosed in Tables 1-4 of US 2015/0218274; or

(f) a VH comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 3; a VHCDR2 amino acid sequence of SEQ ID NO: 30; and a VHCDR3 amino acid sequence of SEQ ID NO: 5; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6, a VLCDR2 amino acid sequence of SEQ ID NO: 7, and a VLCDR3 amino acid sequence of SEQ ID NO: 8, each disclosed in Tables 1-4 of US 2015/0218274.

Exemplary anti-TIM-3 antibodies are disclosed in U.S. Patent No.: 8,552,156, WO 2011/155607, EP 2581113 and U.S Publication No.: 2014/044728.

Exemplary CTLA-4 Inhibitors

In one embodiment, a combination described herein includes a CTLA-4 inhibitor. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor or a hematologic malignancy.

Exemplary anti-CTLA4 antibodies include Tremelimumab (IgG2 monoclonal antibody available from Pfizer, formerly known as ticilimumab, CP-675,206); and Ipilimumab (CTLA-4 antibody, also known as MDX-010, CAS No. 477202-00-9).

In one embodiment, the combination includes an anti-PD-1 antibody molecule, *e.g.*, as described herein, and an anti-CTLA-4 antibody, *e.g.*, ipilimumab. Exemplary doses that can be use include a dose of anti-PD-1 antibody molecule of about 1 to 10 mg/kg, *e.g.*, 3 mg/kg, and a dose of an anti-CTLA-4 antibody, *e.g.*, ipilimumab, of about 3 mg/kg.

Other exemplary anti-CTLA-4 antibodies are disclosed, *e.g.*, in U.S. Pat. No. 5,811,097.

Exemplary IAP Inhibitors

In one embodiment, a combination described herein includes an inhibitor of Inhibitor of Apoptosis Protein (IAP). In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a breast cancer (*e.g.*, a triple negative breast cancer), an ovarian cancer, a lung cancer (*e.g.*, a non-small cell lung cancer), a colorectal cancer, or a pancreatic cancer), *e.g.*, a hematologic malignancy (*e.g.*, a multiple myeloma).

In some embodiments, the IAP inhibitor is (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide (Compound A21) or a compound disclosed in U.S. Patent No. 8,552,003.

In some embodiments, the IAP inhibitor, *e.g.*, (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide (Compound A21) or a compound disclosed in U.S. Patent No. 8,552,003, is administered at a dose of approximately 1800 mg, *e.g.*, once weekly.

Exemplary EGFR Inhibitors

In one embodiment, a combination described herein includes an inhibitor of Epidermal Growth Factor Receptor (EGFR). In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a lung cancer (*e.g.*, a non-small cell lung cancer), a pancreatic cancer, a breast cancer (*e.g.*, a triple negative breast cancer), or a colon cancer).

In some embodiments, the EGFR inhibitor is (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication No. WO 2013/184757.

In some embodiments, the EGFR inhibitor, *e.g.*, (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication No. WO 2013/184757, is administered at a dose of 150-250 mg, *e.g.*, per day. In some embodiments, the EGFR inhibitor, *e.g.*, (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication

No. WO 2013/184757, is administered at a dose of about 150, 200, or 250 mg, or about 150-200 or 200-250 mg.

In some embodiments, the EGFR inhibitor is chosen from one or more of erlotinib, gefitinib, cetuximab, panitumumab, necitumumab, PF-00299804, nimotuzumab, or RO5083945.

Exemplary mTOR Inhibitors

In one embodiment, a combination described herein includes an inhibitor of target of rapamycin (mTOR). In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a prostate cancer, a breast cancer (*e.g.*, a triple negative breast cancer), a brain cancer, a bladder cancer, a pancreatic cancer, a renal cancer, a liver cancer, a lung cancer (*e.g.*, a small cell lung cancer or a non-small cell lung cancer), a respiratory/thoracic cancer, a sarcoma, a bone cancer, an endocrine cancer, an astrocytoma, a cervical cancer, a neurologic cancer, a colorectal cancer, a gastric cancer, or a melanoma), *e.g.*, a hematologic malignancy (*e.g.*, a leukemia (*e.g.*, lymphocytic leukemia), *e.g.*, a lymphoma, or *e.g.*, a multiple myeloma).

In some embodiments, the mTOR inhibitor is dactolisib (Compound A4) or 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydroimidazo[4,5-c]quinolin-2-one (Compound A41), or a compound disclosed in PCT Publication No. WO 2006/122806.

In some embodiments, the mTOR inhibitor is everolimus (also known as AFINITOR®; Compound A36) or a compound disclosed in PCT Publication No. WO 2014/085318.

In some embodiments, the mTOR inhibitor, *e.g.*, everolimus (Compound A36) or a compound disclosed in PCT Publication No. WO 2014/085318, is administered at a dose of about 2.5-20 mg/day. In one embodiment, the TOR inhibitor, *e.g.*, everolimus (Compound A36) or a compound disclosed in PCT Publication No. WO 2014/085318, is administered at a dose of about 2.5, 5, 10, or 20 mg/day, *e.g.*, about 2.5-5, 5-10, or 10-20 mg/day.

In some embodiments, the mTOR inhibitor is chosen from one or more of rapamycin, temsirolimus (TORISEL®), AZD8055, BEZ235, BGT226, XL765, PF-4691502, GDC0980, SF1126, OSI-027, GSK1059615, KU-0063794, WYE-354, Palomid 529 (P529), PF-04691502, or PKI-587. ridaforolimus (formally known as deferolimus, (1R,2R,4S)-4-[(2R)-2-[(1R,9S,12S,15R,16E,18R,19R,21R, 23S,24E,26E,28Z,30S,32S,35R)-1,18-dihydroxy-19,30-

dimethoxy-15,17,21,23, 29,35-hexamethyl-2,3,10,14,20-penta-oxo-11,36-dioxo-4-azatricyclo[30.3.1.0^{4,9}] hexatriaconta-16,24,26,28-tetraen-12-yl]propyl]-2-methoxycyclohexyl dimethylphosphinate, also known as AP23573 and MK8669, and described in PCT Publication No. WO 03/064383); everolimus (AFINITOR® or RAD001); rapamycin (AY22989, SIROLIMUS®); simapimod (CAS Registry Number: 164301-51-3); (5-{2,4-Bis[(3S)-3-methylmorpholin-4-yl]pyrido[2,3-d]pyrimidin-7-yl}-2-methoxyphenyl)methanol (AZD8055); 2-Amino-8-[trans-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-d]pyrimidin-7(8H)-one (PF04691502, CAS Registry Number: 1013101-36-4); N²-[1,4-dioxo-4-[[4-(4-oxo-8-phenyl-4H-1-benzopyran-2-yl)morpholinium-4-yl]methoxy]butyl]-L-arginylglycyl-L- α -aspartyl-L-serine inner salt (SEQ ID NO: 304) (SF1126, CAS Registry Number: 936487-67-1), or XL765 (SAR245409).

Other exemplary mTOR Inhibitors include, but are not limited to, temsirolimus; ridaforolimus (1*R*,2*R*,4*S*)-4-[(2*R*)-2 [(1*R*,9*S*,12*S*,15*R*,16*E*,18*R*,19*R*,21*R*,23*S*,24*E*,26*E*,28*Z*,30*S*,32*S*,35*R*)-1,18-dihydroxy-19,30-dimethoxy-15,17,21,23, 29,35-hexamethyl-2,3,10,14,20-penta-oxo-11,36-dioxo-4-azatricyclo[30.3.1.0^{4,9}] hexatriaconta-16,24,26,28-tetraen-12-yl]propyl]-2-methoxycyclohexyl dimethylphosphinate, also known as AP23573 and MK8669; everolimus (RAD001); rapamycin (AY22989); simapimod; (5-{2,4-bis[(3*S*)-3-methylmorpholin-4-yl]pyrido[2,3-*d*]pyrimidin-7-yl}-2-methoxyphenyl)methanol (AZD8055); 2-amino-8-[*trans*-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PF04691502); and N²-[1,4-dioxo-4-[[4-(4-oxo-8-phenyl-4*H*-1-benzopyran-2-yl)morpholinium-4-yl]methoxy]butyl]-L-arginylglycyl-L- α -aspartyl-L-serine- (SEQ ID NO: 304), inner salt (SF1126); and XL765.

Exemplary IL-15 Agonists

In one embodiment, a combination described herein includes an interleukin-15 (IL-15) agonist. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a refractory solid tumor), (*e.g.*, a melanoma (*e.g.*, a metastatic or advanced melanoma), a kidney cancer (*e.g.*, a renal cell cancer), a non-small cell lung cancer, a squamous cell head and neck cancer, or a bladder cancer (*e.g.*, a non-muscle invasive bladder cancer)), *e.g.*, a hematologic malignancy (*e.g.*, a leukemia, *e.g.*, an acute myelogenous leukemia (*e.g.*, a refractory or relapsed acute myelogenous leukemia), *e.g.*, a lymphoma, *e.g.*, a non-

Hodgkin lymphoma (*e.g.*, a relapsed/refractory indolent B cell non-Hodgkin lymphoma), *e.g.*, or a multiple myeloma (*e.g.*, a relapsed or refractory multiple myeloma)).

IL-15, secreted by mononuclear phagocytes (and some other cell types) following viral infection, regulates T and natural killer cell activation and proliferation. This cytokine induces activation of transcription activators STAT3, STAT5, and STAT6 via JAK kinase signal transduction pathways in mast cells, T cells, and dendritic epidermal T cells. IL-15 and interleukin-2 (IL-2) are structurally similar and share many biological activities; both may bind to common hematopoietin receptor subunits, negatively regulating each other's activity. CD8+ memory T cell number can be regulated by a balance between IL-15 and IL-2.

In some embodiments, the IL-15 agonist is a recombinant human IL-15 (rhIL-15), *e.g.*, CYP0150 (Cytune). CYP0150 is a recombinant protein consisting of a human IL-15 linked to the Sushi+ domain of the human alpha chain receptor (transpresentation).

CYP0150 is disclosed, *e.g.*, in PCT Publication No. WO 2007/046006. CYP0150 has the amino acid sequence of :

MAPRRARGCRTLGLPALLLLLLLRPPATRGDYKDDDDKIEGRITCPPPMSVEHADIWVK
 SYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPALVHQRPA
 P SGGSGGGGSGGGSGGGGSLQNWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTA
 MKCFLELQVISLESGDASIHTVENLIILANNSLSSNGNVTESGCKECELEEKNIKEFLQ
 SFVHIVQMFINTS (SEQ ID NO: 305) (disclosed as SEQ ID NO: 60 in WO 2007/046006) or
 MDSKGSSQKAGSRLLLLLVVSNLLLCQGVVSTTRDYKDDDDKIEGRNWNVVISDLKKIE
 DLIQSMHIDATLYTESDVHPSCKVTAMKCFLELQVISLESGDASIHTVENLIILANNSL
 SSNGNVTESGCKECELEEKNIKEFLQSFVHIVQMFINTSSGGGSGGGGSGGGGSGGGGS
 GGGSLQITCPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNV
 AHWTTPSLKCIRDPALVHQRPA (SEQ ID NO: 306) (disclosed as SEQ ID NO: 62 in WO
 2007/046006).

In some embodiments, the IL-15 agonist is ALT-803 (Altor BioScience). ALT-803 is an IL-15N72D:IL-15R α Su/Fc soluble complex, produced from a high-yield recombinant mammalian cell line that co-expresses IL-15N72D and IL-15R α Su/Fc fusion protein. The IL-15 mutant (N72D) has enhanced IL-15 biological activity (Zhu *et al.* 2009, *J Immunol.* 183:3598). The IL-15N72D mutant and the soluble domain of IL-15R α can form stable heterodimeric complexes in solution and this complex exhibits increased biological activity (approximately 25-

fold more active) compared to the non-complexed IL-15. ALT-803 is disclosed, *e.g.*, in PCT Publication No. WO 2012/040323 and U.S. Patent No. 8,507,222.

In some embodiments, the IL-15 agonist is hetIL-15 (Admune). HetIL-15 is a heterodimeric human IL-15 (IL-15/sIL-15Ra). HetIL-15 is disclosed, *e.g.*, in PCT Publication Nos. WO 2009/002562 and WO 2014/066527.

Exemplary CD40 Agonists

In one embodiment, the combination includes a CD40 agonist. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a lung cancer, an esophageal carcinoma, a melanoma, or a renal cell carcinoma), *e.g.*, a hematologic malignancy (*e.g.*, a leukemia (*e.g.*, a chronic lymphocytic leukemia (CLL)), *e.g.*, a lymphoma (*e.g.*, a non-Hodgkin's lymphoma), *e.g.*, or a multiple myeloma).

In one embodiment, the CD40 agonist is ADC-1013 (Alligator/BioInvent). ADC-1013 is a fully human IgG agonistic monoclonal antibody against human CD40. CD40, an integral membrane protein found on the surface of B lymphocytes, is a member of the tumor necrosis factor receptor superfamily and is highly expressed in a number of cancers such as B-cell malignancies. CD40 agonists, *e.g.*, anti-CD40 antibodies, are able to substitute effectively for T cell helper activity (Ridge, J. *et al.* (1998) *Nature* 393: 474-478).

ADC-1013 is disclosed, *e.g.*, in PCT Publication No. WO 2015/091853. ADC-1013 clones include, *e.g.*, 1136/1137, 1132/1133, 1148/1149, 1140/1135, 1134/1135, 1107/1108, 1142/1135, 1146/1147, and 1150/1151.

The heavy chain variable region of 1132/1133 has the amino acid sequence of:
 EVQLLES~~GG~~GLVQPGGSLRLS~~CA~~ASGFTFSSYAMSWVRQAPGKGLEWVSGIGSYGGGT
 YYADSVKGRFTISRDN~~SK~~N~~T~~LYLQMNSLRAEDTAVYYCARYVNF~~GM~~DYWGQGT~~LV~~TV
 SS (SEQ ID NO: 307) (disclosed as SEQ ID NO: 65 in WO 2015/091853). The light chain
 variable region of 1132/1133 has the amino acid sequence of:
 DIQMTQSPSSLSASV~~GD~~RVTITCRASQSISSYL~~NW~~YQQKPGKAPKLLIYAASSLQSGVPSR
 FSGSGSGTDF~~LT~~LISS~~LQ~~PEDFATYYCQQYGRNPPTFGQGTKLEIK (SEQ ID NO: 308)
 (disclosed as SEQ ID NO: 66 in WO 2015/091853). The heavy chain CDR1 of 1132/1133 has
 the amino acid sequence of: GFTFSSYA (SEQ ID NO: 309) (disclosed as SEQ ID NO: 13 in
 WO 2015/091853). The heavy chain CDR2 of 1132/1133 has the amino acid sequence of:

IGSYGGGT (SEQ ID NO: 310) (disclosed as SEQ ID NO: 14 in WO 2015/091853). The heavy chain CDR3 of 1132/1133 has the amino acid sequence of: ARYVNFGMDY (SEQ ID NO: 311) (disclosed as SEQ ID NO: 15 in WO 2015/091853). The light chain CDR1 of 1132/1133 has the amino acid sequence of: QSISSY (SEQ ID NO: 312) (disclosed as SEQ ID NO: 16 in WO 2015/091853). The light chain CDR2 of 1132/1133 has the amino acid sequence of: AAS (SEQ ID NO: 313) (disclosed as SEQ ID NO: 17 in WO 2015/091853). The light chain CDR3 of 1132/1133 has the amino acid sequence of: QQYGRNPPT (SEQ ID NO: 314) (disclosed as SEQ ID NO: 18 in WO 2015/091853).

The heavy chain variable region of 1107/1108 has the amino acid sequence of: EVQLLES GGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTY YADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARRVWGF DYWGQGLVTVSS (SEQ ID NO: 315) (disclosed as SEQ ID NO: 79 in WO 2015/091853). The light chain variable region of 1107/1108 has the amino acid sequence of: DIQMTQSPSSLSASVGD RVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSR FSGSGSGT DFTLTIS SLQPEDFATYYCQQYGVYPFTFGQGTKLEIK (SEQ ID NO: 316) (disclosed as SEQ ID NO: 80 in WO 2015/091853). The heavy chain CDR1 of 1107/1108 has the amino acid sequence of: GFTFSSYA (SEQ ID NO: 309) (disclosed as SEQ ID NO: 55 in WO 2015/091853). The heavy chain CDR2 of 1107/1108 has the amino acid sequence of: ISGSGGST (SEQ ID NO: 317) (disclosed as SEQ ID NO: 56 in WO 2015/091853). The heavy chain CDR3 of 1107/1108 has the amino acid sequence of: ARRVWGF DY (SEQ ID NO: 318) (disclosed as SEQ ID NO: 57 in WO 2015/091853). The light chain CDR1 of 1107/1108 has the amino acid sequence of: QSISSY (SEQ ID NO: 312) (disclosed as SEQ ID NO: 58 in WO 2015/091853). The light chain CDR2 of 1107/1108 has the amino acid sequence of: AAS (SEQ ID NO: 313) (disclosed as SEQ ID NO: 59 in WO 2015/091853). The light chain CDR3 of 1107/1108 has the amino acid sequence of: QQYGVYPFT (SEQ ID NO: 319) (disclosed as SEQ ID NO: 60 in WO 2015/091853).

In some embodiments, the CD40 agonist is ISF35. ISF35 is a chimeric CD154. ISF is disclosed in PCT Publication Nos. WO 2003/099340 and WO 2008/070743.

In some embodiments, the CD40 agonist is dacetuzumab. Dacetuzumab is also known as SGN-40 or huS2C6. Dacetuzumab is a humanized monoclonal antibody that targets CD40.

Dacetuzumab is disclosed, *e.g.*, in Advani *et al. J Clin Oncol.* 2009; 27(26):4371-7; and Khubchandani *et al. Curr Opin Investig Drugs.* 2009; 10(6):579-87.

In some embodiments, the CD40 agonist is lucatumumab (CAS Registry Number: 903512-50-5). Lucatumumab is also known as CHIR-12.12 or HCD-122. Lucatumumab binds to and inhibits CD40, thereby inhibiting CD40 ligand-induced cell proliferation and triggering cell lysis via antibody-dependent cellular cytotoxicity (ADCC) in cells overexpressing CD40. Lucatumumab is disclosed, *e.g.*, in Tai *et al. Cancer Res.* 2005;65(13):5898-906.

Anti-CD40 antibodies are able to substitute effectively for T cell helper activity (Ridge, J. *et al.* (1998) *Nature* 393: 474-478) and can be used in conjunction with PD-1 antibodies (Ito, N. *et al.* (2000) *Immunobiology* 201 (5) 527-40).

Exemplary OX40 Agonists

In one embodiment, a combination described herein includes an OX40 agonist. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a breast cancer, a melanoma, a head and neck cancer, or a prostate cancer), *e.g.*, a hematologic malignancy (*e.g.*, a lymphoma (*e.g.*, a B-cell lymphoma)).

OX40, also known as CD134, is a cell surface glycoprotein and member of the tumor necrosis factor (TNF) receptor superfamily, is expressed on T-lymphocytes and provides a co-stimulatory signal for the proliferation and survival of activated T-cells. OX40 activation can induce proliferation of effector T-lymphocytes, which promotes an immune response against the tumor cells that express tumor-associated antigens (TAAs).

In some embodiments, the OX40 agonist is chosen from mAb 106-222, humanized 106-222 (Hu106), mAb 119-122, or humanized 119-122 (Hu119).

MAb 106-222, humanized 106-222 (Hu106), mAb 119-122, and humanized 119-122 (Hu119) are disclosed, *e.g.*, in PCT Publication No. WO 2012/027328 and U.S. Patent No. 9,006,399. The amino acid sequence of the heavy chain variable region of mAb 106-222 is disclosed as SEQ ID NO: 4 in WO 2012/027328. The amino acid sequence of the light chain variable region of mAb 106-222 is disclosed as SEQ ID NO: 10 in WO 2012/027328. The amino acid sequence of the heavy chain variable region of humanized 106-222 (Hu106) is disclosed as SEQ ID NO: 5 in WO 2012/027328. The amino acid sequence of the light chain variable region of humanized 106-222 (Hu106) is disclosed as SEQ ID NO: 11 in WO

2012/027328. The amino acid sequence of the heavy chain variable region of mAb 119-122 is disclosed as SEQ ID NO: 16 in WO 2012/027328. The amino acid sequence of the light chain variable region of mAb 119-122 is disclosed as SEQ ID NO: 22 in WO 2012/027328. The amino acid sequence of the heavy chain variable region of humanized 119-122 (Hu119) is disclosed as SEQ ID NO: 17 in WO 2012/027328. The amino acid sequence of the light chain variable region of humanized 119-122 (Hu119) is disclosed as SEQ ID NO: 23 in WO 2012/027328.

In some embodiments, the OX40 agonist is a humanized monoclonal antibody disclosed in U.S. Patent No. 7,959,925 and PCT Publication No. WO 2006/121810.

In some embodiments, the OX40 agonist is chosen from MEDI6469, MEDI0562, or MEDI6383. MEDI6469 is a murine monoclonal antibody against OX40. MEDI0562 is a humanized monoclonal antibody against OX40. MEDI6383 is a monoclonal antibody against OX40.

In some embodiments, the OX40 agonist, *e.g.*, MEDI6469, is administered intravenously at a dose of approximately 0.4 mg/kg, *e.g.*, every other day.

Other exemplary anti-OX-40 antibodies are disclosed, *e.g.*, in Weinberg, A. *et al.* (2000) *Immunol* 164: 2160-2169).

Exemplary CD27 Agonists

In one embodiment, a combination described herein includes a CD27 agonist. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a melanoma, a renal cell carcinoma, a hormone-refractory prostate adenocarcinoma, an ovarian cancer, a breast cancer, a colorectal adenocarcinoma, or a non-small cell lung cancer), *e.g.*, a hematologic malignancy (*e.g.*, a lymphoma (*e.g.*, a Hodgkin's lymphoma, a Burkett's lymphoma, a mantle cell lymphoma, a primary lymphoma of the central nervous system, or a marginal zone B-cell lymphoma), or a leukemia (*e.g.*, a chronic lymphocytic leukemia (CLL)).

In one embodiment, the CD27 agonist is Varlilumab (CAS Registry Number: 1393344-72-3). Varlilumab is also known as CDX-1127 (Celldex) or 1F5. Varlilumab is a fully human monoclonal antibody (mAb) that targets CD27, molecule in the activation pathway of lymphocytes. CDX-1127 is an agonist anti-CD27 mAb that can activate human T cells in the

context of T cell receptor stimulation and therefore mediate anti-tumor effects. CDX-1127 can also provide direct therapeutic effects against tumors with CD27 expression.

Varlilumab is disclosed, *e.g.*, in Vitale *et al.*, *Clin Cancer Res.* 2012;18(14):3812-21, WO 2008/051424, and US 8,481,029.

In one embodiment, the CD27 agonist is BION-1402 (BioNovion). BION-1402 is also known as hCD27.15. BION-1402 is an anti-human CD27 monoclonal antibody. BION-1402 can stimulate the proliferation and/or survival of CD27+ cells. BION-1402 can activate human CD27 more effectively than its ligand CD70, which results in a significantly increased effect on proliferation of CD8+ and CD4+ T-cells.

BION-1402 is disclosed, *e.g.*, as hCD27.15 in WO 2012/004367. This antibody is produced by hybridoma hCD27.15, which was deposited with the ATCC in on June 2, 2010 under number PTA-11008. The heavy chain variable region of hCD27.15 has the amino acid sequence of:

EVRLQQSGADLVKPGASVKLSCASGFIKATYMHWVRQRPEQGLEWIGRIDPANGE KY
DPKFQVKAITADTSSSTAYLQLNSLTSDDTAVYYCARYAWYFDVWGAGTTVTVSSAKT
TPPXVYPXXPGS (SEQ ID NO: 320) (disclosed as SEQ ID NO: 3 in WO 2012/004367). The

light chain variable region of hCD27.15 has the amino acid sequence of:

DIQMTQSPASLSASVGDVTITCRASENIYSFLAWYHQKQGRSPQLLVYHAKTLAEGVP
SRFSGSGSGTQFSLKINSLQAEDFGSYQCQHYGSPFTFGAGTKLEVKRADAAPTVSIFP
PSSEELSL (SEQ ID NO: 321) (disclosed as SEQ ID NO: 4 in WO 2012/004367). The heavy

chain CDR1 of hCD27.15 has the amino acid sequence of: GFIKATYMH (SEQ ID NO: 322) (disclosed as SEQ ID NO: 5 in WO 2012/004367). The heavy chain CDR2 of hCD27.15 has the

amino acid sequence of: RIDPANGETKYDPKFQV (SEQ ID NO: 323) (disclosed as SEQ ID

NO: 6 in WO 2012/004367). The heavy chain CDR3 of hCD27.15 has the amino acid sequence of: YAWYFDV (SEQ ID NO: 324) (disclosed as SEQ ID NO: 7 in WO 2012/004367). The

light chain CDR1 of hCD27.15 has the amino acid sequence of: RASENIYSFLA (SEQ ID NO: 325) (disclosed as SEQ ID NO: 8 in WO 2012/004367). The light chain CDR2 of hCD27.15 has

the amino acid sequence of: HAKTLAE (SEQ ID NO: 326) (disclosed as SEQ ID NO: 9 in WO 2012/004367). The light chain CDR3 of hCD27.15 has the amino acid sequence of:

QHYYGSPLT (SEQ ID NO: 327) (disclosed as SEQ ID NO: 10 in WO 2012/004367).

Exemplary LAG-3 Inhibitors

The immune system has the capability of recognizing and eliminating tumor cells; however, tumors can use multiple strategies to evade immunity. Blockade of immune checkpoints is one of the approaches to activating or reactivating therapeutic antitumor immunity. Lymphocyte Activation Gene-3 (LAG-3) has been described as an inhibitory receptor in the immunological synapse (Chen and Flies (2013) *Nat Rev Immunol.* 13(4):227-42). Thus, blocking of LAG-3 can lead to enhancement of antitumor immunity.

Several cell types express LAG-3. For example, LAG-3 is expressed on activated CD4⁺ and CD8⁺ T cells, T_{reg} cells, natural killer (NK) cells, and plasmacytoid dendritic cells (DCs). LAG-3 is expressed in tumor-infiltrating lymphocytes, *e.g.*, infiltrating lymphocytes in head and neck squamous cell carcinoma (HNSCC). LAG-3 is expressed on highly suppressive induced and natural Tregs. For example, highly suppressive FoxP3⁺ nTregs and FoxP3⁻ iTregs are LAG-3 positive in melanoma and colorectal cancer (Camisaschi *et al.* (2010) *J. Immunol.* 184(11):6545-6551; Scurr *et al.* (2014) *Mucosal. Immunol.* 7(2):428-439).

LAG-3 negatively regulates T cell signaling and functions. Ligands for LAG-3 includes, *e.g.*, MHC Class II and L-SECTin. Anti-LSECTin has been shown to inhibit B16 melanoma cell growth (Xu *et al.* (2014) *Cancer Res.* 74(13):3418-3428). Blockade of LAG-3 can restore activities of effector cells, diminish suppressor activity of T_{regs}, and/or enhance anti-PD-1 antitumor activity.

LAG-3 is typically though not exclusively co-expressed on PD-1⁺ cells and single blockade can restore *in vitro* activities of the cells. The degree of CD8⁺ T cell exhaustion, *e.g.*, as shown by the percentages of dual IFN- γ /TNF- α producers, correlates with the number of inhibitory receptors expressed (Blackburn *et al.* (2009) *Nat. Immunol.* 10(1): 29-37). High PD-1/LAG-3 expression correlates with T cell infiltration in melanoma. Co-blockade of LAG-3 with anti-PD-1 or PD-L1 can result in tumor suppressive activities in preclinical models. For example, anti-LAG-3 and anti-PD-1 blockade show efficacy in Sa1N fibrosarcoma and MC38 colon carcinoma models (Woo *et al.* (2012) *Cancer Res.* 72(4):917-27).

LAG-3 blockade is also efficacious in a lymphocytic choriomeningitis virus (LCMV) model. For example, PD-L1 plus LAG-3 blockade during chronic LCMV infection enhances antiviral CD8⁺ T cell responses (Blackburn *et al.* (2009) *Nat. Immunol.* 10(1): 29-37).

The term “Lymphocyte Activation Gene-3” or “LAG-3” include all isoforms, mammalian, *e.g.*, human LAG-3, species homologs of human LAG-3, and analogs comprising at least one common epitope with LAG-3. The amino acid and nucleotide sequences of LAG-3, *e.g.*, human LAG-3, is known in the art, *e.g.*, Triebel *et al.* (1990) *J. Exp. Med.* 171:1393-1405.

In certain embodiments, the combinations described herein include a LAG-3 inhibitor, *e.g.*, an anti-LAG-3 antibody molecule (*e.g.*, humanized antibody molecules) as described herein. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor or a hematologic malignancy. In some embodiments, the cancer is a lung cancer (*e.g.*, a non-small cell lung cancer), a skin cancer (*e.g.*, a melanoma), or a renal cancer (*e.g.*, a renal cell carcinoma).

In some embodiments, the LAG-3 antibody molecule (*e.g.*, an isolated or recombinant antibody molecule) has one or more of the following properties:

(i) binds to LAG-3, *e.g.*, human LAG-3, with high affinity, *e.g.*, with an affinity constant of at least about 10^7 M^{-1} , typically about 10^8 M^{-1} , and more typically, about 10^9 M^{-1} to 10^{10} M^{-1} or stronger;

(ii) binds to LAG-3, *e.g.*, a LAG-3-CHO transfectant, with a K_D of less than: 5 nM, 4 nM, 3 nM, 2 nM, 1 nM, *e.g.*, 1 to 3 nM (*e.g.*, about 1.92 nM or about 2.3 nM);

(iii) does not substantially bind to CD4;

(iv) inhibits binding of LAG-3 to a major histocompatibility (MHC) class II molecule, *e.g.*, shows an IC_{50} of about 1 to 20 nM, 5 to 15 nM, *e.g.*, 5.5 nM;

(v) binds to the D1 domain of LAG-3 (*e.g.*, human LAG-3), *e.g.*, binds to the D1 domain, but does not bind to the extra loop region of the D1 domain;

(vi) modulates (*e.g.*, stimulates, enhances, or restores) an immune response, *e.g.*, an antigen-specific T cell response or anti-tumor response;

(vii) binds specifically to an epitope on LAG-3, *e.g.*, the same or similar epitope as the epitope recognized by murine monoclonal antibody BAP050 or chimeric antibody BAP050-chi;

(viii) binds to a different epitope on LAG-3 than the one recognized by antibody BMS-986016;

(ix) shows the same or similar binding affinity or specificity, or both, as any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11,

BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J.

(x) shows the same or similar binding affinity or specificity, or both, as an antibody molecule (*e.g.*, an heavy chain variable region and light chain variable region) described in Table 1;

(xi) shows the same or similar binding affinity or specificity, or both, as an antibody molecule (*e.g.*, an heavy chain variable region and light chain variable region) having an amino acid sequence shown in Table 1;

(xii) shows the same or similar binding affinity or specificity, or both, as an antibody molecule (*e.g.*, an heavy chain variable region and light chain variable region) encoded by the nucleotide sequence shown in Table 1;

(xiii) inhibits, *e.g.*, competitively inhibits, the binding of a second antibody molecule to LAG-3, wherein the second antibody molecule is an antibody molecule described herein, *e.g.*, an antibody molecule chosen from, *e.g.*, any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J;

(xiv) binds the same or an overlapping epitope with a second antibody molecule to LAG-3, wherein the second antibody molecule is an antibody molecule described herein, *e.g.*, an

antibody molecule chosen from, *e.g.*, any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J;

(xv) competes for binding, and/or binds the same epitope, with a second antibody molecule to LAG-3, *e.g.*, as measured by a Biacore method, a FACS method, or both, wherein the second antibody molecule is an antibody molecule described herein, *e.g.*, an antibody molecule chosen from, *e.g.*, any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J;

(xvi) has one or more biological properties of an antibody molecule described herein, *e.g.*, an antibody molecule chosen from, *e.g.*, any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-

hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J;

(xvii) has one or more pharmacokinetic properties of an antibody molecule described herein, *e.g.*, an antibody molecule chosen from, *e.g.*, any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or

(xviii) inhibits one or more activities of LAG-3, *e.g.*, results in one or more of: an increase in antigen-dependent stimulation of CD4⁺ T lymphocytes; an increase in T cell proliferation; an increase in expression of an activation antigen, *e.g.*, CD25; an increase in expression of a cytokine, *e.g.*, interferon-gamma (IFN- γ), interleukin-2 (IL-2), or interleukin-4 (IL-4); an increase in expression of a chemokine, *e.g.*, CCL3, CCL4, or CCL5; a decrease in the suppressor activity of T_{reg} cells; an increase in T cell homeostasis; an increase in tumor infiltrating lymphocytes; or a decrease in immune evasion by the cancerous cells.

As used herein, “huBAP050(Ser)” refers to a humanized BAP050 antibody molecule, *e.g.*, any of the humanized BAP050 antibody molecule described herein, *e.g.*, as described in Table 1, that has a Cys to Ser substitution at position 84 of the heavy chain framework region 3 (VHFW3). In some embodiments, the huBAP050(Ser) antibody molecule is chosen from BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser.

In some embodiments, the anti-LAG-3 antibody molecule binds to LAG-3 with high affinity, *e.g.*, with a dissociation equilibrium constant (K_D) that is about the same, or at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80% or 90% higher or lower than the K_D of a murine or chimeric anti-LAG-3 antibody molecule, *e.g.*, a murine or chimeric anti-LAG-3 antibody molecule described herein. In one embodiment, the anti-LAG-3 antibody molecule binds to LAG-3, *e.g.*, a LAG-3-CHO transfectant, with a K_D of less than: 5 nM, 4 nM, 3 nM, 2nM, *e.g.*, 1 to 3 nM (*e.g.*, about 1.92 nM or about 2.3 nM).

In some embodiments, the expression level of the anti-LAG-3 antibody molecule is about the same, higher or lower, *e.g.*, at least about 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10-fold higher or lower, than the expression level of a murine or chimeric antibody molecule, *e.g.*, a murine or chimeric anti-LAG-3 antibody molecule described herein. In some embodiments, the antibody molecule is expressed in CHO cells.

In some embodiments, the anti-LAG-3 antibody molecule reduces one or more LAG-3-associated activities with an IC_{50} (concentration at 50% inhibition) that is about the same, higher or lower, *e.g.*, at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80% or 90% higher or lower, than the IC_{50} of a murine or chimeric anti-LAG-3 antibody molecule, *e.g.*, a murine or chimeric anti-LAG-3 antibody molecule described herein. In some embodiments, the LAG-3-associated activity is the binding of an MHC class II molecule to LAG-3. In some embodiments, the LAG-3-associated activity is the binding of L-SECTin to LAG-3. In one embodiment, the anti-LAG-3 antibody has an IC_{50} of about 1 to 20 nM, 5 to 15 nM, 5.5 nM (*e.g.*, detected by inhibition of MHC class II or L-SECTin binding).

In some embodiments, the anti-LAG-3 antibody molecule has about the same or improved stability, *e.g.*, at least about 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10-fold more stable *in vivo* or *in vitro*, than a murine or chimeric anti-LAG-3 antibody molecule, *e.g.*, a murine or chimeric anti-LAG-3 antibody molecule described herein.

In one embodiment, the anti-LAG-3 antibody molecule is a humanized antibody molecule and has a risk score based on T cell epitope analysis of 800 to 1200, 850 to 1150, 900 to 1100, 950 to 1050, or a risk score as described herein.

In another embodiment, the anti-LAG-3 antibody molecule comprises at least one antigen-binding region, *e.g.*, a variable region or an antigen-binding fragment thereof, from an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-

hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In yet another embodiment, the anti-LAG-3 antibody molecule comprises at least one, two, three or four variable regions from an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences. In one embodiment, the antibody molecule includes a substitution (*e.g.*, a Cys to Ser substitution at position 84) in the heavy chain framework region 3 (VHFW3) (*e.g.*, as shown in Tables 1 and 2).

In yet another embodiment, the anti-LAG-3 antibody molecule comprises at least one or two heavy chain variable regions from an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-

hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In yet another embodiment, the anti-LAG-3 antibody molecule comprises at least one or two light chain variable regions from an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In yet another embodiment, the anti-LAG-3 antibody molecule includes a heavy chain constant region for an IgG4, *e.g.*, a human IgG4. In one embodiment, the human IgG4 includes a substitution at position 228 (*e.g.*, a Ser to Pro substitution). In still another embodiment, the anti-LAG-3 antibody molecule includes a heavy chain constant region for an IgG1, *e.g.*, a human IgG1. In one embodiment, the human IgG1 includes a substitution at position 297 (*e.g.*, an Asn to Ala substitution). In one embodiment, the human IgG1 includes a substitution at position 265,

a substitution at position 329, or both (*e.g.*, an Asp to Ala substitution at position 265 and/or a Pro to Ala substitution at position 329). In one embodiment, the human IgG1 includes a substitution at position 234, a substitution at position 235, or both (*e.g.*, a Leu to Ala substitution at position 234 and/or a Leu to Ala substitution at position 235). In one embodiment, the heavy chain constant region comprises an amino sequence set forth in Table 3, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto.

In yet another embodiment, the anti-LAG-3 antibody molecule includes a kappa light chain constant region, *e.g.*, a human kappa light chain constant region. In one embodiment, the light chain constant region comprises an amino sequence set forth in Table 3, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto.

In another embodiment, the anti-LAG-3 antibody molecule includes a heavy chain constant region for an IgG4, *e.g.*, a human IgG4, and a kappa light chain constant region, *e.g.*, a human kappa light chain constant region, *e.g.*, a heavy and light chain constant region comprising an amino sequence set forth in Table 3, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto. In one embodiment, the constant region is a mutated IgG4, *e.g.*, a mutated human IgG4 (*e.g.*, has a mutation at position 228 (*e.g.*, a S228P mutation)). In yet another embodiment, the anti-LAG-3 antibody molecule includes a heavy chain constant region for an IgG1, *e.g.*, a human IgG1, and a kappa light chain constant region, *e.g.*, a human kappa light chain constant region, *e.g.*, a heavy and light chain constant region comprising an amino sequence set forth in Table 3, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto. In one embodiment, the human IgG1 includes a substitution at position 297 (*e.g.*, an Asn to Ala substitution). In one embodiment, the human IgG1 includes a substitution at position 265, a substitution at position 329, or both (*e.g.*, an Asp to Ala substitution at position 265 and/or a Pro to Ala substitution at position 329). In one embodiment, the human IgG1 includes a substitution at position 234, a substitution at position 235, or both (*e.g.*, a Leu to Ala substitution at position 234 and/or a Leu to Ala substitution at position 235).

In another embodiment, the anti-LAG-3 antibody molecule includes a heavy chain variable domain and a constant region, a light chain variable domain and a constant region, or

both, comprising the amino acid sequence of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences. The anti-LAG-3 antibody molecule, optionally, comprises a leader sequence from a heavy chain, a light chain, or both, as shown in Table 4; or a sequence substantially identical thereto.

In yet another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but

not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs shown in Table 1.

In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

In yet another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, or three complementarity determining regions (CDRs) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs shown in Table 1.

In yet another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

In another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid shown in Table 1, or encoded by a nucleotide sequence shown in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs shown in Table 1.

In another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in Table 1, or encoded by a nucleotide sequence shown in Table 1.

In one embodiment, the anti-LAG-3 antibody molecule includes all six CDRs from an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1, or closely related CDRs, *e.g.*, CDRs which are identical or which have at least one amino acid alteration, but not

more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs shown in Table 1. In one embodiment, the anti-LAG-3 antibody molecule may include any CDR described herein.

In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three CDRs according to Kabat (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in Table 1) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Kabat shown in Table 1.

In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three CDRs according to Kabat (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in Table 1) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-

hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Kabat shown in Table 1.

In yet another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, three, four, five, or six CDRs according to Kabat (*e.g.*, at least one, two, three, four, five, or six CDRs according to the Kabat definition as set out in Table 1) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to at least one, two, three, four, five, or six CDRs according to Kabat *et al.* shown in Table 1. In one embodiment, the anti-LAG-3 antibody molecule may include any CDR described herein.

In yet another embodiment, the anti-LAG-3 antibody molecule includes all six CDRs according to Kabat (*e.g.*, all six CDRs according to the Kabat definition as set out in Table 1) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody

chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to Kabat *et al.* shown in Table 1. In one embodiment, the anti-LAG-3 antibody molecule may include any CDR described herein.

In another embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three hypervariable loops (*e.g.*, at least one, two, or three hypervariable loops according to the Chothia definition as set out in Table 1) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, according to Chothia (*e.g.*, at least one, two, or three hypervariable loops according to the Chothia definition as set out in Table 1); or encoded by the nucleotide sequence in Table 1; or a

sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three hypervariable loops according to Chothia shown in Table 1.

In another embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three hypervariable loops according to Chothia (*e.g.*, at least one, two, or three CDRs according to the Chothia definition as set out in Table 1) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J,; or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three hypervariable loops according to Chothia shown in Table 1.

In yet another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, three, four, five, or six hypervariable loops (*e.g.*, at least one, two, three, four, five, or six hypervariable loops according to the Chothia definition as set out in Table 1) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20,

huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1; or encoded by the nucleotide sequence in Table 1; or at least the amino acids from those hypervariable loops that contact LAG-3. In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two, three, four, five, or six Chothia hypervariable loops of Table 1.

In one embodiment, the anti-LAG-3 antibody molecule includes all six hypervariable loops (*e.g.*, all six hypervariable loops according to the Chothia definition as set out in Table 1) of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, or closely related hypervariable loops, *e.g.*, hypervariable loops which are identical or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six hypervariable loops shown in Table 1. In one embodiment, the anti-LAG-3 antibody molecule may include any hypervariable loop described herein.

In still another embodiment, the anti-LAG-3 antibody molecule includes at least one, two, or three hypervariable loops that have the same canonical structures as the corresponding hypervariable loop of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10,

BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, *e.g.*, the same canonical structures as at least loop 1 and/or loop 2 of the heavy and/or light chain variable domains of an antibody described herein. *See, e.g.*, Chothia *et al.*, (1992) *J. Mol. Biol.* 227:799-817; Tomlinson *et al.*, (1992) *J. Mol. Biol.* 227:776-798 for descriptions of hypervariable loop canonical structures. These structures can be determined by inspection of the tables described in these references.

In certain embodiments, the anti-LAG-3 antibody molecule includes a combination of CDRs or hypervariable loops defined according to the Kabat *et al.* and Chothia *et al.*

In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three CDRs or hypervariable loops from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, according to the Kabat and Chothia definition (*e.g.*, at least one, two, or three CDRs or hypervariable loops according to the Kabat and Chothia definition as set out in Table 1); or encoded by the nucleotide sequence in Table 1; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*,

substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs or hypervariable loops according to Kabat and/or Chothia shown in Table 1.

For example, the anti-LAG-3 antibody molecule can include VH CDR1 according to Kabat *et al.* or VH hypervariable loop 1 according to Chothia *et al.*, or a combination thereof, *e.g.*, as shown in Table 1. In one embodiment, the combination of Kabat and Chothia CDR of VH CDR1 comprises the amino acid sequence GFTLTNYGMN (SEQ ID NO: 286), or an amino acid sequence substantially identical thereto (*e.g.*, having at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions)). The anti-LAG-3 antibody molecule can further include, *e.g.*, VH CDRs 2-3 according to Kabat *et al.* and VL CDRs 1-3 according to Kabat *et al.*, *e.g.*, as shown in Table 1. Accordingly, in some embodiments, framework regions are defined based on a combination of CDRs defined according to Kabat *et al.* and hypervariable loops defined according to Chothia *et al.* For example, the anti-LAG-3 antibody molecule can include VH FR1 defined based on VH hypervariable loop 1 according to Chothia *et al.* and VH FR2 defined based on VH CDRs 1-2 according to Kabat *et al.*, *e.g.*, as shown in Table 1. The anti-LAG-3 antibody molecule can further include, *e.g.*, VH FRs 3-4 defined based on VH CDRs 2-3 according to Kabat *et al.* and VL FRs 1-4 defined based on VL CDRs 1-3 according to Kabat *et al.*

The anti-LAG-3 antibody molecule can contain any combination of CDRs or hypervariable loops according to the Kabat and Chothia definitions. In one embodiment, the anti-LAG-3 antibody molecule includes at least one, two or three CDRs from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-

I, or BAP050-Clone-J, according to the Kabat and Chothia definition (*e.g.*, at least one, two, or three CDRs according to the Kabat and Chothia definition as set out in Table 1).

In an embodiment, *e.g.*, an embodiment comprising a variable region, CDR (*e.g.*, CDR or Kabat CDR), or other sequence referred to herein, *e.g.*, in Table 1, the antibody molecule is a monospecific antibody molecule, a bispecific antibody molecule, or is an antibody molecule that comprises an antigen binding fragment of an antibody, *e.g.*, a half antibody or antigen binding fragment of a half antibody. In certain embodiments, the antibody molecule is a bispecific antibody molecule having a first binding specificity for LAG-3 and a second binding specificity for PD-1, TIM-3, CEACAM (*e.g.*, CEACAM-1 and/or CEACAM-5), PD-L1 or PD-L2.

In one embodiment, the anti-LAG-3 antibody includes:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15;

(b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15; or

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12.

In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region

(VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15;

In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12;

In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15; or

In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12.

In one embodiment, the antibody molecule is a humanized antibody molecule. In another embodiment, the antibody molecule is a monospecific antibody molecule. In yet another embodiment, the antibody molecule is a bispecific antibody molecule.

In one embodiment, the anti-LAG-3 antibody includes:

(i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and

(ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12.

In another embodiment, the anti-LAG-3 antibody molecule includes:

(i) a heavy chain variable region (VH) including a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and

(ii) a light chain variable region (VL) including a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15.

In one embodiment, the anti-LAG-3 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 1. In another embodiment, the anti-LAG-3 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 4. In yet another embodiment, the anti-LAG-3 antibody molecule comprises the VHCDR1 amino acid sequence of SEQ ID NO: 286.

In one embodiment, the light or the heavy chain variable framework (*e.g.*, the region encompassing at least FR1, FR2, FR3, and optionally FR4) of the anti-LAG-3 antibody molecule can be chosen from: (a) a light or heavy chain variable framework including at least 80%, 85%, 87%, 90%, 92%, 93%, 95%, 97%, 98%, or preferably 100% of the amino acid residues from a human light or heavy chain variable framework, *e.g.*, a light or heavy chain variable framework residue from a human mature antibody, a human germline sequence, or a human consensus sequence; (b) a light or heavy chain variable framework including from 20% to 80%, 40% to 60%, 60% to 90%, or 70% to 95% of the amino acid residues from a human light or heavy chain variable framework, *e.g.*, a light or heavy chain variable framework residue from a human mature antibody, a human germline sequence, or a human consensus sequence; (c) a non-human framework (*e.g.*, a rodent framework); or (d) a non-human framework that has been modified, *e.g.*, to remove antigenic or cytotoxic determinants, *e.g.*, deimmunized, or partially humanized. In one embodiment, the light or heavy chain variable framework region (particularly FR1, FR2 and/or FR3) includes a light or heavy chain variable framework sequence at least 70, 75, 80, 85, 87, 88, 90, 92, 94, 95, 96, 97, 98, 99% identical or identical to the frameworks of a VL or VH segment of a human germline gene.

In certain embodiments, the anti-LAG-3 antibody molecule comprises a heavy chain variable domain having at least one, two, three, four, five, six, seven, ten, fifteen, twenty or more changes, *e.g.*, amino acid substitutions or deletions, from an amino acid sequence of BAP050-chi-HC, *e.g.*, the amino acid sequence of the FR region in the entire variable region, *e.g.*, shown in Figures. 9A-9B, or SEQ ID NO: 20 or 22. In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain variable domain having one or more of: E at position 1, V at position 2, A at position 9, V at position 11, A at position 16, S at position 17, L at position 18, R

at position 19, V at position 20, V or G at position 24, I at position 37, A or S at position 40, R or T at position 41, S at position 42, Q or R at position 43, R at position 44, E at position 46, I or L at position 48, V at position 68, V or T at position 69, I at position 70, A at position 72, D at position 73, K at position 74, V or I at position 76, Y at position 80, W at position 83, C or S at position 84, S or T at position 85, A at position 88, E or S at position 89, V or M at position 93, or Y at position 95 of amino acid sequence of BAP050-chi-HC, *e.g.*, the amino acid sequence of the FR in the entire variable region, *e.g.*, shown in Figures. 9A-9B, or SEQ ID NO: 20 or 22. In one embodiment, the antibody molecule includes a substitution (*e.g.*, a Cys to Ser substitution at position 84) in the heavy chain framework region 3 (VHFW3) (*e.g.*, as shown in Table 2).

Alternatively, or in combination with the heavy chain substitutions of BAP050-chi-HC described herein, the anti-LAG-3 antibody molecule comprises a light chain variable domain having at least one, two, three, four, five, six, seven, ten, fifteen, twenty or more amino acid changes, *e.g.*, amino acid substitutions or deletions, from an amino acid sequence of BAP050-chi-LC, *e.g.*, the amino acid sequence shown in Figures. 10A-10B, or SEQ ID NO: 24 or 26. In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain variable domain having one or more of: E or A at position 1, V at position 3, L at position 4, S at position 7, P at position 8, A or L or D at position 9, T or F at position 10, Q at position 11, P at position 12, V or L at position 13, T at position 14, V or P at position 15, K at position 16, Q or E at position 17, T or P or K at position 18, A at position 19, S at position 20, L at position 21, T at position 22, L at position 37, G at position 41, K or Q at position 42, A or S at position 43, P at position 44, R or Q at position 45, L at position 46, I at position 58, P or D at position 60, Y at position 67, E at position 70, F at position 71, T at position 72, F at position 73, N at position 76, S or R at position 77, I at position 78, Q at position 79, A or S or P at position 80, D at position 81, A or F at position 83, Y or V at position 85, or F at position 87 of the amino acid sequence of BAP050-chi-LC, *e.g.*, the amino acid sequence shown in Figures. 10A-10B, or SEQ ID NO: 24 or 26.

In other embodiments, the anti-LAG-3 antibody molecule includes one, two, three, or four heavy chain framework regions (*e.g.*, a VHFW amino acid or nucleotide sequence shown in Table 2, or encoded by the nucleotide sequence shown in Table 2), or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved

substitutions). In one embodiment, the antibody molecule includes a substitution (*e.g.*, a Cys to Ser substitution at position 84) in the heavy chain framework region 3 (VHFW3) (*e.g.*, as shown in Table 2).

In yet other embodiments, the anti-LAG-3 antibody molecule includes one, two, three, or four light chain framework regions (*e.g.*, a VLFW amino acid sequence shown in Table 2, or encoded by the nucleotide sequence shown in Table 2), or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In other embodiments, the anti-LAG-3 antibody molecule includes one, two, three, or four heavy chain framework regions (*e.g.*, a VHFW amino acid sequence shown in Table 2, or encoded by the nucleotide sequence shown in Table 2), or a sequence substantially identical thereto; and one, two, three, or four light chain framework regions (*e.g.*, a VLFW amino acid sequence shown in Table 2, or encoded by the nucleotide sequence shown in Table 2), or a sequence substantially identical thereto.

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework region 1 (VHFW1) of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum14, BAP050-hum15, BAP050-hum18, BAP050-hum19, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, BAP050-Clone-F, or BAP050-Clone-G (*e.g.*, SEQ ID NO: 187). In some embodiments, the antibody molecule comprises the heavy chain framework region 1 (VHFW1) of BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, or BAP050-hum20, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone J (*e.g.*, SEQ ID NO: 190). In some embodiments, the antibody molecule comprises the heavy chain framework region 1 (VHFW1) of BAP050-hum16 (*e.g.*, SEQ ID NO: 194). In some embodiments, the antibody molecule comprises the heavy chain framework region 1 (VHFW1) of BAP050-hum17 (*e.g.*, SEQ ID NO: 196). In other embodiments, the antibody molecule comprises a heavy chain framework region 1 (VHFW1) having a sequence, or encoded by a

sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework region 2 (VHFW2) of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum13, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum13-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, BAP050-Clone-F, BAP050-Clone-G, or BAP050-Clone-J (*e.g.*, SEQ ID NO: 198). In some embodiments, the antibody molecule comprises the heavy chain framework region 2 (VHFW2) of BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum20, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum20-Ser, or BAP050-Clone-I (*e.g.*, SEQ ID NO: 202). In some embodiments, the antibody molecule comprises the heavy chain framework region 2 (VHFW2) of BAP050-hum14, BAP050-hum15, BAP050-hum14-Ser, or BAP050-hum15-Ser (*e.g.*, SEQ ID NO: 206). In some embodiments, the antibody molecule comprises the heavy chain framework region 2 (VHFW2) of BAP050-hum16 (*e.g.*, SEQ ID NO: 208). In other embodiments, the antibody molecule comprises a heavy chain framework region 2 (VHFW2) having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework region 3 (VHFW3) of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum18, BAP050-hum19, or BAP050-hum20 (*e.g.*, SEQ ID NO: 210). In some embodiments, the antibody molecule comprises the heavy chain framework region 3 (VHFW3) of BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-

hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, BAP050-hum20-Ser, BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J (*e.g.*, SEQ ID NO: 212). In some embodiments, the antibody molecule comprises the heavy chain framework region 3 (VHFW3) of BAP050-hum16 (*e.g.*, SEQ ID NO: 217). In some embodiments, the antibody molecule comprises the heavy chain framework region 3 (VHFW3) of BAP050-hum17 (*e.g.*, SEQ ID NO: 219). In other embodiments, the antibody molecule comprises a heavy chain framework region 3 (VHFW3) having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework region 4 (VHFW4) of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, or BAP050-hum20, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, BAP050-hum20-Ser, BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J (*e.g.*, SEQ ID NO: 221). In other embodiments, the antibody molecule comprises a heavy chain framework region 4 (VHFW4) having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the light chain framework region 1 (VLFW1) of BAP050-hum01, BAP050-hum02, BAP050-hum04, BAP050-hum07, BAP050-hum09, BAP050-hum11, BAP050-hum13, BAP050-hum17, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum04-Ser, BAP050-hum07-Ser, BAP050-hum09-Ser, BAP050-hum11-Ser, BAP050-hum13-Ser, BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J (*e.g.*, SEQ ID NO: 226). In some embodiments,

the antibody molecule comprises the light chain framework region 1 (VLFW1) of BAP050-hum03, BAP050-hum10, BAP050-hum14, BAP050-hum03-Ser, BAP050-hum10-Ser, or BAP050-hum14-Ser (*e.g.*, SEQ ID NO: 230). In some embodiments, the antibody molecule comprises the light chain framework region 1 (VLFW1) of BAP050-hum05 or BAP050-hum05-Ser (*e.g.*, SEQ ID NO: 232). In some embodiments, the antibody molecule comprises the light chain framework region 1 (VLFW1) of BAP050-hum06, BAP050-hum20, BAP050-hum06-Ser, or BAP050-hum20-Ser (*e.g.*, SEQ ID NO: 234). In some embodiments, the antibody molecule comprises the light chain framework region 1 (VLFW1) of BAP050-hum08, BAP050-hum12, BAP050-hum15, BAP050-hum16, BAP050-hum19, BAP050-hum08-Ser, BAP050-hum12-Ser, BAP050-hum15-Ser, or BAP050-hum19-Ser (*e.g.*, SEQ ID NO: 236). In some embodiments, the antibody molecule comprises the light chain framework region 1 (VLFW1) of BAP050-hum18 or BAP050-hum18-Ser (*e.g.*, SEQ ID NO: 238). In other embodiments, the antibody molecule comprises a light chain framework region 1 (VLFW1) having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the light chain framework region 2 (VLFW2) of BAP050-hum01, BAP050-hum02, BAP050-hum05, BAP050-hum09, BAP050-hum13, BAP050-hum17, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum05-Ser, BAP050-hum09-Ser, BAP050-hum13-Ser, BAP050-hum17-Ser, BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J (*e.g.*, SEQ ID NO: 240). In some embodiments, the antibody molecule comprises the light chain framework region 2 (VLFW2) of BAP050-hum03, BAP050-hum06, BAP050-hum08, BAP050-hum10, BAP050-hum12, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum18, BAP050-hum19, BAP050-hum20, BAP050-hum03-Ser, BAP050-hum06-Ser, BAP050-hum08-Ser, BAP050-hum10-Ser, BAP050-hum12-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, or BAP050-hum20-Ser (*e.g.*, SEQ ID NO: 244). In some embodiments, the antibody molecule comprises the light chain framework region 2 (VLFW2) of BAP050-hum04 or BAP050-hum04-Ser (*e.g.*, SEQ ID NO: 246). In some embodiments, the antibody molecule comprises the light chain framework region 2 (VLFW2) of BAP050-hum07, BAP050-hum11, BAP050-hum07-Ser, or BAP050-hum11-Ser (*e.g.*, SEQ ID NO: 248). In other

embodiments, the antibody molecule comprises a light chain framework region 2 (VLFW2) having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the light chain framework region 3 (VLFW3) of BAP050-hum01, BAP050-hum03, BAP050-hum05, BAP050-hum10, BAP050-hum14, BAP050-hum19, BAP050-hum01-Ser, BAP050-hum03-Ser, BAP050-hum05-Ser, BAP050-hum10-Ser, BAP050-hum14-Ser, BAP050-hum19-Ser, or BAP050-Clone-F (*e.g.*, SEQ ID NO: 252). In some embodiments, the antibody molecule comprises the light chain framework region 3 (VLFW3) of BAP050-hum02, BAP050-hum09, BAP050-hum13, BAP050-hum02-Ser, BAP050-hum09-Ser, BAP050-hum13-Ser, BAP050-Clone-G, BAP050-Clone-H, or BAP050-Clone-J (*e.g.*, SEQ ID NO: 255). In some embodiments, the antibody molecule comprises the light chain framework region 3 (VLFW3) of BAP050-hum04 or BAP050-hum04-Ser (*e.g.*, SEQ ID NO: 259). In some embodiments, the antibody molecule comprises the light chain framework region 3 (VLFW3) of BAP050-hum06, BAP050-hum07, BAP050-hum11, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum11-Ser, or BAP050-Clone-I (*e.g.*, SEQ ID NO: 261). In some embodiments, the antibody molecule comprises the light chain framework region 3 (VLFW3) of BAP050-hum08, BAP050-hum12, BAP050-hum15, BAP050-hum16, BAP050-hum18, BAP050-hum08-Ser, BAP050-hum12-Ser, BAP050-hum15-Ser, or BAP050-hum18-Ser (*e.g.*, SEQ ID NO: 265). In some embodiments, the antibody molecule comprises the light chain framework region 3 (VLFW3) of BAP050-hum17 (*e.g.*, SEQ ID NO: 267). In some embodiments, the antibody molecule comprises the light chain framework region 3 (VLFW3) of BAP050-hum20 or BAP050-hum20-Ser (*e.g.*, SEQ ID NO: 269). In other embodiments, the antibody molecule comprises a light chain framework region 3 (VHLW3) having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the light chain framework region 4 (VLFW4) of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14,

BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, BAP050-hum20-Ser, BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J (*e.g.*, SEQ ID NO: 271). In other embodiments, the antibody molecule comprises a light chain framework region 4 (VLFW4) having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum18, BAP050-hum19 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)). In some embodiments, the antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum20 (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 210 (VHFW3)). In some embodiments, the antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum13 (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)). In some embodiments, the antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum14 or BAP050-hum15 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 206 (VHFW2), and SEQ ID NO: 210 (VHFW3)). In some embodiments, the antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum16 (*e.g.*, SEQ ID NO: 194 (VHFW1), SEQ ID NO: 208 (VHFW2), and SEQ ID NO: 217 (VHFW3)). In some embodiments, the antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum17 (*e.g.*, SEQ ID NO: 196 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 219 (VHFW3)). In some embodiments, the antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, BAP050-Clone-F,

or BAP050-Clone-G (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)). In some embodiments, the antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum20-Ser, BAP050-Clone-H, or BAP050-Clone I (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 212 (VHFW3)). In some embodiments, the antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum13-Ser or BAP050-Clone-J (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)). In some embodiments, the antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum14-Ser or BAP050-hum15-Ser (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 206 (VHFW2), and SEQ ID NO: 212 (VHFW3)). In some embodiments, the antibody molecule further comprises the heavy chain framework region 4 of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum05-Ser, BAP050-hum09-Ser, BAP050-hum11-Ser, BAP050-hum13-Ser, BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J (*e.g.*, SEQ ID NO: 221). In other embodiments, the antibody molecule comprises a heavy chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum01, BAP050-hum01-Ser, or BAP050-Clone-F (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 240 (VLFW2), and SEQ ID NO: 252 (VLFW3)). In some embodiments, the antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum02, BAP050-hum09, BAP050-hum13, BAP050-hum02-Ser, BAP050-hum09-Ser, BAP050-hum13-Ser, BAP050-Clone-G, BAP050-Clone-H, or BAP050-Clone-J (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 240 (VLFW2), and SEQ ID NO: 255 (VLFW3)). In some embodiments, the antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum03, BAP050-hum10, BAP050-hum14, BAP050-hum03-Ser, BAP050-hum10-Ser,

or BAP050-hum14-Ser (*e.g.*, SEQ ID NO: 230 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 252 (VLFW3)). In some embodiments, the antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum04 or BAP050-hum04-Ser (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 246 (VLFW2), and SEQ ID NO: 259 (VLFW3)). In some embodiments, the antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum05 or BAP050-hum05-Ser (*e.g.*, SEQ ID NO: 232 (VLFW1), SEQ ID NO: 240 (VLFW2), and SEQ ID NO: 252 (VLFW3)). In some embodiments, the antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum06 or BAP050-hum06-Ser (*e.g.*, SEQ ID NO: 234 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 261 (VLFW3)). In some embodiments, the antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum07, BAP050-hum11, BAP050-hum07-Ser, BAP050-hum11-Ser, or BAP050-Clone-I (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 248 (VLFW2), and SEQ ID NO: 261 (VLFW3)). In some embodiments, the antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum08, BAP050-hum12, BAP050-hum15, BAP050-hum16, BAP050-hum08-Ser, BAP050-hum12-Ser, or BAP050-hum15-Ser (*e.g.*, SEQ ID NO: 236 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 265 (VLFW3)). In some embodiments, the antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum17 (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 240 (VLFW2), and SEQ ID NO: 267 (VLFW3)). In some embodiments, the antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum18 or BAP050-hum18-Ser (*e.g.*, SEQ ID NO: 238 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 265 (VLFW3)). In some embodiments, the antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum19 or BAP050-hum19-Ser (*e.g.*, SEQ ID NO: 236 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 252 (VLFW3)). In some embodiments, the antibody molecule comprises the light chain framework regions 1-3 of BAP050-hum20 or BAP050-hum20-Ser (*e.g.*, SEQ ID NO: 234 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 269 (VLFW3)). In some embodiments, the antibody molecule further comprises the heavy chain framework region 4 of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19,

BAP050-hum20, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum03-Ser, BAP050-hum04-Ser, BAP050-hum05-Ser, BAP050-hum06-Ser, BAP050-hum07-Ser, BAP050-hum08-Ser, BAP050-hum09-Ser, BAP050-hum10-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser, BAP050-hum14-Ser, BAP050-hum15-Ser, BAP050-hum18-Ser, BAP050-hum19-Ser, BAP050-hum20-Ser, BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J (*e.g.*, SEQ ID NO: 271). In other embodiments, the antibody molecule comprises a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum01 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum01-Ser or BAP050-Clone-F (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum01, BAP050-hum01-Ser, or BAP050-Clone-F (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 240 (VLFW2), and SEQ ID NO: 252 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum02 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum02-Ser or BAP050-Clone-G (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum02, BAP050-hum02-Ser, or BAP050-Clone-G (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 240 (VLFW2), and SEQ ID NO: 255 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%,

90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum03 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum03-Ser (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum03 (*e.g.*, SEQ ID NO: 230 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 252 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum04 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum04-Ser (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum04 (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 246 (VLFW2), and SEQ ID NO: 259 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum05 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)) or BAP050-hum05-Ser (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum05 or BAP050-hum05-Ser (*e.g.*, SEQ ID NO: 232 (VLFW1), SEQ ID NO: 240 (VLFW2), and SEQ ID NO: 252 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework

region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum06 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum06-Ser (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum06 (*e.g.*, SEQ ID NO: 234 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 261 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum07 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum07-Ser (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum07 (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 248 (VLFW2), and SEQ ID NO: 261 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum08 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum08-Ser (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum08 (*e.g.*,

SEQ ID NO: 236 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 265 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum09 (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or BAP050-hum09-Ser or BAP050-Clone-H (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum09, BAP050-hum09-Ser, or BAP050-Clone-H (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 240 (VLFW2), and SEQ ID NO: 255 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum10 (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum10-Ser (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum10 (*e.g.*, SEQ ID NO: 230 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 252 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum11 (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or BAP050-hum11-Ser, or BAP050-Clone-I (*e.g.*,

SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum11, BAP050-hum11-Ser, or BAP050-Clone-I (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 248 (VLFW2), and SEQ ID NO: 261 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum12 (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 210 (VHFW3)) or BAP050-hum12-Ser (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum12 or BAP050-hum12-Ser (*e.g.*, SEQ ID NO: 236 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 265 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum13 (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum13-Ser or BAP050-Clone-J (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum13, BAP050-hum13-Ser, or BAP050-Clone-J (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 240 (VLFW2), and SEQ ID NO: 255 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum14 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 206 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum14-Ser (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 206 (VHFW2), and SEQ ID NO: 210 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum14 (*e.g.*, SEQ ID NO: 230 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 252 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum15 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 206 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum15-Ser (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 206 (VHFW2), and SEQ ID NO: 210 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum15 (*e.g.*, SEQ ID NO: 236 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 265 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum16 (*e.g.*, SEQ ID NO: 194 (VHFW1), SEQ ID NO: 208 (VHFW2), and SEQ ID NO: 217 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum16 (*e.g.*, SEQ ID NO: 236 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 265 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum17 (*e.g.*, SEQ ID NO: 196 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 219 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum17 (*e.g.*, SEQ ID NO: 226 (VLFW1), SEQ ID NO: 240 (VLFW2), and SEQ ID NO: 267 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum18 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum18-Ser (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum18 (*e.g.*, SEQ ID NO: 238 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 265 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum19 (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or the heavy chain framework regions 1-3 of BAP050-hum18-Ser (*e.g.*, SEQ ID NO: 187 (VHFW1), SEQ ID NO: 198 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum19 (*e.g.*, SEQ ID NO: 236 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 252 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises the heavy chain framework regions 1-3 of BAP050-hum20 (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 210 (VHFW3)), or BAP050-hum20-Ser (*e.g.*, SEQ ID NO: 190 (VHFW1), SEQ ID NO: 202 (VHFW2), and SEQ ID NO: 212 (VHFW3)); and the light chain framework regions 1-3 of BAP050-hum20 (*e.g.*, SEQ ID NO: 234 (VLFW1), SEQ ID NO: 244 (VLFW2), and SEQ ID NO: 269 (VLFW3)). In other embodiments, the antibody molecule comprises a heavy chain and a light chain framework region having a sequence, or encoded by a sequence, substantially identical (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical) to any of the aforesaid sequences, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions).

In some embodiments, the anti-LAG-3 antibody molecule comprises a heavy chain framework region having a combination of framework regions FW1, FW2 and FW3 as shown in Figures. 4 or 6. In other embodiment, antibody molecule comprises a light chain framework region having a combination of framework regions FW1, FW2 and FW3 as shown in Figures. 4 or 6. In yet other embodiments, the antibody molecule comprises a heavy chain framework region having a combination of framework regions FW1, FW2 and FW3 as shown in Figures. 4 or 6, and a light chain framework region having a combination of framework regions FW1, FW2 and FW3 as shown in Figures. 4 or 6.

In one embodiment, the heavy or light chain variable domain, or both, of the anti-LAG-3 antibody molecule includes an amino acid sequence, which is substantially identical to an amino acid disclosed herein, *e.g.*, at least 70%, 75%, 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical to a variable region of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum05-Ser, BAP050-hum09-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J; or as described in Table 1, or encoded by the nucleotide sequence in Table 1; or which

differs at least 1 or 5 residues, but less than 40, 30, 20, or 10 residues, from a variable region of an antibody described herein.

In one embodiment, the heavy or light chain variable region, or both, of the anti-LAG-3 antibody molecule includes an amino acid sequence encoded by a nucleic acid sequence described herein or a nucleic acid that hybridizes to a nucleic acid sequence described herein (*e.g.*, a specific nucleic acid sequence or a nucleic acid sequence that encodes an amino acid sequence described herein, *e.g.*, as shown in Tables 1 and 2) or its complement, *e.g.*, under low stringency, medium stringency, or high stringency, or other hybridization condition described herein.

In another embodiment, the anti-LAG-3 antibody molecule comprises at least one, two, three, or four antigen-binding regions, *e.g.*, variable regions, having an amino acid sequence as set forth in Table 1, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the sequences shown in Table 1). In another embodiment, the anti-LAG-3 antibody molecule includes a VH and/or VL domain encoded by a nucleic acid having a nucleotide sequence as set forth in Table 1, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 70%, 75%, 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 3, 6, 15, 30, or 45 nucleotides from the sequences shown in Table 1).

In yet another embodiment, the anti-LAG-3 antibody molecule comprises at least one, two, or three CDRs from a heavy chain variable region having an amino acid sequence as set forth in Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions). In yet another embodiment, the anti-LAG-3 antibody molecule comprises at least one, two, or three CDRs from a light chain variable region having an amino acid sequence as set forth in Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions). In yet another embodiment, the anti-LAG-3 antibody molecule comprises at least one, two, three, four, five or six CDRs from heavy and light chain variable regions having an amino acid sequence as set forth in Table 1), or a sequence substantially homologous thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical

thereto, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions). In one embodiment, at least one, two, three, four, five or six CDR is defined according to Kabat, *e.g.*, as shown in Table 1. In another embodiment, at least one, two, three, four, five or six CDR is defined according to Chothia, *e.g.*, as shown in Table 1.

In one embodiment, the anti-LAG-3 antibody molecule comprises at least one, two, or three CDRs and/or hypervariable loops from a heavy chain variable region having an amino acid sequence of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum05-Ser, BAP050-hum09-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, as summarized in Table 1, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions). In another embodiment, the anti-LAG-3 antibody molecule comprises at least one, two, or three CDRs from a light chain variable region having an amino acid sequence of an antibody described herein, *e.g.*, an antibody chosen from any of BAP050-hum01, BAP050-hum02, BAP050-hum03, BAP050-hum04, BAP050-hum05, BAP050-hum06, BAP050-hum07, BAP050-hum08, BAP050-hum09, BAP050-hum10, BAP050-hum11, BAP050-hum12, BAP050-hum13, BAP050-hum14, BAP050-hum15, BAP050-hum16, BAP050-hum17, BAP050-hum18, BAP050-hum19, BAP050-hum20, huBAP050(Ser) (*e.g.*, BAP050-hum01-Ser, BAP050-hum02-Ser, BAP050-hum05-Ser, BAP050-hum09-Ser, BAP050-hum11-Ser, BAP050-hum12-Ser, BAP050-hum13-Ser), BAP050-Clone-F, BAP050-Clone-G, BAP050-Clone-H, BAP050-Clone-I, or BAP050-Clone-J, as summarized in Table 1, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions or deletions, *e.g.*, conserved substitutions). In one embodiment, the anti-LAG-3 antibody molecule comprises all six CDRs and/or hypervariable loops described herein, *e.g.*, described in Table 1.

In one embodiment, the anti-LAG-3 antibody molecule has a variable region that is identical in sequence, or which differs by 1, 2, 3, or 4 amino acids from a variable region described herein (*e.g.*, an FR region disclosed herein).

In one embodiment, the anti-LAG-3 antibody molecule is a full antibody or fragment thereof (*e.g.*, a Fab, F(ab')₂, Fv, or a single chain Fv fragment (scFv)). In certain embodiments, the anti-LAG-3 antibody molecule is a monoclonal antibody or an antibody with single specificity. The anti-LAG-3 antibody molecule can also be a humanized, chimeric, camelid, shark, or *in vitro*-generated antibody molecules. In one embodiment, the anti-LAG-3 antibody molecule thereof is a humanized antibody molecule. The heavy and light chains of the anti-LAG-3 antibody molecule can be full-length (*e.g.*, an antibody can include at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains) or can include an antigen-binding fragment (*e.g.*, a Fab, F(ab')₂, Fv, a single chain Fv fragment, a single domain antibody, a diabody (dAb), a bivalent or bispecific antibody or fragment thereof, a single domain variant thereof, or a camelid antibody).

In yet other embodiments, the anti-LAG-3 antibody molecule has a heavy chain constant region (Fc) chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE; particularly, chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4, more particularly, the heavy chain constant region of IgG1, IgG2 or IgG4 (*e.g.*, human IgG1, IgG2 or IgG4). In one embodiment, the heavy chain constant region is human IgG1 or human IgG4. In another embodiment, the anti-LAG-3 antibody molecule has a light chain constant region chosen from, *e.g.*, the light chain constant regions of kappa or lambda, preferably kappa (*e.g.*, human kappa). In one embodiment, the constant region is altered, *e.g.*, mutated, to modify the properties of the anti-LAG-3 antibody molecule (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function). For example, the constant region is mutated at positions 296 (M to Y), 298 (S to T), 300 (T to E), 477 (H to K) and 478 (N to F) to alter Fc receptor binding (*e.g.*, the mutated positions correspond to positions 132 (M to Y), 134 (S to T), 136 (T to E), 313 (H to K) and 314 (N to F) of SEQ ID NOs: 212 or 214; or positions 135 (M to Y), 137 (S to T), 139 (T to E), 316 (H to K) and 317 (N to F) of SEQ ID NOs: 215, 216, 217 or 218). In another embodiment, the heavy chain constant region of an IgG4, *e.g.*, a human IgG4, is mutated at position 228 (*e.g.*, S to P), *e.g.*, as shown in Table 3. In

certain embodiments, the anti-LAG-3 antibody molecules comprises a human IgG4 mutated at position 228 (*e.g.*, S to P), *e.g.*, as shown in Table 3; and a kappa light chain constant region, *e.g.*, as shown in Table 3. In still another embodiment, the heavy chain constant region of an IgG1, *e.g.*, a human IgG1, is mutated at one or more of position 297 (*e.g.*, N to A), position 265 (*e.g.*, D to A), position 329 (*e.g.*, P to A), position 234 (*e.g.*, L to A), or position 235 (*e.g.*, L to A), *e.g.*, as shown in Table 3. In certain embodiments, the anti-LAG-3 antibody molecules comprises a human IgG1 mutated at one or more of the aforesaid positions, *e.g.*, as shown in Table 3; and a kappa light chain constant region, *e.g.*, as shown in Table 3.

In certain embodiments, the anti-LAG-3 antibody molecule is in the form of a bispecific or a multispecific antibody molecule. In one embodiment, the bispecific antibody molecule has a first binding specificity for LAG-3 and a second binding specificity for PD-1, TIM-3, CEACAM (*e.g.*, CEACAM-1 and/or CEACAM-5), PD-L1 or PD-L2. In one embodiment, the bispecific antibody molecule binds to LAG-3 and PD-1. In another embodiment, the bispecific antibody molecule binds to LAG-3 and TIM-3. In another embodiment, the bispecific antibody molecule binds to LAG-3 and CEACAM (*e.g.*, CEACAM-1 and/or CEACAM-5). In another embodiment, the bispecific antibody molecule binds to LAG-3 and CEACAM-1. In yet another embodiment, the bispecific antibody molecule binds to LAG-3 and CEACAM-5. In another embodiment, the bispecific antibody molecule binds to LAG-3 and PD-L1. In yet another embodiment, the bispecific antibody molecule binds to LAG-3 and PD-L2. Any combination of the aforesaid molecules can be made in a multispecific antibody molecule, *e.g.*, a trispecific antibody that includes a first binding specificity to LAG-3, and a second and third binding specificity to one or more of: PD-1, TIM-3, CEACAM (*e.g.*, CEACAM-1 or CEACAM-5), PD-L1 or PD-L2.

In other embodiments, the anti-LAG-3 antibody molecule is used in combination with a bispecific molecule comprising one or more of: PD-1, TIM-3, CEACAM (*e.g.*, CEACAM-1 or CEACAM-5), PD-L1 or PD-L2. In one embodiment, the bispecific antibody molecule used in combination binds to CEACAM (*e.g.*, CEACAM-1 and/or CEACAM-5) and PD-1. In another embodiment, the bispecific antibody molecule used in combination binds to CEACAM (*e.g.*, CEACAM-1 and/or CEACAM-5) and TIM-3. In another embodiment, the bispecific antibody molecule used in combination binds to PD-1 and TIM-3.

In one embodiment, the anti-LAG-3 antibody molecule is isolated or recombinant.

In one embodiment, the anti-LAG-3 antibody molecule is a humanized antibody molecule.

In one embodiment, the anti-LAG-3 antibody molecule has a risk score based on T cell epitope analysis of less than 1200, 1150, 1100, 1050, 1000, 950, 900, 850, or 800.

In one embodiment, the anti-LAG-3 antibody molecule is a humanized antibody molecule and has a risk score based on T cell epitope analysis of 800 to 1200, 850 to 1150, 900 to 1100, 950 to 1050, or a risk score as described herein.

In certain embodiments, the anti-LAG-3 antibody molecule comprises:

(i) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and

(ii) a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12.

In other embodiments, the anti-LAG-3 antibody molecule comprises:

(i) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and

(ii) a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15.

In embodiments of the aforesaid antibody molecules, the VHCDR1 comprises the amino acid sequence of SEQ ID NO: 1. In other embodiments, the VHCDR1 comprises the amino acid sequence of SEQ ID NO: 4. In yet other embodiments, the VHCDR1 amino acid sequence of SEQ ID NO: 286.

In embodiments, the aforesaid antibody molecules have a heavy chain variable region comprising at least one framework (FW) region comprising the amino acid sequence of any of SEQ ID NOs: 187, 190, 194, 196, 198, 202, 206, 208, 210, 212, 217, 219, or 221, or an amino acid sequence at least 90% identical thereto, or having no more than two amino acid substitutions, insertions or deletions compared to the amino acid sequence of any of SEQ ID NOs: 187, 190, 194, 196, 198, 202, 206, 208, 210, 212, 217, 219, or 221.

In other embodiments, the aforesaid antibody molecules have a heavy chain variable region comprising at least one framework region comprising the amino acid sequence of any of SEQ ID NOs: 187, 190, 194, 196, 198, 202, 206, 208, 210, 212, 217, 219, or 221.

In yet other embodiments, the aforesaid antibody molecules have a heavy chain variable region comprising at least two, three, or four framework regions comprising the amino acid sequences of any of SEQ ID NOs: 187, 190, 194, 196, 198, 202, 206, 208, 210, 212, 217, 219, or 221.

In other embodiments, the aforesaid antibody molecules comprise a VHFW1 amino acid sequence of SEQ ID NO: 187, 190, 194, or 196, a VHFW2 amino acid sequence of SEQ ID NO: 198, 202, 206, or 208, and a VHFW3 amino acid sequence of SEQ ID NO: 210, 212, 217, or 219, and, optionally, further comprising a VHFW4 amino acid sequence of SEQ ID NO: 221.

In other embodiments, the aforesaid antibody molecules have a light chain variable region comprising at least one framework region comprising the amino acid sequence of any of SEQ ID NOs: 226, 230, 232, 234, 236, 238, 240, 244, 246, 248, 252, 255, 259, 261, 265, 267, 269, or 271, or an amino acid sequence at least 90% identical thereto, or having no more than two amino acid substitutions, insertions or deletions compared to the amino acid sequence of any of 226, 230, 232, 234, 236, 238, 240, 244, 246, 248, 252, 255, 259, 261, 265, 267, 269, or 271.

In other embodiments, the aforesaid antibody molecules have a light chain variable region comprising at least one framework region comprising the amino acid sequence of any of SEQ ID NOs: 226, 230, 232, 234, 236, 238, 240, 244, 246, 248, 252, 255, 259, 261, 265, 267, 269, or 271.

In other embodiments, the aforesaid antibody molecules have a light chain variable region comprising at least two, three, or four framework regions comprising the amino acid sequences of any of SEQ ID NOs: 226, 230, 232, 234, 236, 238, 240, 244, 246, 248, 252, 255, 259, 261, 265, 267, 269, or 271.

In other embodiments, the aforesaid antibody molecules comprise a VLFW1 amino acid sequence of SEQ ID NO: 226, 230, 232, 234, 236, or 2385, a VLFW2 amino acid sequence of SEQ ID NO: 240, 244, 246, or 248, and a VLFW3 amino acid sequence of SEQ ID NO: 252, 255, 259, 261, 265, 267, or 269, and, optionally, further comprising a VLFW4 amino acid sequence of SEQ ID NO: 271.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising an amino acid sequence at least 85% identical to any of SEQ ID NOs: 8, 28, 64, 68, 72, 76, 80, 100, 104, or 108.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 8, 28, 64, 68, 72, 76, 80, 100, 104, or 108.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising an amino acid sequence at least 85% identical to any of SEQ ID NOs: 32, 36, 40, 44, 48, 52, 56, 60, 84, 88, 92, or 96.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 32, 36, 40, 44, 48, 52, 56, 60, 84, 88, 92, or 96.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 8.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 18.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 30.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 66.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 68.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 70.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 72.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 74.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 76.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 78.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 80.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 82.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 100.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 102 or SEQ ID NO: 113.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 104.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 106.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 122.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 108.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 110.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 134.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 32.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 34.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 36.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 38.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 40.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 42.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 44.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 46.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 48.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 50.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 52.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 54.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 56.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 58.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 62.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 84.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 86.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 88.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 90.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 92.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 94.

In other embodiments, the aforesaid antibody molecules comprise a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 96.

In other embodiments, the aforesaid antibody molecules comprise a light chain comprising the amino acid sequence of SEQ ID NO: 98.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 32.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 36.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 40.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 44.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 48.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 52.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 56.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 36.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 40.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 56.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 68 or SEQ ID NO: 108; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 36.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 72 or SEQ ID NO: 8; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 40.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 72 or SEQ ID NO: 8; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 76 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 80 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 84.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 88.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 92.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 96.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 30 or SEQ ID NO: 102; and a light chain comprising the amino acid sequence of SEQ ID NO: 34.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 30 or SEQ ID NO: 102; and a light chain comprising the amino acid sequence of SEQ ID NO: 38.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 30 or SEQ ID NO: 102; and a light chain comprising the amino acid sequence of SEQ ID NO: 42.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 30 or SEQ ID NO: 102; and a light chain comprising the amino acid sequence of SEQ ID NO: 46.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 30 or SEQ ID NO: 102; and a light chain comprising the amino acid sequence of SEQ ID NO: 50.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 30 or SEQ ID NO: 102; and a light chain comprising the amino acid sequence of SEQ ID NO: 54.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 30 or SEQ ID NO: 102; and a light chain comprising the amino acid sequence of SEQ ID NO: 58.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 30 or SEQ ID NO: 102; and a light chain comprising the amino acid sequence of SEQ ID NO: 62.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 66 or SEQ ID NO: 106; and a light chain comprising the amino acid sequence of SEQ ID NO: 38.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 66 or SEQ ID NO: 106; and a light chain comprising the amino acid sequence of SEQ ID NO: 42.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 66 or SEQ ID NO: 106; and a light chain comprising the amino acid sequence of SEQ ID NO: 58.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 66 or SEQ ID NO: 106; and a light chain comprising the amino acid sequence of SEQ ID NO: 62.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 70 or SEQ ID NO: 110; and a light chain comprising the amino acid sequence of SEQ ID NO: 38.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 74 or SEQ ID NO: 18; and a light chain comprising the amino acid sequence of SEQ ID NO: 42.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 74 or SEQ ID NO: 18; and a light chain comprising the amino acid sequence of SEQ ID NO: 62.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 78 and a light chain comprising the amino acid sequence of SEQ ID NO: 62.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 82 and a light chain comprising the amino acid sequence of SEQ ID NO: 86.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 30 or SEQ ID NO: 102; and a light chain comprising the amino acid sequence of SEQ ID NO: 94.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 66 or SEQ ID NO: 106; and a light chain comprising the amino acid sequence of SEQ ID NO: 98.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 113 and a light chain comprising the amino acid sequence of SEQ ID NO: 34.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 113 and a light chain comprising the amino acid sequence of SEQ ID NO: 38.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 122 and a light chain comprising the amino acid sequence of SEQ ID NO: 38.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 122 and a light chain comprising the amino acid sequence of SEQ ID NO: 58.

In other embodiments, the aforesaid antibody molecules comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 134 and a light chain comprising the amino acid sequence of SEQ ID NO: 38.

In other embodiments, the aforesaid antibody molecules are chosen from a Fab, F(ab')₂, Fv, or a single chain Fv fragment (scFv).

In other embodiments, the aforesaid antibody molecules comprise a heavy chain constant region selected from IgG1, IgG2, IgG3, and IgG4.

In other embodiments, the aforesaid antibody molecules comprise a light chain constant region chosen from the light chain constant regions of kappa or lambda.

In other embodiments, the aforesaid antibody molecules comprise a human IgG4 heavy chain constant region with a mutation at position 228 according to EU numbering or position 108 of SEQ ID NO: 275 or 277 and a kappa light chain constant region.

In other embodiments, the aforesaid antibody molecules comprise a human IgG4 heavy chain constant region with a Serine to Proline mutation at position 228 according to EU numbering or position 108 of SEQ ID NO: 275 or 277 and a kappa light chain constant region.

In other embodiments, the aforesaid antibody molecules comprise a human IgG1 heavy chain constant region with an Asparagine to Alanine mutation at position 297 according to EU numbering or position 180 of SEQ ID NO: 279 and a kappa light chain constant region.

In other embodiments, the aforesaid antibody molecules comprise a human IgG1 heavy chain constant region with an Aspartate to Alanine mutation at position 265 according to EU numbering or position 148, and Proline to Alanine mutation at position 329 according to EU numbering or position 212 of SEQ ID NO: 280 and a kappa light chain constant region.

In other embodiments, the aforesaid antibody molecules comprise a human IgG1 heavy chain constant region with a Leucine to Alanine mutation at position 234 according to EU numbering or position 117 and Leucine to Alanine mutation at position 235 according to EU numbering or position 118 of SEQ ID NO: 281 and a kappa light chain constant region.

In other embodiments, the aforesaid antibody molecules are capable of binding to human LAG-3 with a dissociation constant (K_D) of less than about 0.2 nM.

In some embodiments, the aforesaid antibody molecules bind to human LAG-3 with a K_D of less than about 0.2 nM, 0.15 nM, 0.1 nM, 0.05 nM, or 0.02 nM, *e.g.*, about 0.05 nM to 0.15 nM, *e.g.*, about 0.11 nM, *e.g.*, as measured by a Biacore method.

In other embodiments, the aforesaid antibody molecules bind to cynomolgus LAG-3 with a K_D of less than about 0.2 nM, 0.15 nM, 0.1 nM, 0.05 nM, or 0.02 nM, *e.g.*, about 0.05 nM to 0.15 nM, *e.g.*, as measured by a Biacore method.

In certain embodiments, the aforesaid antibody molecules bind to both human LAG-3 and cynomolgus LAG-3 with similar K_D , *e.g.*, in the nM range, *e.g.*, as measured by a Biacore method. In some embodiments, the aforesaid antibody molecules bind to a human LAG-3-Ig

fusion protein with a K_D of less than about 0.5 nM, 0.2 nM, 0.1 nM, 0.05 nM, 0.025 nM, or 0.01 nM, *e.g.*, as measured by ELISA.

In some embodiments, the aforesaid antibody molecules bind to CHO cells that express human LAG-3 (*e.g.*, human LAG-3-transfected CHO cells) with a K_D of less than about 4 nM, 2.5 nM, 2 nM, 1.5 nM, 1 nM, 0.75 nM, 0.5 nM, 0.4 nM, 0.3 nM, 0.2 nM, 0.1 nM, or 0.05 nM, *e.g.*, about 2.3, 1.92 nM or about 0.2 nM, *e.g.*, as measured by FACS analysis.

In some embodiments, the aforesaid antibody molecules bind to human T cells with a K_D of less than about 0.5 nM, 0.4 nM, 0.3 nM, 0.2 nM, 0.1 nM, or 0.05 nM, *e.g.*, about 0.26 nM, *e.g.*, as measured by FACS analysis.

In some embodiments, the aforesaid antibody molecules bind to cells that express LAG-3 (*e.g.*, human LAG-3-expressing 300.19 cells) with a K_D of less than about 20 nM, 15 nM, 10 nM, 5 nM, 2 nM, or 1 nM, *e.g.*, about 13.6 nM, *e.g.*, as measured by FACS analysis.

In some embodiments, the aforesaid antibody molecules bind to cells that express rhesus LAG-3 (*e.g.*, cells transfected with rhesus LAG-3) with a K_D of less than about 15 nM, 10 nM, 9 nM, 8 nM, 6 nM, 5 nM, 2 nM, or 1 nM, *e.g.*, about 8.03 nM, *e.g.*, as measured by FACS analysis.

In certain embodiments, the aforesaid antibody molecules are not cross-reactive with mouse LAG-3. In some embodiments, the aforesaid antibodies are not cross-reactive with rat LAG-3. In other embodiments, the aforesaid antibodies are cross-reactive with rhesus LAG-3. In some embodiments, the aforesaid antibodies are cross-reactive with rat LAG-3. For example, the cross-reactivity can be measured by a Biacore method or a binding assay using cells that expresses LAG-3 (*e.g.*, human LAG-3-expressing 300.19 cells).

In other embodiments, the aforesaid antibody molecules bind an extracellular Ig-like domain of LAG-3 (*e.g.*, human LAG-3), *e.g.*, any of Domain 1 (D1), Domain 2 (D2), Domain 3 (D3), or Domain 4 (D4). In some embodiments, the aforesaid antibody molecules bind one or more amino acid residues in D1. In some embodiments, the aforesaid antibody molecules do not bind the extra loop of D1 or a fragment thereof (*e.g.*, as measured by a Biacore method or a FACS method). In some embodiments, the aforesaid antibodies do not bind D2. In some embodiments, the aforesaid antibody molecules bind both D1 and D2. In some embodiments, the aforesaid antibody molecules bind one or more amino acid residues in D1 and/or D2 that bind an MHC class II molecule. In other embodiments, the aforesaid antibody molecules are

capable of reducing binding of LAG-3 to a major histocompatibility (MHC) class II molecule, or a cell that expresses an MHC class II molecule. In some embodiments, the aforesaid antibody molecules reduce (*e.g.*, block) LAG-3-Ig binding to a MHC class II molecule, *e.g.*, on Raji cells or Daudi cells, with an IC₅₀ of less than about 10 nM, 8 nM, 5 nM, 4 nM, 3 nM, 2 nM, 1 nM, or 0.5 nM, *e.g.*, between about 8 nM and about 10 nM or between about 2 nM and about 3 nM, *e.g.*, about 5.5 nM or about 2.3 nM.

In other embodiments, the aforesaid antibody molecules are capable of enhancing an antigen-specific T cell response.

In embodiments, the antibody molecule is a monospecific antibody molecule or a bispecific antibody molecule. In embodiments, the antibody molecule has a first binding specificity for LAG-3 and a second binding specificity for PD-1, TIM-3, CEACAM (*e.g.*, CEACAM-1 and/or CEACAM-5), PD-L1 or PD-L2. In embodiments, the antibody molecule comprises an antigen binding fragment of an antibody, *e.g.*, a half antibody or antigen binding fragment of a half antibody.

In some embodiments, the aforesaid antibody molecules increase the expression of IL-2 from cells activated by Staphylococcal enterotoxin B (SEB) (*e.g.*, at 25 µg/mL) by at least about 2, 3, 4, 5-fold, *e.g.*, about 2 to 3-fold, compared to the expression of IL-2 when an isotype control (*e.g.*, IgG4) is used, *e.g.*, as measured in a SEB T cell activation assay or a human whole blood *ex vivo* assay.

In some embodiments, the aforesaid antibody molecules increase the expression of IFN-γ from T cells stimulated by anti-CD3 (*e.g.*, at 0.1 µg/mL) by at least about 0.5, 1, 2, 3, 4, 5, 6, 7, or 8-fold, *e.g.*, about 0.9 to 5.1-fold, *e.g.*, about 3-fold, compared to the expression of IFN-γ when an isotype control (*e.g.*, IgG4) is used, *e.g.*, as measured in an IFN-γ activity assay.

In some embodiments, the aforesaid antibody molecules increase the expression of IFN-γ from T cells activated by SEB (*e.g.*, at 3 pg/mL) by at least about 2, 3, 4, 5-fold, *e.g.*, about 1.2 to 2-fold, *e.g.*, about 1.6-fold, compared to the expression of IFN-γ when an isotype control (*e.g.*, IgG4) is used, *e.g.*, as measured in an IFN-γ activity assay.

In some embodiments, the aforesaid antibody molecules do not increase the expression of IL-2 or IFN-γ without T cell receptor activation (*e.g.* in the absence of SEB).

In some embodiments, the aforesaid antibody molecules increase the expression of IFN-γ from T cells activated with an CMV peptide by at least about 2, 3, 4, 5-fold, *e.g.*, about 1.1 to

1.7-fold, *e.g.*, about 1.4-fold, compared to the expression of IFN- γ when an isotype control (*e.g.*, IgG4) is used, *e.g.*, as measured in an IFN- γ activity assay. In some embodiments, the aforesaid antibody molecules increase the proliferation of CD8⁺ T cells activated with an CMV peptide by at least about 1, 2, 3, 4, 5-fold, *e.g.*, about 1.5-fold, compared to the proliferation of CD8⁺ T cells when an isotype control (*e.g.*, IgG4) is used, *e.g.*, as measured by the percentage of CD8⁺ T cells that passed through at least *n* (*e.g.*, *n* = 2 or 4) cell divisions.

In certain embodiments, the aforesaid antibody molecules has a C_{max} between about 50 $\mu\text{g/mL}$ and about 400 $\mu\text{g/mL}$, between about 100 $\mu\text{g/mL}$ and about 350 $\mu\text{g/mL}$, between about 150 $\mu\text{g/mL}$ and about 300 $\mu\text{g/mL}$, or between about 200 $\mu\text{g/mL}$ and about 250 $\mu\text{g/mL}$, *e.g.*, about 166 $\mu\text{g/mL}$, *e.g.*, as measured in an animal.

In certain embodiments, the aforesaid antibody molecules has a T_{1/2} between about 50 hours and about 400 hours, between about 100 hours and about 350 hours, between about 150 hours and about 300 hours, or between about 200 hours and about 250 hours, *e.g.*, about 231.9 hours, *e.g.*, as measured in an animal.

In some embodiments, the aforesaid antibody molecules bind to LAG-3 with a K_d slower than 5×10^{-4} , 1×10^{-4} , 5×10^{-5} , or $1 \times 10^{-5} \text{ s}^{-1}$, *e.g.*, about $7 \times 10^{-5} \text{ s}^{-1}$, *e.g.*, as measured by a Biacore method. In some embodiments, the aforesaid antibodies bind to LAG-3 with a K_a faster than 1×10^4 , 5×10^4 , 1×10^5 , 5×10^5 , or $1 \times 10^6 \text{ M}^{-1}\text{s}^{-1}$, *e.g.*, about $6.41 \times 10^5 \text{ M}^{-1}\text{s}^{-1}$, *e.g.*, as measured by a Biacore method.

In another aspect, the invention provides an isolated nucleic acid molecule encoding any of the aforesaid antibody molecules, vectors and host cells thereof.

In one embodiment, the isolated nucleic acid encodes the antibody heavy chain variable region or light chain variable region, or both, of any the aforesaid antibody molecules.

In one embodiment, the isolated nucleic acid encodes heavy chain CDRs 1-3, wherein said nucleic acid comprises a nucleotide sequence of SEQ ID NO: 140-144, 151-155, 162-166, 173-177, 184-186, or 287.

In another embodiment, the isolated nucleic acid encodes light chain CDRs 1-3, wherein said nucleic acid comprises a nucleotide sequence of SEQ ID NO: 145-150, 156-161, 167-172, or 178-183.

In other embodiments, the aforesaid nucleic acid further comprises a nucleotide sequence encoding a heavy chain variable domain, wherein said nucleotide sequence is at least 85%

identical to any of SEQ ID NO: 9, 29, 65, 69, 73, 77, 81, 101, 105, 109, 112, 121, 124, 125, 132, or 133.

In other embodiments, the aforesaid nucleic acid further comprises a nucleotide sequence encoding a heavy chain variable domain, wherein said nucleotide sequence comprises any of SEQ ID NO: 9, 29, 65, 69, 73, 77, 81, 101, 105, 109, 112, 121, 124, 125, 132, or 133.

In other embodiments, the aforesaid nucleic acid further comprises a nucleotide sequence encoding a heavy chain, wherein said nucleotide sequence is at least 85% identical to any of SEQ ID NO: 19, 31, 67, 71, 75, 79, 83, 103, 107, 111, 114, 123, 126, 127, 135, or 136.

In other embodiments, the aforesaid nucleic acid further comprises a nucleotide sequence encoding a heavy chain, wherein said nucleotide sequence comprises any of SEQ ID NO: 19, 31, 67, 71, 75, 79, 83, 103, 107, 111, 114, 123, 126, 127, 135, or 136.

In other embodiments, the aforesaid nucleic acid further comprises a nucleotide sequence encoding a light chain variable domain, wherein said nucleotide sequence is at least 85% identical to any of SEQ ID NO: 33, 37, 41, 45, 49, 53, 57, 61, 85, 89, 93, 97, 115, 118, 128, 129, or 137.

In other embodiments, the aforesaid nucleic acid further comprises a nucleotide sequence encoding a light chain variable domain, wherein said nucleotide sequence comprises any of SEQ ID NO: 33, 37, 41, 45, 49, 53, 57, 61, 85, 89, 93, 97, 115, 118, 128, 129, or 137.

In other embodiments, the aforesaid nucleic acid further comprises a nucleotide sequence encoding a light chain, wherein said nucleotide sequence is at least 85% identical to any of SEQ ID NO: 35, 39, 43, 47, 51, 55, 59, 63, 87, 91, 95, 99, 117, 120, 130, 131, 138, or 139.

In other embodiments, the aforesaid nucleic acid further comprises a nucleotide sequence encoding a light chain, wherein said nucleotide sequence comprises any of SEQ ID NO: 35, 39, 43, 47, 51, 55, 59, 63, 87, 91, 95, 99, 117, 120, 130, 131, 138, or 139.

In certain embodiments, one or more expression vectors and host cells comprising the aforesaid nucleic acids are provided.

A method of producing an antibody molecule or fragment thereof, comprising culturing the host cell as described herein under conditions suitable for gene expression is also provided.

In one aspect, the invention features a method of providing an antibody molecule described herein. The method includes: providing a LAG-3 antigen (*e.g.*, an antigen comprising at least a portion of a LAG-3 epitope); obtaining an antibody molecule that specifically binds to

the LAG-3 polypeptide; and evaluating if the antibody molecule specifically binds to the LAG-3 polypeptide, or evaluating efficacy of the antibody molecule in modulating, *e.g.*, inhibiting, the activity of the LAG-3. The method can further include administering the antibody molecule to a subject, *e.g.*, a human or non-human animal.

In another aspect, the invention provides, compositions, *e.g.*, pharmaceutical compositions, which include a pharmaceutically acceptable carrier, excipient or stabilizer, and at least one of the therapeutic agents, *e.g.*, anti-LAG-3 antibody molecules described herein. In one embodiment, the composition, *e.g.*, the pharmaceutical composition, includes a combination of the antibody molecule and one or more agents, *e.g.*, a therapeutic agent or other antibody molecule, as described herein. In one embodiment, the antibody molecule is conjugated to a label or a therapeutic agent.

Additional Inhibitors of LAG-3

In one embodiment, a combination described herein includes a LAG-3 inhibitor. In some embodiments, the LAG-3 inhibitor is an anti-LAG-3 antibody molecule other than the anti-LAG-3 antibody molecule of Table 1. In certain embodiments, the LAG-3 inhibitor comprises an anti-LAG-3 antibody molecule of Table 1 and an anti-LAG-3 antibody molecule other than the antibody molecule of Table 1. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor or a hematologic malignancy.

In some embodiments, the anti-LAG-3 antibody is BMS-986016. BMS-986016 (also referred to as BMS986016; Bristol-Myers Squibb) is a monoclonal antibody that binds to LAG-3. BMS-986016 and other humanized anti-LAG-3 antibodies are disclosed in US 2011/0150892, WO2010/019570, and WO2014/008218

Exemplary CSF-1/IR Binding Agents

In one embodiment, a combination described herein includes a CSF-1/IR binding agent. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a prostate cancer, a breast cancer, or pigmented villonodular synovitis (PVNS)). In some embodiments, the cancer is a brain cancer (*e.g.*, a glioblastoma multiforme), a pancreatic cancer, an ovarian cancer, or a breast cancer (*e.g.*, a triple negative breast cancer).

In some embodiments, the CSF-1/1R binding agent is an inhibitor of macrophage colony-stimulating factor (M-CSF).

In another embodiment, the CSF-1/1R binding agent is a CSF-1R tyrosine kinase inhibitor, 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-methylpicolinamide (Compound A15), or a compound disclosed in PCT Publication No. WO 2005/073224.

In some embodiments, the CSF-1/1R binding agent is an M-CSF inhibitor, Compound A33, or a binding agent to CSF-1 disclosed in PCT Publication No. WO 2004/045532 or PCT Publication No. WO 2005/068503 including RX1 or 5H4 (*e.g.*, an antibody molecule or Fab fragment against M-CSF).

In some embodiments, the CSF-1/1R binding agent, *e.g.*, an M-CSF inhibitor, Compound A33, or a compound disclosed in PCT Publication No. WO 2004/045532 (*e.g.*, an antibody molecule or Fab fragment against M-CSF), is administered at an average dose of about 10mg/kg.

In some embodiments, the CSF-1/1R binding agent is a CSF1R inhibitor or 4-(2-((1R, 2R)-2-hydroxycyclohexylamino)benzothiazol-6-yloxy)-N-methylpicolinamide. 4-(2-((1R, 2R)-2-hydroxycyclohexylamino)benzothiazol-6-yloxy)-N-methylpicolinamide is disclosed as example 157 at page 117 of PCT Publication No. WO 2007/121484.

In some embodiments, the CSF-1/1R binding agent is pexidartinib (CAS Registry Number 1029044-16-3). Pexidartinib is also known as PLX3397 or 5-((5-chloro-1H-pyrrolo[2,3-b]pyridin-3-yl)methyl)-N-((6-(trifluoromethyl)pyridin-3-yl)methyl)pyridin-2-amine. Pexidartinib is a small-molecule receptor tyrosine kinase (RTK) inhibitor of KIT, CSF1R and FLT3. FLT3, CSF1R and FLT3 are overexpressed or mutated in many cancer cell types and play major roles in tumor cell proliferation and metastasis. PLX3397 can bind to and inhibit phosphorylation of stem cell factor receptor (KIT), colony-stimulating factor-1 receptor (CSF1R) and FMS-like tyrosine kinase 3 (FLT3), which may result in the inhibition of tumor cell proliferation and down-modulation of macrophages, osteoclasts and mast cells involved in the osteolytic metastatic disease. In some embodiments, the CSF-1/1R binding agent, *e.g.*, pexidartinib, is used in combination with a PD-1 inhibitor, *e.g.*, an anti-PD-1 antibody molecule described herein.

In some embodiments, the CSF-1/1R binding agent is emactuzumab. Emactuzumab is also known as RG7155 or RO5509554. Emactuzumab is a humanized IgG1 mAb targeting

CSF1R. In some embodiments, the CSF-1/1R binding agent, *e.g.*, pexidartinib, is used in combination with a PD-L1 inhibitor, *e.g.*, an anti-PD-L1 antibody molecule described herein. In some embodiments, the CSF-1/1R binding agent is FPA008. FPA008 is a humanized mAb that inhibits CSF1R. In some embodiments, the CSF-1/1R binding agent, *e.g.*, FPA008, is used in combination with a PD-1 inhibitor, *e.g.*, an anti-PD-1 antibody molecule described herein.

Exemplary IL-17 Inhibitors

In one embodiment, a combination described herein includes an interleukine-17 (IL-17) inhibitor. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor, *e.g.*, breast cancer (*e.g.*, a triple negative breast cancer), lung cancer (*e.g.*, a non-small cell lung cancer), or colon cancer.

In some embodiments, the IL-17 inhibitor is secukinumab (CAS Registry Numbers: 875356-43-7 (heavy chain) and 875356-44-8 (light chain)). Secukinumab is also known as AIN457 and COSENTYX®. Secukinumab is a recombinant human monoclonal IgG1/κ antibody that binds specifically to IL-17A. It is expressed in a recombinant Chinese Hamster Ovary (CHO) cell line.

Secukinumab is described, *e.g.*, in WO 2006/013107, US 7,807,155, US 8,119,131, US 8,617,552, and EP 1776142. The heavy chain variable region of secukinumab has the amino acid sequence of:

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYWMNWVRQAPGKGLEWVAAINQDGSE
KYYVGSVKGRFTISRDNKNSLYLQMNSLRVEDTAVYYCVRDYYDILTDYYIHYWYFD
LWGRGTLVTVSS (SEQ ID NO: 328) (disclosed as SEQ ID NO: 8 in WO 2006/013107). The light chain variable region of secukinumab has the amino acid sequence of:

EIVLTQSPGTLSSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPD
RFGSGSGTDFTLISRLEPEDFAVYYCQQYGSSPCTFGQGRLEIKR (SEQ ID NO: 329)

(disclosed as SEQ ID NO: 10 in WO 2006/013107). The heavy chain CDR1 of secukinumab has the amino acid sequence of NYWMN (SEQ ID NO: 330) (disclosed as SEQ ID NO: 1 in WO 2006/013107). The heavy chain CDR2 of secukinumab has the amino acid sequence of AINQDGSEKYYVGSVKG (SEQ ID NO: 331) (disclosed as SEQ ID NO: 2 in WO 2006/013107). The heavy chain CDR3 of secukinumab has the amino acid sequence of DYYDILTDYYIHYWYFDL (SEQ ID NO: 332) (disclosed as SEQ ID NO: 3 in WO

2006/013107). The light chain CDR1 of secukinumab has the amino acid sequence of RASQSVSSSYLA (SEQ ID NO: 333) (disclosed as SEQ ID NO: 4 in WO 2006/013107). The light chain CDR2 of secukinumab has the amino acid sequence of GASSRAT (SEQ ID NO: 334) (disclosed as SEQ ID NO: 5 in WO 2006/013107). The light chain CDR3 of secukinumab has the amino acid sequence of QQYGSSPCT (SEQ ID NO: 335) (disclosed as SEQ ID NO: 6 in WO 2006/013107).

In some embodiments, the IL-17 inhibitor is CJM112. CJM112 is also known as XAB4. CJM112 is a fully human monoclonal antibody that targets IL-17A.

CJM112 is disclosed, *e.g.*, in WO 2014/122613. The heavy chain of CJM112 has the amino acid sequence of:

EVQLVESGGDLVQPGGSLRLSCAASGFTFSSYWMSWVRQAPGKGLEWVANIKQDGSE
 KYYVDSVKGRFTISRDNKNSLYLQMNSLRAEDTAVYYCARDRGSLYYWGQGTLLVTV
 SSASTKGPSVFPLAPSSKSTSGGTAAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ
 SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELL
 GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE
 QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP
 SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTV
 DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 336) (disclosed as
 SEQ ID NO: 14 in WO 2014/122613). The light chain of CJM112 has the amino acid sequence
 of:

AIQLTQSPSSLSASVGDRVTITCRPSQGINWELAWYQQKPGKAPKLLIYDASSLEQGVPS
 RFGSGSGTDFLTISLQPEDFATYYCQQFNQSYPLTFGGGTKVEIKRTVAAPSVEFIFPPSD
 EQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTL
 SKADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 337) (disclosed as SEQ ID
 NO: 44 in WO 2014/122613).

In some embodiments, the IL-17 inhibitor is ixekizumab (CAS Registry Number: 1143503-69-8). Ixekizumab is also known as LY2439821. Ixekizumab is a humanized IgG4 monoclonal antibody that targets IL-17A.

Ixekizumab is described, *e.g.*, in WO 2007/070750, US 7,838,638, and US 8,110,191. The heavy chain variable region of ixekizumab has the amino acid sequence of:

QVQLVQSGAEVKKPGSSVKVSKASGYSFTDYHIHWVRQAPGQGLEWMGVINPMYGT

TDYNNRQRFKGRVTITADESTSTAYMELSSLRSEDVAVYYCARYDYFTGTGVVYWGQGTLV
TVSS (SEQ ID NO: 338) (disclosed as SEQ ID NO: 118 in WO 2007/070750). The light chain
variable region of ixekizumab has the amino acid sequence of:

DIVMTQTPLSLSVTPGQPASISCRSSRSLVHSRGNTYLHWYLQKPGQSPQLLIYKVSNRFI
GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHLPFTFGQGTKLEIK (SEQ ID NO:
339) (disclosed as SEQ ID NO: 241 in WO 2007/070750).

In some embodiments, the IL-17 inhibitor is brodalumab (CAS Registry Number:
1174395-19-7). Brodalumab is also known as AMG 827 or AM-14. Brodalumab binds to the
interleukin-17 receptor A (IL-17RA) and prevents IL-17 from activating the receptor.

Brodalumab is disclosed, *e.g.*, in WO 2008/054603, US 7,767,206, US 7,786,284, US
7,833,527, US 7,939,070, US 8,435,518, US 8,545,842, US 8,790,648, and US 9,073,999. The
heavy chain CDR1 of brodalumab has the amino acid sequence of RYGIS (SEQ ID NO: 340) (as
disclosed as SEQ ID NO: 146 in WO 2008/054603). The heavy chain CDR2 of brodalumab has
the amino acid sequence of WISTYSGNTNYAQKLQG (SEQ ID NO: 341) (as disclosed as
SEQ ID NO: 147 in WO 2008/054603). The heavy chain CDR3 of brodalumab has the amino
acid sequence of RQLYFDY (SEQ ID NO: 342) (as disclosed as SEQ ID NO: 148 in WO
2008/054603). The light chain CDR1 of brodalumab has the amino acid sequence of
RASQSVSSNLA (SEQ ID NO: 343) (as disclosed as SEQ ID NO: 224 in WO 2008/054603).
The heavy chain CDR2 of brodalumab has the amino acid sequence of DASTRAT (SEQ ID NO:
344) (as disclosed as SEQ ID NO: 225 in WO 2008/054603). The heavy chain CDR3 of
brodalumab has the amino acid sequence of QQYDNWPLT (SEQ ID NO: 345) (as disclosed as
SEQ ID NO: 226 in WO 2008/054603).

Exemplary IL-1 β Inhibitors

In one embodiment, a combination described herein includes an interleukine-1 beta (IL-
1 β) inhibitor. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer
described herein, *e.g.*, a hematologic malignancy (*e.g.*, a lymphoma (*e.g.*, Hodgkin lymphoma), a
leukemia (*e.g.*, an acute or chronic leukemia), or a multiple myeloma).

In some embodiments, the IL-1 β inhibitor is canakinumab. Canakinumab is also known
as ACZ885 or ILARIS®. Canakinumab is a human monoclonal IgG1/ κ antibody that neutralizes
the bioactivity of human IL-1 β .

Canakinumab is disclosed, *e.g.*, in WO 2002/16436, US 7,446,175, and EP 1313769. The heavy chain variable region of canakinumab has the amino acid sequence of: MEFGLSWVFLVALLRGVQCQVQLVESGGGVVQPGRSLRLSCAASGFTFSVYGMNWVR QAPGKGLEWVAIIWYDGDNQYYADSVKGRFTISRDN SKNTLYLQMNGLRAEDTAVYY CARDLRTGPFDYWGQGLTVTVSS (SEQ ID NO: 346) (disclosed as SEQ ID NO: 1 in US 7,446,175). The light chain variable region of canakinumab has the amino acid sequence of: MLPSQLIGFLLLWVPASRGEIVLTQSPDFQSVTPKEKVTITCRASQSIGSSLHWYQQKPD QSPKLLIKYASQSFSGVPSRFSGSGSGTDFTLTINSLEAEDAAAYYCHQSSSLPFTFGPGT KVDIK (SEQ ID NO: 347) (disclosed as SEQ ID NO: 2 in US 7,446,175).

Exemplary CXCR2 Inhibitors

In one embodiment, a combination described herein includes an inhibitor of chemokine (C-X-C motif) receptor 2 (CXCR2) inhibitor. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor, *e.g.*, a breast cancer, a metastatic sarcoma, a pancreatic cancer, a melanoma, a renal cell carcinoma (RCC), a non-small cell lung cancer (NSCLC), or a pediatric tumor (*e.g.*, a rhabdomyosarcoma).

In some embodiments, the CXCR2 inhibitor is danirixin (CAS Registry Number: 954126-98-8). Danirixin is also known as GSK1325756 or 1-(4-chloro-2-hydroxy-3-piperidin-3-ylsulfonylphenyl)-3-(3-fluoro-2-methylphenyl)urea. Danirixin is disclosed, *e.g.*, in Miller *et al. Eur J Drug Metab Pharmacokinet* (2014) 39:173–181; and Miller *et al. BMC Pharmacology and Toxicology* (2015), 16:18.

In some embodiments, the CXCR2 inhibitor is reparixin (CAS Registry Number: 266359-83-5). Reparixin is also known as repertaxin or (2R)-2-[4-(2-methylpropyl)phenyl]-N-methylsulfonylpropanamide. Reparixin is a non-competitive allosteric inhibitor of CXCR1/2. Reparixin is disclosed, *e.g.*, in Zarbock *et al. British Journal of Pharmacology* (2008), 1–8.

In some embodiments, the CXCR2 inhibitor is navarixin. Navarixin is also known as MK-7123, SCH 527123, PS291822, or 2-hydroxy-N,N-dimethyl-3-[[2-[[[(1R)-1-(5-methylfuran-2-yl)propyl]amino]-3,4-dioxocyclobuten-1-yl]amino]benzamide. Navarixin is disclosed, *e.g.*, in Ning *et al. Mol Cancer Ther.* 2012;11(6):1353-64.

Exemplary PI3K- γ , - δ Inhibitors

In one embodiment, a combination described herein includes an inhibitor of phosphatidylinositol-4,5-bisphosphate 3-kinase (PI3K), *e.g.*, phosphatidylinositol-4,5-bisphosphate 3-kinase gamma and/or delta (PI3K- γ , δ). In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a prostate cancer, a breast cancer, a brain cancer, a bladder cancer, a pancreatic cancer, a renal cancer, a solid tumor, a liver cancer, a non-small cell lung cancer, an endocrine cancer, an ovarian cancer, a melanoma, a female reproductive system cancer, a digestive/gastrointestinal cancer, a glioblastoma multiforme, a head and neck cancer, or a colon cancer), *e.g.*, a hematologic malignancy (*e.g.*, a leukemia (*e.g.*, a lymphocytic leukemia, *e.g.*, chronic lymphocytic leukemia (CLL) (*e.g.*, relapsed CLL)), *e.g.*, a lymphoma (*e.g.*, non-Hodgkin lymphoma (*e.g.*, relapsed follicular B-cell non-Hodgkin lymphoma (FL) or relapsed small lymphocytic lymphoma (SLL)), or *e.g.*, a multiple myeloma).

In some embodiments, the PI3K inhibitor is an inhibitor of delta and gamma isoforms of PI3K. Exemplary PI3K inhibitors that can be used in combination are described in, *e.g.*, WO 2010/036380, WO 2010/006086, WO 09/114870, WO 05/113556, GSK 2126458, GDC-0980, GDC-0941, Sanofi XL147, XL756, XL147, PF-46915032, BKM 120, CAL-101, CAL 263, SF1126, PX-886, and a dual PI3K inhibitor (*e.g.*, Novartis BEZ235).

In some embodiments, the PI3K- γ , δ inhibitor is idelalisib (CAS Registry Number: 870281-82-6). Idelalisib is also known as ZYDELIG®, GS-1101, CAL-101, or 5-Fluoro-3-phenyl-2-[(1S)-1-(7H-purin-6-ylamino)propyl]-4(3H)-quinazolinone. Idelalisib blocks P110 δ , the delta isoform of PI3K. Idelalisib is disclosed, *e.g.*, in Wu *et al. Journal of Hematology & Oncology* (2013) 6: 36.

In some embodiments, the PI3K- γ , δ inhibitor is dactolisib (Compound A4) or 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydroimidazo[4,5-c]quinolin-2-one (Compound A41), or a compound disclosed in PCT Publication No. WO 2006/122806.

In some embodiments, the PI3K- γ , δ inhibitor is buparlisib (Compound A6) or a compound disclosed in PCT Publication No. WO 2007/084786.

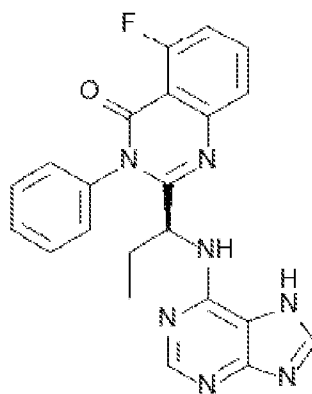
In one embodiment, the PI3K- γ,δ inhibitor, *e.g.*, buparlisib (Compound A6) or a compound disclosed in PCT Publication No. WO 2007/084786, is administered at a dose of about 100 mg (*e.g.*, per day).

Other exemplary PI3K- γ,δ inhibitors that can be used in the combination include, *e.g.*, pictilisib (GDC-0941), LY294002, pilaralisib (XL147), PI-3065, PI-103, VS-5584 (SB2343), CZC24832, duvelisib (IPI-145, INK1197), TG100-115, CAY10505, GSK1059615, PF-04691502, AS-605240, voxtalisib (SAR245409, XL765), IC-87114, omipalisib (GSK2126458, GSK458), TG100713, gedatolisib (PF-05212384, PKI-587), PKI-402, XL147 analogue, PIK-90, PIK-293, PIK-294, 3-Methyladenine (3-MA), AS-252424, AS-604850, or apitolisib (GDC-0980, RG7422).

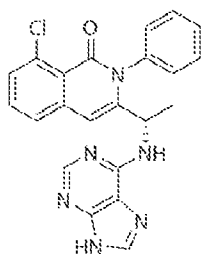
In some embodiments, the PI3K inhibitor is Compound A8 or a compound described in PCT Publication No. WO2010/029082.

In some embodiments, the PI3K inhibitor is a pan-PI3K inhibitor, (4S,5R)-3-(2'-amino-2-morpholino-4'-(trifluoromethyl)-[4,5'-bipyrimidin]-6-yl)-4-(hydroxymethyl)-5-methyloxazolidin-2-one (Compound A13) or a compound disclosed in PCT Publication No. WO2013/124826.

Exemplary PI3K- $\gamma, -\delta$ inhibitors include, but are not limited to, duvelisib and idelalisib. Idelalisib (also called GS-1101 or CAL-101; Gilead) is a small molecule that blocks the delta isoform of PI3K. The structure of idelalisib (5-Fluoro-3-phenyl-2-[(1S)-1-(7H-purin-6-ylamino)propyl]-4(3H)-quinazolinone) is shown below.



Duvelisib (also called IPI-145; Infinity Pharmaceuticals and Abbvie) is a small molecule that blocks PI3K- δ,γ . The structure of duvelisib (8-Chloro-2-phenyl-3-[(1S)-1-(9H-purin-6-ylamino)ethyl]-1(2H)-isoquinolinone) is shown below.



In one embodiment, the inhibitor is a dual phosphatidylinositol 3-kinase (PI3K) and mTOR inhibitor selected from 2-Amino-8-[*trans*-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PF-04691502); *N*-[4-[[4-(Dimethylamino)-1-piperidinyl]carbonyl]phenyl]-*N'*-[4-(4,6-di-4-morpholinyl-1,3,5-triazin-2-yl)phenyl]urea (PF-05212384, PKI-587); 2-Methyl-2-{4-[3-methyl-2-oxo-8-(quinolin-3-yl)-2,3-dihydro-1*H*-imidazo[4,5-*c*]quinolin-1-yl]phenyl}propanenitrile (BEZ-235); apitolisib (GDC-0980, RG7422); 2,4-Difluoro-*N*-{2-(methoxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide (GSK2126458); 8-(6-methoxypyridin-3-yl)-3-methyl-1-(4-(piperazin-1-yl)-3-(trifluoromethyl)phenyl)-1*H*-imidazo[4,5-*c*]quinolin-2(3*H*)-one Maleic acid (NVP-BGT226); 3-[4-(4-Morpholinyl)pyrido[3',2':4,5]furo[3,2-*d*]pyrimidin-2-yl]phenol (PI-103); 5-(9-isopropyl-8-methyl-2-morpholino-9*H*-purin-6-yl)pyrimidin-2-amine (VS-5584, SB2343); or *N*-[2-[(3,5-Dimethoxyphenyl)amino]quinoxalin-3-yl]-4-[(4-methyl-3-methoxyphenyl)carbonyl]aminophenylsulfonamide (XL765).

Exemplary BAFF-R Inhibitors

In one embodiment, a combination described herein includes a B-cell-activating factor receptor (BAFF-R) inhibitor. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a hematologic malignancy, *e.g.*, a leukemia (*e.g.*, chronic lymphocytic leukemia (CLL), *e.g.*, relapsed or refractory chronic lymphocytic leukemia).

In one embodiment, the BAFF-R inhibitor is VAY736. VAY736 is a fully human combinatorial antibody library (HuCAL)-derived monoclonal antibody targeting BAFF-R. BAFF-R, also known as tumor necrosis factor receptor superfamily member 13C, is overexpressed in certain tumor cell types and autoimmune diseases. VAY736 has both anti-inflammatory and antineoplastic activities. In cancer cells, BAFF-R plays a key role in B-cell proliferation and survival. VAY736 targets and binds to BAFF-R, which inhibits both

BAFF/BAFF-R interaction and BAFF-R-mediated signaling. This may decrease cell growth in tumor cells expressing BAFF-R.

VAY736 is disclosed, *e.g.*, in US 8,106,163. The heavy chain CDR1 of VAY736 has the amino acid sequence of GDSVSSNSAAWG (SEQ ID NO: 348) (disclosed as SEQ ID NO: 3 in US 8,106,163). The heavy chain CDR2 of VAY736 has the amino acid sequence of RIYYRSKWYNSYAVSVKS (SEQ ID NO: 349) (disclosed as SEQ ID NO: 10 in US 8,106,163). The heavy chain CDR3 of VAY736 has the amino acid sequence of YDWVPKIGVFDS (SEQ ID NO: 350) (disclosed as SEQ ID NO: 17 in US 8,106,163). The light chain CDR1 of VAY736 has the amino acid sequence of RASQFISSSYLS (SEQ ID NO: 351) (disclosed as SEQ ID NO: 24 in US 8,106,163). The light chain CDR2 of VAY736 has the amino acid sequence of LLIYGSSSRAT (SEQ ID NO: 352) (disclosed as SEQ ID NO: 31 in US 8,106,163). The light chain CDR3 of VAY736 has the amino acid sequence of QQLYSSPM (SEQ ID NO: 353) (disclosed as SEQ ID NO: 38 in US 8,106,163). The heavy chain variable region of VAY736 has the amino acid sequence of:

QVQLQQSGPGLVKPSQTLTLTCAISGDSVSSNSAAWGWIRQSPGRGLEWLGRIYYRSKW
YNSYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCARYDWVPKIGVFDSWGQGT
LVTVSS (SEQ ID NO: 354) (disclosed as SEQ ID NO: 52 in US 8,106,163). The light chain variable region of VAY736 has the amino acid sequence of:

DIVLTQSPATLSLSPGERATLSCRASQFISSSYLSWYQQKPGQAPRLLIYGSSSRATGVPA
RFGSGSGTDFTLTISLEPEDFAVYYCQQLYSSPMFTFGQGTKVEIKRT (SEQ ID NO: 355)
(disclosed as SEQ ID NO: 45 in US 8,106,163). The heavy chain of VAY736 has the amino acid sequence of:

QVQLQQSGPGLVKPSQTLTLTCAISGDSVSSNSAAWGWIRQSPGRGLEWLGRIYYRSKW
YNSYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCARYDWVPKIGVFDSWGQGT
LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP
AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVKDKRVEPKSCDKTHTCPPCPA
PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTK
PREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV
YTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYS
KLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 356) (disclosed
as SEQ ID NO: 75 in US 8,106,163). The light chain variable region of VAY736 has the amino

acid sequence of:

DIVLTQSPATLSLSPGERATLSCRASQFISSSYLSWYQQKPGQAPRLLIYGSSSRATGVPA
RFSGSGSGTDFTLTISSLEPEDFAVYYCQQLYSSPMTFGQGTKVEIKRTVAAPSVFIFPPSD
EQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDESTYLSSTLTL
SKADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 357) (disclosed as SEQ ID
NO: 71 in US 8,106,163).

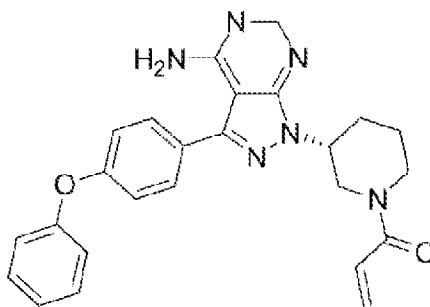
Exemplary MALT-1/BTK Inhibitors

In one embodiment, a combination described herein includes an inhibitor of MALT-1 and/or BTK. In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein.

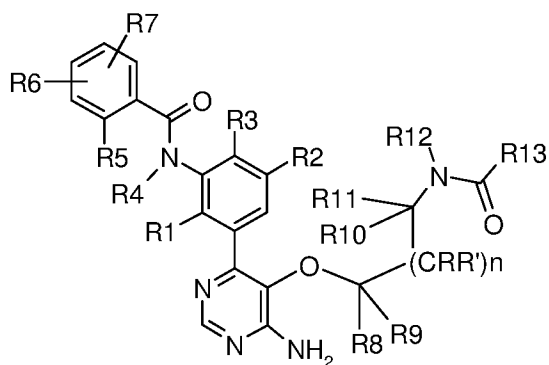
Exemplary MALT-1/BTK inhibitors include, but are not limited to, (S)-1-(6-(2H-1,2,3-triazol-2-yl)-5-(trifluoromethyl)pyridin-3-yl)-3-(2-chloro-7-(1-methoxyethyl)pyrazolo[1,5-a]pyrimidin-6-yl)urea, (S)-1-(2-chloro-7-(1-methoxyethyl)pyrazolo[1,5-a]pyrimidin-6-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea, (S)-1-(2-chloro-7-(1-methoxyethyl)pyrazolo[1,5-a]pyrimidin-6-yl)-3-(1-methyl-2-oxo-5-(trifluoromethyl)-1,2-dihydropyridin-3-yl)urea, (R)-1-(6-(2H-1,2,3-triazol-2-yl)-5-(trifluoromethyl)pyridin-3-yl)-3-(2-chloro-7-(1-methoxy-2-methylpropyl)pyrazolo[1,5-a]pyrimidin-6-yl)urea, (R)-1-(5-chloro-6-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)-3-(2-chloro-7-(1-methoxy-2-methylpropyl)pyrazolo[1,5-a]pyrimidin-6-yl)urea, (S)-1-(7-(1-methoxyethyl)-2-methylpyrazolo[1,5-a]pyrimidin-6-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea, (S)-1-(2-fluoro-7-(1-methoxyethyl)pyrazolo[1,5-a]pyrimidin-6-yl)-3-(2-(trifluoromethyl)pyridin-4-yl)urea, (S)-1-(2-chloro-7-(1-methoxyethyl)pyrazolo[1,5-a]pyrimidin-6-yl)-3-(5-cyanopyridin-3-yl)urea,

Exemplary BTK inhibitors include, but are not limited to, ibrutinib (PCI-32765); GDC-0834; RN-486; CGI-560; CGI-1764; HM-71224; CC-292; ONO-4059; CNX-774; or LFM-A13. In one embodiment, the BTK inhibitor does not reduce or inhibit the kinase activity of interleukin-2-inducible kinase (ITK), *e.g.*, is selected from GDC-0834; RN-486; CGI-560; CGI-1764; HM-71224; CC-292; ONO-4059; CNX-774; or LFM-A13.

In one embodiment, the kinase inhibitor is a BTK inhibitor, *e.g.*, ibrutinib (PCI-32765). The structure of ibrutinib (1-[(3*R*)-3-[4-Amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-d]pyrimidin-1-yl]piperidin-1-yl]prop-2-en-1-one) is shown below.



In other embodiments, the BTK inhibitor is a BTK inhibitor described in International Application WO/2015/079417, which is herein incorporated by reference in its entirety. For instance, in some embodiments, the BTK inhibitor is a compound of formula (I) or a pharmaceutically acceptable salt thereof;



(I)

wherein,

R1 is hydrogen, C1-C6 alkyl optionally substituted by hydroxy;

R2 is hydrogen or halogen;

R3 is hydrogen or halogen;

R4 is hydrogen;

R5 is hydrogen or halogen;

or R4 and R5 are attached to each other and stand for a bond, -CH₂-, -CH₂-CH₂-, -CH=CH-, -CH=CH-CH₂-; -CH₂-CH=CH-; or -CH₂-CH₂-CH₂-;

R6 and R7 stand independently from each other for H, C1-C6 alkyl optionally substituted by hydroxyl, C3-C6 cycloalkyl optionally substituted by halogen or hydroxy, or halogen;

R8, R9, R, R', R10 and R11 independently from each other stand for H, or C1-C6 alkyl optionally substituted by C1-C6 alkoxy; or any two of R8, R9, R, R', R10 and R11 together with the carbon atom to which they are bound may form a 3 – 6 membered saturated carbocyclic ring;

R12 is hydrogen or C1-C6 alkyl optionally substituted by halogen or C1-C6 alkoxy;

or R12 and any one of R8, R9, R, R', R10 or R11 together with the atoms to which they are bound may form a 4, 5, 6 or 7 membered azacyclic ring, which ring may optionally be substituted by halogen, cyano, hydroxyl, C1-C6 alkyl or C1-C6 alkoxy;

n is 0 or 1; and

R13 is C2-C6 alkenyl optionally substituted by C1-C6 alkyl, C1-C6 alkoxy or N,N-di-C1-C6 alkyl amino; C2-C6 alkynyl optionally substituted by C1-C6 alkyl or C1-C6 alkoxy; or C2-C6 alkylenyl oxide optionally substituted by C1-C6 alkyl.

In some embodiments, the BTK inhibitor of Formula I is chosen from: N-(3-(5-((1-Acryloylazetid-3-yl)oxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (E)-N-(3-(6-Amino-5-((1-(but-2-enoyl)azetid-3-yl)oxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(6-Amino-5-((1-propioloylazetid-3-yl)oxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(6-Amino-5-((1-(but-2-ynoyl)azetid-3-yl)oxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(5-((1-Acryloylpiperidin-4-yl)oxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(6-Amino-5-(2-(N-methylacrylamido)ethoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (E)-N-(3-(6-Amino-5-(2-(N-methylbut-2-enamido)ethoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(6-Amino-5-(2-(N-methylpropiolamido)ethoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (E)-N-(3-(6-Amino-5-(2-(4-methoxy-N-methylbut-2-enamido)ethoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(6-Amino-5-(2-(N-methylbut-2-ynamido)ethoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(2-((4-Amino-6-(3-(4-cyclopropyl-2-fluorobenzamido)-5-fluoro-2-methylphenyl)pyrimidin-5-yl)oxy)ethyl)-N-methyloxirane-2-carboxamide; N-(2-((4-Amino-6-(3-(6-cyclopropyl-8-fluoro-1-oxoisoquinolin-2(1H)-yl)phenyl)pyrimidin-5-yl)oxy)ethyl)-N-methylacrylamide; N-(3-(5-(2-Acrylamidoethoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(6-Amino-5-(2-(N-ethylacrylamido)ethoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(6-Amino-5-(2-(N-(2-fluoroethyl)acrylamido)ethoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(5-((1-Acrylamidocyclopropyl)methoxy)-6-aminopyrimidin-4-yl)-5-

fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (S)-N-(3-(5-(2-Acrylamidopropoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (S)-N-(3-(6-Amino-5-(2-(but-2-ynamido)propoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (S)-N-(3-(6-Amino-5-(2-(N-methylacrylamido)propoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (S)-N-(3-(6-Amino-5-(2-(N-methylbut-2-ynamido)propoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(6-Amino-5-(3-(N-methylacrylamido)propoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (S)-N-(3-(5-((1-Acryloylpyrrolidin-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (S)-N-(3-(6-Amino-5-((1-(but-2-ynoyl)pyrrolidin-2-yl)methoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (S)-2-(3-(5-((1-Acryloylpyrrolidin-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-(hydroxymethyl)phenyl)-6-cyclopropyl-3,4-dihydroisoquinolin-1(2H)-one; N-(2-((4-Amino-6-(3-(6-cyclopropyl-1-oxo-3,4-dihydroisoquinolin-2(1H)-yl)-5-fluoro-2-(hydroxymethyl)phenyl)pyrimidin-5-yl)oxy)ethyl)-N-methylacrylamide; N-(3-(5-(((2S,4R)-1-Acryloyl-4-methoxypyrrolidin-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(6-Amino-5-(((2S,4R)-1-(but-2-ynoyl)-4-methoxypyrrolidin-2-yl)methoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; 2-(3-(5-(((2S,4R)-1-Acryloyl-4-methoxypyrrolidin-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-(hydroxymethyl)phenyl)-6-cyclopropyl-3,4-dihydroisoquinolin-1(2H)-one; N-(3-(5-(((2S,4S)-1-Acryloyl-4-methoxypyrrolidin-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(6-Amino-5-(((2S,4S)-1-(but-2-ynoyl)-4-methoxypyrrolidin-2-yl)methoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(5-(((2S,4R)-1-Acryloyl-4-fluoropyrrolidin-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(6-Amino-5-(((2S,4R)-1-(but-2-ynoyl)-4-fluoropyrrolidin-2-yl)methoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (S)-N-(3-(5-((1-Acryloylazetidid-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (S)-N-(3-(6-Amino-5-((1-propioloylazetidid-2-yl)methoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (S)-2-(3-(5-((1-Acryloylazetidid-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-

fluoro-2-(hydroxymethyl)phenyl)-6-cyclopropyl-3,4-dihydroisoquinolin-1(2H)-one; (R)-N-(3-(5-((1-Acryloylazetid-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; (R)-N-(3-(5-((1-Acryloylpiperidin-3-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(5-(((2R,3S)-1-Acryloyl-3-methoxypyrrolidin-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; N-(3-(5-(((2S,4R)-1-Acryloyl-4-cyanopyrrolidin-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide; or N-(3-(5-(((2S,4S)-1-Acryloyl-4-cyanopyrrolidin-2-yl)methoxy)-6-aminopyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2-fluorobenzamide.

Unless otherwise provided, the chemical terms used above in describing the BTK inhibitor of Formula I are used according to their meanings as set out in International Application WO/2015/079417, which is herein incorporated by reference in its entirety.

Exemplary JAK Inhibitors

In one embodiment, a combination described herein includes an inhibitor of Janus kinase (JAK). In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, a colon cancer, a prostate cancer, a lung cancer, a breast cancer, or a pancreatic cancer), *e.g.*, a hematologic malignancy (*e.g.*, a leukemia (*e.g.*, a myeloid leukemia or a lymphocytic leukemia), *e.g.*, a lymphoma (*e.g.*, a non-Hodgkin lymphoma), or *e.g.*, a multiple myeloma.

In some embodiments, the JAK inhibitor is 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof, or a compound disclosed in PCT Publication No. WO 2007/070514.

In some embodiments, the JAK inhibitor, *e.g.*, 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof, or a compound disclosed in PCT Publication No. WO 2007/070514, is administered at a dose of about 400-600 mg (*e.g.*, per day), *e.g.*, about 400, 500, or 600 mg, or about 400-500 or 500-600 mg.

In some embodiment, the JAK inhibitor is ruxolitinib phosphate (also known as JAKAFI; Compound A18) or a compound disclosed in PCT Publication No. WO 2007/070514.

In one embodiment, the JAK inhibitor, *e.g.*, ruxolitinib phosphate (also known as JAKAFI; Compound A18) or a compound disclosed in PCT Publication No. WO 2007/070514, is administered at a dose of about 15-25 mg, *e.g.*, twice daily. In some embodiments, the dose is about 15, 20, or 25 mg, or about 15-20 or 20-25 mg.

Exemplary CRTH2 Inhibitors

In one embodiment, a combination described herein includes an inhibitor of chemoattractant receptor homologous to the T helper 2 cell (CRTH2). In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein.

In some embodiments, the CRTH2 inhibitor is QAV680 (CAS Registry Number: 872365-16-7). QAV680 is also known as 2-[2-methyl-1-[(4-methylsulfonylphenyl)methyl]pyrrolo[2,3-b]pyridin-3-yl]acetic acid. QAV680 is disclosed, *e.g.*, in Sandham *et al. Bioorg Med Chem.* 2013;21(21):6582-91.

In some embodiments, the CRTH2 inhibitor is QAW039 (CAS Number: 872365-14-5).

Other CRTH2 inhibitors that can be used in the combination include, *e.g.*, AZD1981, ARRY-502, setipiprant (ACT-453859), and ACT-129968.

Exemplary PFKFB3 inhibitors

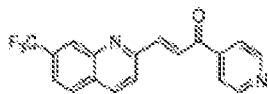
In one embodiment, a combination described herein includes an inhibitor of 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 (PFKFB3). In some embodiments, the combination is used to treat a cancer, *e.g.*, a cancer described herein, *e.g.*, a solid tumor (*e.g.*, an advanced solid tumor).

In some embodiments, the PFKFB3 inhibitor is PFK-158. PFK-158 is also known as ACT-PFK-158 or (E)-1-(pyridin-4-yl)-3-(7-(trifluoromethyl)quinolin-2-yl)-prop-2-en-1-one. PFK-158 is a derivative of 3-(3-pyridinyl)-1-[4-pyridinyl]-2-propen-1-one (3PO). PFKFB3, which catalyzes the conversion of fructose-6-phosphate to fructose-2,6-bisphosphate, is highly expressed and active in human cancer cells and plays a key role in increasing both glycolytic flux and proliferation of cancer cells. PFKFB3 inhibitors, *e.g.*, PFK-158, can bind to and inhibit the activity of PFKFB3, which leads to the inhibition of both the glycolytic pathway and glucose uptake by cancer cells. This prevents the production of macromolecules and energy that

causes the enhanced cellular proliferation in cancer cells as compared to that of normal, healthy cells. Depriving cancer cells of nutrients and energy leads to the inhibition of cancer cell growth.

PFK158 is disclosed, *e.g.*, at page 5 of WO 2013/148228.

In some embodiments, the PFKFB3 inhibitor has the following structure:



Pharmaceutical Compositions and Kits

In another aspect, the present invention provides compositions, *e.g.*, pharmaceutically acceptable compositions, which include combination molecules (*e.g.*, antibody molecules) described herein, formulated together with a pharmaceutically acceptable carrier. As used herein, "pharmaceutically acceptable carrier" includes any and all solvents, dispersion media, isotonic and absorption delaying agents, and the like that are physiologically compatible. The carrier can be suitable for intravenous, intramuscular, subcutaneous, parenteral, rectal, spinal or epidermal administration (*e.g.*, by injection or infusion).

The compositions of this invention may be in a variety of forms. These include, for example, liquid, semi-solid and solid dosage forms, such as liquid solutions (*e.g.*, injectable and infusible solutions), dispersions or suspensions, liposomes and suppositories. The preferred form depends on the intended mode of administration and therapeutic application. Typical preferred compositions are in the form of injectable or infusible solutions. The preferred mode of administration is parenteral (*e.g.*, intravenous, subcutaneous, intraperitoneal, intramuscular). In a preferred embodiment, the antibody is administered by intravenous infusion or injection. In another preferred embodiment, the antibody is administered by intramuscular or subcutaneous injection.

The phrases "parenteral administration" and "administered parenterally" as used herein means modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal, epidural and intrasternal injection and infusion.

Therapeutic compositions typically should be sterile and stable under the conditions of manufacture and storage. The composition can be formulated as a solution, microemulsion, dispersion, liposome, or other ordered structure suitable to high antibody concentration. Sterile injectable solutions can be prepared by incorporating the active compound (*i.e.*, antibody or antibody portion) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof. The proper fluidity of a solution can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prolonged absorption of injectable compositions can be brought about by including in the composition an agent that delays absorption, for example, monostearate salts and gelatin.

The combination molecules (*e.g.*, antibody molecules) can be administered by a variety of methods known in the art, although for many therapeutic applications, the preferred route/mode of administration is intravenous injection or infusion. In one embodiment, the antibody molecule is administered by intravenous infusion at a rate of more than 20 mg/min, *e.g.*, 20-40 mg/min, and preferably greater than or equal to 40 mg/min to reach a dose of about 35 to 440 mg/m², preferably about 70 to 310 mg/m², and more preferably, about 110 to 130 mg/m². In another embodiment, the antibody molecule is administered by intravenous infusion at a rate of less than 10mg/min; preferably less than or equal to 5 mg/min to reach a dose of about 1 to 100 mg/m², preferably about 5 to 50 mg/m², about 7 to 25 mg/m² and more preferably, about 10 mg/m². As will be appreciated by the skilled artisan, the route and/or mode of administration will vary depending upon the desired results. In certain embodiments, the active compound may be prepared with a carrier that will protect the compound against rapid release, such as a controlled release formulation, including implants, transdermal patches, and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and

polylactic acid. Many methods for the preparation of such formulations are patented or generally known to those skilled in the art. *See, e.g., Sustained and Controlled Release Drug Delivery Systems*, J. R. Robinson, ed., Marcel Dekker, Inc., New York, 1978.

In certain embodiments, an antibody molecule can be orally administered, for example, with an inert diluent or an assimilable edible carrier. The compound (and other ingredients, if desired) may also be enclosed in a hard or soft shell gelatin capsule, compressed into tablets, or incorporated directly into the subject's diet. For oral therapeutic administration, the compounds may be incorporated with excipients and used in the form of ingestible tablets, buccal tablets, troches, capsules, elixirs, suspensions, syrups, wafers, and the like. To administer a compound of the invention by other than parenteral administration, it may be necessary to coat the compound with, or co-administer the compound with, a material to prevent its inactivation. Therapeutic compositions can also be administered with medical devices known in the art.

Dosage regimens are adjusted to provide the optimum desired response (*e.g.*, a therapeutic response). For example, a single bolus may be administered, several divided doses may be administered over time or the dose may be proportionally reduced or increased as indicated by the exigencies of the therapeutic situation. It is especially advantageous to formulate parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subjects to be treated; each unit contains a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on (a) the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and (b) the limitations inherent in the art of compounding such an active compound for the treatment of sensitivity in individuals.

An exemplary, non-limiting range for a therapeutically or prophylactically effective amount of an antibody molecule is 0.1-30 mg/kg, more preferably 1-25 mg/kg. Dosages and therapeutic regimens of the anti-LAG-3 antibody molecule can be determined by a skilled artisan. In certain embodiments, the anti-LAG-3 antibody molecule is administered by injection (*e.g.*, subcutaneously or intravenously) at a dose of about 1 to 40 mg/kg, *e.g.*, 1 to 30 mg/kg, *e.g.*, about 5 to 25 mg/kg, about 10 to 20 mg/kg, about 1 to 5 mg/kg, 1 to 10 mg/kg, 5 to 15 mg/kg, 10 to 20 mg/kg, 15 to 25 mg/kg, or about 3 mg/kg. The dosing schedule can vary from *e.g.*, once a

week to once every 2, 3, or 4 weeks. In one embodiment, the anti-LAG-3 antibody molecule is administered at a dose from about 10 to 20 mg/kg every other week. The antibody molecule can be administered by intravenous infusion at a rate of more than 20 mg/min, *e.g.*, 20-40 mg/min, and preferably greater than or equal to 40 mg/min to reach a dose of about 35 to 440 mg/m², preferably about 70 to 310 mg/m², and more preferably, about 110 to 130 mg/m². In embodiments, the infusion rate of about 110 to 130 mg/m² achieves a level of about 3 mg/kg. In one embodiment, the anti-LAG-3 antibody molecule is administered (*e.g.*, intravenously) at a dose from about 3 to 800 mg, *e.g.*, about 3, 20, 80, 240, or 800 mg. In certain embodiments, the anti-LAG-3 antibody molecule is administered alone at a dose from about 20 to 800 mg, *e.g.*, about 3, 20, 80, 240, or 800 mg. In other embodiments, the anti-LAG-3 antibody molecule is administered at a dose from about 3 to 240 mg, *e.g.*, about 3, 20, 80, or 240 mg, in combination with a second agent or therapeutic modality, *e.g.*, a second agent or therapeutic modality described herein. In one embodiment, the anti-LAG-3 antibody molecule is administered every 2 weeks (*e.g.*, during weeks 1, 3, 5, 7) during each 8 week cycle, *e.g.*, up to 96 weeks.

The antibody molecule can be administered by intravenous infusion at a rate of more than 20 mg/min, *e.g.*, 20-40 mg/min, and preferably greater than or equal to 40 mg/min to reach a dose of about 35 to 440 mg/m², preferably about 70 to 310 mg/m², and more preferably, about 110 to 130 mg/m². In embodiments, the infusion rate of about 110 to 130 mg/m² achieves a level of about 3 mg/kg. In other embodiments, the antibody molecule is administered by intravenous infusion at a rate of less than 10 mg/min, *e.g.*, less than or equal to 5 mg/min to reach a dose of about 1 to 100 mg/m², *e.g.*, about 5 to 50 mg/m², about 7 to 25 mg/m², and more preferably, about 10 mg/m². In some embodiments, the antibody is infused over a period of about 30 min.

It is to be noted that dosage values may vary with the type and severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that dosage ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed composition.

The pharmaceutical compositions of the invention may include a "therapeutically effective amount" or a "prophylactically effective amount" of an antibody or antibody portion of the invention. A "therapeutically effective amount" refers to an amount effective, at dosages and

for periods of time necessary, to achieve the desired therapeutic result. A therapeutically effective amount of the modified antibody or antibody fragment may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the antibody or antibody portion to elicit a desired response in the individual. A therapeutically effective amount is also one in which any toxic or detrimental effects of the modified antibody or antibody fragment is outweighed by the therapeutically beneficial effects. A "therapeutically effective dosage" preferably inhibits a measurable parameter, *e.g.*, tumor growth rate by at least about 20%, more preferably by at least about 40%, even more preferably by at least about 60%, and still more preferably by at least about 80% relative to untreated subjects. The ability of a compound to inhibit a measurable parameter, *e.g.*, cancer, can be evaluated in an animal model system predictive of efficacy in human tumors. Alternatively, this property of a composition can be evaluated by examining the ability of the compound to inhibit, such inhibition *in vitro* by assays known to the skilled practitioner

A "prophylactically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired prophylactic result. Typically, since a prophylactic dose is used in subjects prior to or at an earlier stage of disease, the prophylactically effective amount will be less than the therapeutically effective amount.

Also within the scope of the invention is a kit comprising an antibody molecule described herein. The kit can include one or more other elements including: instructions for use; other reagents, *e.g.*, a label, a therapeutic agent, or an agent useful for chelating, or otherwise coupling, an antibody to a label or therapeutic agent, or a radioprotective composition; devices or other materials for preparing the antibody for administration; pharmaceutically acceptable carriers; and devices or other materials for administration to a subject.

Uses of Anti-LAG-3 Antibody Molecules

The combinations, *e.g.*, the anti-LAG-3 antibody molecules disclosed herein, have *in vitro* and *in vivo* diagnostic, as well as therapeutic and prophylactic utilities. For example, these molecules can be administered to cells in culture, *in vitro* or *ex vivo*, or to a subject, *e.g.*, a human subject, *e.g.*, *in vivo*, to enhance immunity. In one embodiment, the anti-LAG-3 antibody molecules enhance an immune response in a subject, *e.g.*, by blockade of LAG-3 (*e.g.*, by blockade of LAG-3 binding to an MHC molecule or other ligands).

Accordingly, in one aspect, the invention provides a method of modifying an immune response in a subject comprising administering to the subject the antibody, molecule described herein, such that the immune response in the subject is modified. In one embodiment, the immune response is enhanced, stimulated or up-regulated. In some embodiments, the anti-LAG-3 antibody molecule restores, enhances or stimulates an antigen-specific T cell response, *e.g.*, interleukin-2 (IL-2) or interferon-gamma (IFN- γ), production in an antigen-specific T cell response, in the subject. In some embodiments, the immune response is an anti-tumor response. The methods and compositions described herein are suitable for treating human patients having a disorder that can be treated by augmenting the T-cell mediated immune response. For example, the anti-LAG-3 antibody molecules, alone or in combination, can be administered to a subject to treat, prevent, and/or diagnose a variety of disorders, such as cancers (melanoma or hepatic cancers), or an infectious disorder.

As used herein, the term "subject" is intended to include human and non-human animals. In one embodiment, the subject is a human subject, *e.g.*, a human patient having a disorder or condition characterized by abnormal LAG-3 functioning. The term "non-human animals" of the invention includes mammals and non-mammals, such as non-human primates. In one embodiment, the subject is a human. In one embodiment, the subject is a human patient in need of enhancement of an immune response. In one embodiment, the subject has, or is at risk of, having a disorder described herein, *e.g.*, a cancer or an infectious disorder as described herein. In certain embodiments, the subject is, or is at risk of being, immunocompromised. For example, the subject is undergoing or has undergone a chemotherapeutic treatment and/or radiation therapy. Alternatively, or in combination, the subject is, or is at risk of being, immunocompromised as a result of an infection. For example, the methods and compositions described herein can enhance a number of immune activities. In one embodiment, the subject has increased number or activity of tumour-infiltrating T lymphocytes (TILs). In another embodiment, the subject has increased expression or activity of interferon-gamma (IFN- γ). In yet another embodiment, the subject has decreased PD-L1 expression or activity. Accordingly, in certain embodiments, any (*e.g.*, one, two, three, or all) of TILs, IFN- γ , CD8, or PD-L1, can be used as biomarkers for the anti-LAG-3 immunotherapies described herein.

Therapeutic Uses

Blockade of LAG-3 by antibodies can enhance an immune response to cancerous cells in a subject. Similar to CD4, LAG-3 interacts with MHC class II molecules but, unlike CD4, LAG-3 does not interact with the human immunodeficiency virus gp120 protein (Baixeras *et al.* (1992) *J. Exp. Med.* 176:327-337). Studies have demonstrated direct and specific binding of LAG-3 to MHC class II on the cell surface (Huard *et al.* (1996) *Eur. J. Immunol.* 26:1180-1186). The LAG-3/MHC class II interaction plays a role in down-regulating antigen-dependent stimulation of CD4⁺ and CD8⁺ T lymphocytes. The addition of anti-LAG-3 antibodies can result in increased T cell proliferation, higher expression of activation antigens such as CD25, and higher concentrations of cytokines such as interferon-gamma and interleukin-4 (Huard *et al.* (1994) *Eur. J. Immunol.* 24:3216-3221). The intra-cytoplasmic region of LAG-3 can also interact with LAP, a signal transduction molecule involved in the downregulation of the CD3/TCR activation pathway (Iouzalen *et al.* (2001) *Eur. J. Immunol.* 31:2885-2891). Further, LAG-3 contributes to the suppressor activity of CD4⁺CD25⁺ regulatory T cells (T_{reg}). T_{reg} cells express LAG-3 upon activation and antibodies to LAG-3 inhibit suppression by induced T_{reg} cells (Huang, C. *et al.* (2004) *Immunity* 21:503-513). LAG-3 can also negatively regulate T cell homeostasis by regulatory T cells in both T cell-dependent and independent mechanisms (Workman, C. J. and Vignali, D. A. (2005) *J. Immunol.* 174:688-695). Thus, inhibition of LAG-3 can result in augmenting an immune response.

Accordingly, in one aspect, a method of treating (*e.g.*, reducing or inhibiting) a cancer or tumor in a subject is provided. The method comprises administering to the subject an anti-LAG-3 antibody molecule described herein, *e.g.*, a therapeutically effective amount of an anti-LAG-3 antibody molecule, alone or in combination, *e.g.*, with one or more agents or procedures. In one embodiment, an anti-LAG-3 antibody molecule may be used alone to inhibit the growth of cancerous tumors. Alternatively, an anti-LAG-3 antibody may be used in combination with one or more of: a standard of care treatment (*e.g.*, for cancers or infectious disorders), another antibody, an immunomodulator (*e.g.*, an activator of a costimulatory molecule or an inhibitor of an inhibitory molecule); a vaccine, *e.g.*, a therapeutic cancer vaccine; or other forms of cellular immunotherapy, as described below. In certain embodiments, the anti-LAG-3 antibody molecule is administered in combination with a modulator of a costimulatory molecule (*e.g.*, an agonist of

a costimulatory molecule) or a modulator of an inhibitory molecule (*e.g.*, an inhibitor of an immune checkpoint inhibitor), *e.g.*, as described herein.

In one embodiment, the methods are suitable for the treatment of cancer *in vivo*. To achieve antigen-specific enhancement of immunity, the anti-LAG-3 antibody molecule can be administered together with an antigen of interest. When antibodies to LAG-3 are administered in combination with one or more agents, the combination can be administered in either order or simultaneously.

In certain embodiments, a method of treating a subject, *e.g.*, reducing or ameliorating, a hyperproliferative condition or disorder (*e.g.*, a cancer), *e.g.*, solid tumor, a hematological cancer, soft tissue tumor, or a metastatic lesion, in a subject is provided. The method includes administering to the subject one or more of the combinations described herein.

As used herein, the term "cancer" is meant to include all types of cancerous growths or oncogenic processes, metastatic tissues or malignantly transformed cells, tissues, or organs, irrespective of histopathologic type or stage of invasiveness. Examples of cancerous disorders include, but are not limited to, solid tumors, hematological cancers, soft tissue tumors, and metastatic lesions. Examples of solid tumors include malignancies, *e.g.*, sarcomas, and carcinomas (including adenocarcinomas and squamous cell carcinomas), of the various organ systems, such as those affecting liver, lung, breast, lymphoid, gastrointestinal (*e.g.*, colon), genitourinary tract (*e.g.*, renal, urothelial cells), prostate and pharynx. Adenocarcinomas include malignancies such as most colon cancers, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine and cancer of the esophagus. Squamous cell carcinomas include malignancies such as those affecting the lung, esophagus, skin, head and neck region, oral cavity, anus, and cervix. Metastatic lesions of the aforementioned cancers can also be treated or prevented using the methods and compositions of the invention.

Exemplary cancers whose growth can be inhibited using the combinations disclosed herein include cancers typically responsive to immunotherapy. Non-limiting examples of preferred cancers for treatment include melanoma (*e.g.*, an advanced stage (*e.g.*, stage II-IV) melanoma or an HLA-A2 positive melanoma), pancreatic cancer (*e.g.*, advanced pancreatic cancer), solid tumors, breast cancer (*e.g.*, metastatic breast carcinoma, a breast cancer that does not express one, two or all of estrogen receptor, progesterone receptor, or Her2/neu, *e.g.*, a triple

negative breast cancer), and renal cell carcinoma (*e.g.*, advanced (*e.g.*, stage IV) or metastatic renal cell carcinoma (MRCC)). Additionally, refractory or recurrent malignancies can be treated using the antibody molecules described herein.

Examples of other cancers that can be treated include, *e.g.*, a solid tumor, *e.g.*, prostate cancer (*e.g.*, hormone refractory prostate adenocarcinoma), colon cancer, lung cancer (*e.g.*, non-small cell lung cancer), bone cancer, skin cancer, cancer of the head or neck (*e.g.*, HPV+ squamous cell carcinoma), cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Merkel cell cancer, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, or squamous cell cancer or a hematological malignancy, *e.g.*, Hodgkin lymphoma, non-Hodgkin lymphoma, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia (*e.g.*, relapsed or refractory chronic lymphocytic leukemia), solid tumors of childhood, lymphocytic lymphoma, multiple myeloma, myelodysplastic syndromes, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers including those induced by asbestos (*e.g.*, mesothelioma), and combinations of said cancers. Treatment of metastatic cancers, *e.g.*, metastatic cancers that express MHC class II molecules or LAG-3, can be effected using the antibody molecules described herein.

While not wishing to be bound by theory, in some embodiments, a patient is more likely to respond to treatment with anti-LAG-3, alone or in combination with anti-PD-1 or PD-L1 antibody molecules (optionally in combination with one or more agents as described herein) if the patient has a cancer that highly expresses PD-L1, and/or the cancer is infiltrated by anti-

tumor immune cells, *e.g.*, TILs. The anti-tumor immune cells may be positive for CD8, PD-L1, and/or IFN- γ ; thus levels of CD8, PD-L1, and/or IFN- γ can serve as a readout for levels of TILs in the microenvironment. In certain embodiments, the cancer microenvironment is referred to as triple-positive for PD-L1/CD8/IFN- γ .

Accordingly, in certain aspects, this application provides methods of determining whether a tumor sample is positive for one or more of PD-L1, CD8, and IFN- γ , and if the tumor sample is positive for one or more, *e.g.*, two, or all three, of the markers, then administering to the patient a therapeutically effective amount of an anti-PD-1 antibody molecule, optionally in combination with one or more other immunomodulators or anti-cancer agents.

In the following indications, a large fraction of patients are triple-positive for PD-L1/CD8/IFN- γ : lung cancer (squamous); lung cancer (adenocarcinoma); head and neck cancer; stomach cancer; NSCLC; HNSCC; gastric cancers (*e.g.*, MSIhi and/or EBV+); CRC (*e.g.*, MSIhi); nasopharyngeal cancer (NPC); cervical cancer (*e.g.*, squamous); thyroid cancer *e.g.*, papillary thyroid; melanoma; TN breast cancer; and DLBCL (Diffuse Large B-Cell Lymphoma). In breast cancer generally and in colon cancer generally, a moderate fraction of patients is triple-positive for PD-L1/CD8/IFN- γ . In the following indications, a small fraction of patients are triple-positive for PD-L1/CD8/IFN- γ : ER+ breast cancer, and pancreatic cancer. These findings are discussed further in Example 4. Regardless of whether a large or small fraction of patients is triple-positive for these markers, screening the patients for these markers allows one to identify a fraction of patients that has an especially high likelihood of responding favorably to therapy with a LAG-3 antibody, alone or in combination with a PD-1 antibody (*e.g.*, a blocking PD-1 antibody), optionally in combination with one or more other immunomodulators (*e.g.*, an anti-TIM-3 antibody molecule or an anti-PD-L1 antibody molecule) and/or anti-cancer agents, *e.g.*, those listed in Table 7 and disclosed in the publications listed in Table 7.

In some embodiments, the cancer sample is classified as triple-positive for PDL1/CD8/IFN- γ . This measurement can roughly be broken down into two thresholds: whether an individual cell is classified as positive, and whether the sample as a whole is classified as positive. First, one can measure, within an individual cell, the level of PD-L1, CD8, and/or IFN- γ . In some embodiments, a cell that is positive for one or more of these markers is a cell that has a higher level of the marker compared to a control cell or a reference value. For example, in some embodiments, a high level of PD-L1 in a given cell is a level higher than the level of PD-

L1 in a corresponding non-cancerous tissue in the patient. As another example, in some embodiments, a high level of CD8 or IFN- γ in a given cell is a level of that protein typically seen in a TIL. Second, one can also measure the percentage of cells in the sample that are positive for PD-L1, CD8, and/or IFN- γ . (It is not necessary for a single cell to express all three markers.) In some embodiments, a triple positive sample is one that has a high percentage of cells, *e.g.*, higher than a reference value or higher than a control sample, that are positive for these markers.

In other embodiments, one can measure the levels of PD-L1, CD8, and/or IFN- γ overall in the sample. In this case, a high level of CD8 or IFN- γ in the sample can be the level of that protein typically seen in a tumor infiltrated with TIL. Similarly, a high level of PD-L1 can be the level of that protein typically seen in a tumor sample, *e.g.*, a tumor microenvironment.

The identification of subsets of patients that are triple-positive for PD-L1/CD8/IFN- γ , as shown in Example 4 herein, reveals certain sub-populations of patients that are likely to be especially responsive to PD-1 antibody therapy. For instance, many IM-TN (immunomodulatory, triple negative) breast cancer patients are triple-positive for PDL1/CD8/IFN- γ . IM-TN breast cancer is described in, *e.g.*, Brian D. Lehmann *et al.*, “Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies”, *J Clin Invest.* Jul 1, 2011; 121(7): 2750–2767. Triple-negative breast cancers are those that do not express estrogen receptor (ER), progesterone receptor (PR) and Her2/neu. These cancers are difficult to treat because they are typically not responsive to agents that target ER, PR, and Her2/neu. Triple-negative breast cancers can be further subdivided into different classes, one of which is immunomodulatory. As described in Lehmann *et al.*, IM-TN breast cancer is enriched for factors involved in immune cell processes, for example, one or more of immune cell signaling (*e.g.*, TH1/TH2 pathway, NK cell pathway, B cell receptor signaling pathway, DC pathway, and T cell receptor signaling), cytokine signaling (*e.g.*, cytokine pathway, IL-12 pathway, and IL-7 pathway), antigen processing and presentation, signaling through core immune signal transduction pathways (*e.g.*, NF κ B, TNF, and JAK/STAT signaling), genes involved in T-cell function, immune transcription, interferon (IFN) response and antigen processing. Accordingly, in some embodiments, the cancer treated is a cancer that is, or is determined to be, positive for one or more marker of IM-TN breast cancer, *e.g.*, a factor that promotes one or more of immune cell signaling (*e.g.*, TH1/TH2 pathway, NK cell pathway, B cell receptor signaling pathway, DC pathway, and T cell receptor signaling), cytokine

signaling (*e.g.*, cytokine pathway, IL-12 pathway, and IL-7 pathway), antigen processing and presentation, signaling through core immune signal transduction pathways (*e.g.*, NF κ B, TNF, and JAK/STAT signaling), genes involved in T-cell function, immune transcription, interferon (IFN) response and antigen processing.

As another example, it is shown herein that a subset of colon cancer patients having high MSI (microsatellite instability) is also triple-positive for PD-L1/CD8/IFN- γ . Accordingly, in some embodiments, a LAG-3 antibody, *e.g.*, a LAG-3 antibody as described herein, alone or in combination with a PD-1 antibody, (optionally in combination with one or more immunomodulators such as a TIM-3 antibody or a PD-L1 antibody, and one or more anti-cancer agents, *e.g.*, an anti-cancer agent described in Table 7 or in a publication in Table 7) is administered to a patient who has, or who is identified as having, colon cancer with high MSI, thereby treating the cancer. In some embodiments, a cell with high MSI is a cell having MSI at a level higher than a reference value or a control cell, *e.g.*, a non-cancerous cell of the same tissue type as the cancer.

As another example, it is shown herein that a subset of gastric cancer patients having high MSI, and/or which is EBV+, is also triple-positive for PD-L1/CD8/IFN- γ . Accordingly, in some embodiments, a LAG-3 antibody, *e.g.*, a LAG-3 antibody as described herein, alone or in combination with a PD-1 antibody, (optionally in combination with one or more immunomodulators such as a TIM-3 antibody or a PD-L1 antibody, and one or more anti-cancer agents, *e.g.*, an anti-cancer agent described in Table 7 or in a publication in Table 7) is administered to a patient who has, or who is identified as having, gastric cancer with high MSI and/or EBV+, thereby treating the cancer. In some embodiments, a cell with high MSI is a cell having MSI at a level higher than a reference value or a control cell, *e.g.*, a non-cancerous cell of the same tissue type as the cancer.

Additionally disclosed herein are methods of assaying a cancer for PD-L1, and then treating the cancer with a LAG-3 antibody, alone or in combination with a PD-1 antibody. As described in Example 5 herein, a cancer sample can be assayed for PD-L1 protein levels or mRNA levels. A sample having levels of PD-L1 (protein or mRNA) higher than a reference value or a control cell (*e.g.*, a non-cancerous cell) can be classified as PD-L1 positive. Accordingly, in some embodiments, a LAG-3 antibody, *e.g.*, a LAG-3 antibody as described herein, alone or in combination with a PD-1 antibody, (optionally in combination with one or

more anti-cancer agents) is administered to a patient who has, or who is identified as having, a cancer that is PD-L1 positive. The cancer may be, *e.g.*, non-small cell lung (NSCLC) adenocarcinoma (ACA), NSCLC squamous cell carcinoma (SCC), or hepatocellular carcinoma (HCC).

In some embodiments, the methods herein involve using a LAG-3 antibody, *e.g.*, a LAG-3 antibody as described herein, *e.g.*, in combination with a PD-1 antibody, for treating a cancer that is (or is identified as being) positive for PD-L1. In some embodiments, the cancer is colorectal cancer (*e.g.*, MSI-high), gastric cancer (*e.g.*, MSI-high and/or EBV+), NPC, cervical cancer, breast cancer (*e.g.*, TN breast cancer), and ovarian cancer. In some embodiments, the cancer is NSCLC, melanoma, or HNSCC. In some embodiments, the LAG-3 antibody is administered at a dose of, *e.g.*, 1, 3, 10, or 20 mg/kg.

Based on, *e.g.* Example 4 herein, it was found that certain gastric cancers that are triple-positive for PDL1/CD8/IFN- γ are also positive for PIK3CA. Accordingly, in some embodiments, a cancer can be treated with a LAG-3 antibody, alone or in combination with an anti-PD1 antibody molecule (optionally in combination with one or more immunomodulators, *e.g.*, an anti-TIM-3 antibody molecule or an anti-PD-L1 antibody molecule) and an agent that inhibits PIK3CA. Exemplary agents in this category are described in Stein RC (September 2001). "Prospects for phosphoinositide 3-kinase inhibition as a cancer treatment". *Endocrine-related Cancer* 8 (3): 237–48 and Marone R, Cmiljanovic V, Giese B, Wymann MP (January 2008). "Targeting phosphoinositide 3-kinase: moving towards therapy". *Biochimica et Biophysica Acta* 1784 (1): 159–85.

Based on, *e.g.* Example 4 herein, CRC, *e.g.*, a patient that has (or is identified as having) MSI-high CRC may be treated with a LAG-3 antibody, alone or in combination with a PD-1 antibody, optionally in combination with a therapeutic that targets one or both of RNF43 and BRAF. For instance, these cancers may be treated with a LAG-3 antibody and a PD-1 antibody, optionally in combination with one or more therapeutics that target one or more of RNF43 and BRAF. In embodiments, the one or more therapeutics include an anti-cancer agent described in Table 7 or a publication listed in Table 7. PD-1 inhibitors, *e.g.*, antibodies, are described herein. RNF43 can be inhibited, *e.g.*, with an antibody, small molecule (*e.g.*, 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28)), siRNA, or a Rspo ligand or derivative thereof. BRAF inhibitors (*e.g.*, vemurafenib or dabrafenib) are described

herein.

Based on, *e.g.*, Example 4 herein, a patient that has (or is identified as having) a squamous cell lung cancer may be treated with a LAG-3 antibody molecule in combination with a therapeutic that targets PD-1, *e.g.*, a PD-1 antibody molecule, and optionally with one or more anti-cancer agents, *e.g.*, an anti-cancer agent described in Table 7 or in a publication in Table 7, or a therapeutic that targets TIM-3, *e.g.*, a TIM-3 antibody.

Based on, *e.g.*, Example 4 herein, a patient that has (or is identified as having) a thyroid cancer may be treated with a LAG-3 antibody molecule, alone or in combination with a PD-1 antibody molecule, optionally in combination with a therapeutic that targets BRAF, and optionally in combination with one or more immunomodulators, *e.g.*, an anti-TIM-3 antibody molecule, and an anti-PD-L1 antibody molecule. BRAF inhibitors (*e.g.*, vemurafenib or dabrafenib) are described herein, *e.g.*, in Table 7 and the publications listed in Table 7.

In some embodiments, the therapies here can be used to treat a patient that has (or is identified as having) a cancer associated with an infection, *e.g.*, a viral or bacterial infection. Exemplary cancers include cervical cancer, anal cancer, HPV-associated head and neck squamous cell cancer, HPV-associated esophageal papillomas, HHV6-associated lymphomas, EBV-associated lymphomas (including Burkitt lymphoma), Gastric MALT lymphoma, other infection-associated MALT lymphomas, HCC, Kaposi's sarcoma. In other embodiments, the cancer is a hematological cancer including but is not limited to a leukemia or a lymphoma. For example, the anti-LAG-3 antibody molecule can be used to treat cancers and malignancies including, but not limited to, *e.g.*, acute leukemias including but not limited to, *e.g.*, B-cell acute lymphoid leukemia ("BALL"), T-cell acute lymphoid leukemia ("TALL"), acute lymphoid leukemia (ALL); one or more chronic leukemias including but not limited to, *e.g.*, chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL); additional hematologic cancers or hematologic conditions including, but not limited to, *e.g.*, B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, Follicular lymphoma, Hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin's lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and "preleukemia" which are a diverse collection of

hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells, and the like.

In one embodiment, the cancer is a melanoma, *e.g.*, an advanced melanoma. In one embodiment, the cancer is an advanced or unresectable melanoma that does not respond to other therapies. In other embodiments, the cancer is a melanoma with a BRAF mutation (*e.g.*, a BRAF V600 mutation). In yet other embodiments, the anti-LAG-3 antibody molecule is administered after treatment with an anti-CTLA4 antibody (*e.g.*, ipilimumab) with or without a BRAF inhibitor (*e.g.*, vemurafenib or dabrafenib).

Methods and compositions disclosed herein are useful for treating metastatic lesions associated with the aforementioned cancers.

Exemplary non-limiting combinations and uses of the anti-LAG-3 antibody molecules are disclosed in US 2015/0259420 (USSN 14/657,260), entitled "Antibody Molecules to LAG-3 and Uses Thereof," incorporated by reference in its entirety.

In certain embodiments, the combination includes an anti-LAG-3 antibody molecule in combination with a modulator of a costimulatory molecule or an inhibitory molecule, *e.g.*, a co-inhibitory ligand or receptor.

In one embodiment, the anti-LAG-3 antibody molecule is administered in combination with a modulator, *e.g.*, agonist, of a costimulatory molecule. In one embodiment, the agonist of the costimulatory molecule is chosen from an agonist (*e.g.*, an agonistic antibody or soluble fusion) of OX40, CD2, CD27, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3, or CD83 ligand.

In another embodiment, the anti-LAG-3 antibody molecule is used in combination with a costimulatory molecule, *e.g.*, an agonist associated with a positive signal that includes a costimulatory domain of CD28, CD27, ICOS and GITR.

In one embodiment, the anti-LAG-3 antibody molecule is administered in combination with an inhibitor of an inhibitory molecule (*e.g.*, an inhibitor of an immune checkpoint molecule). It will be understood by those of ordinary skill in the art, that the term "immune checkpoints" means a group of molecules on the cell surface of CD4 and CD8 T cells. These molecules can effectively serve as "brakes" to down-modulate or inhibit an anti-tumor immune response. Immune checkpoint molecules include, but are not limited to, Programmed Death 1

(PD-1), Cytotoxic T-Lymphocyte Antigen 4 (CTLA-4), B7H1, B7H4, OX-40, CD137, CD40, and TIM-3, which directly inhibit immune cells, immunotherapeutic agents which can act as immune checkpoint inhibitors useful in the methods of the present invention, include, but are not limited to, inhibitors of PD-1, PD-L1, PD-L2, CTLA-4, TIM-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, CEACAM (*e.g.*, CEACAM-1 and/or CEACAM-5), and/or TGF beta. Inhibition of an inhibitory molecule can be performed by inhibition at the DNA, RNA or protein level. In embodiments, an inhibitory nucleic acid (*e.g.*, a dsRNA, siRNA or shRNA), can be used to inhibit expression of an inhibitory molecule. In other embodiments, the inhibitor of an inhibitory signal is, a polypeptide *e.g.*, a soluble ligand, or an antibody or antibody fragment, that binds to the inhibitory molecule. Exemplary TIM-3 antibody molecules include, but are not limited to, MBG220, MBG227, and MBG219. Exemplary TIGIT inhibitors include, but are not limited to, 10A7 and 1F4 (Roche).

Further examples of modulators include but are not limited to B7-H5, ENTPD1, ENTPD2, SIGGIR, B7-1, B7-2, VSIG4, TIM-1, CD200, RANKL, and P2X7.

In one embodiment, the inhibitor is a soluble ligand (*e.g.*, a CTLA-4-Ig or a TIM-3-Ig), or an antibody or antibody fragment that binds to PD-L1, PD-L2 or CTLA4. For example, the anti-LAG-3 antibody molecule can be administered in combination with an anti-CTLA-4 antibody, *e.g.*, ipilimumab. Exemplary anti-CTLA4 antibodies include Tremelimumab (IgG2 monoclonal antibody available from Pfizer, formerly known as ticilimumab, CP-675,206); and Ipilimumab (CTLA-4 antibody, also known as MDX-010, CAS No. 477202-00-9). In one embodiment, the anti-LAG-3 antibody molecule is administered after treatment, *e.g.*, after treatment of a melanoma, with an anti-CTLA4 antibody (*e.g.*, ipilimumab) with or without a BRAF inhibitor (*e.g.*, vemurafenib or dabrafenib). In one embodiment, the anti-CTLA-4 antibody, *e.g.*, ipilimumab, is administered at a dose of about 3 mg/kg. The anti-LAG-3 antibody molecule can be administered in combination at a dose from about 20 to 800 mg, *e.g.*, about 20, 80, 240, or 800 mg. In one embodiment, the anti-LAG-3 antibody molecule is administered every 2 weeks (*e.g.*, during weeks 1, 3, 5, 7) during each 8 week cycle, *e.g.*, up to 96 weeks.

In another embodiment, the anti-LAG-3 antibody molecule is administered in combination with an anti-PD-1 antibody molecule. Exemplary doses that can be use include a dose of anti-PD-1 antibody molecule of about 1 to 10 mg/kg, *e.g.*, 3 mg/kg. The anti-LAG-3

antibody molecule can be administered in combination at a dose from about 20 to 800 mg, *e.g.*, about 20, 80, 240, or 800 mg. In one embodiment, the anti-LAG-3 antibody molecule is administered every 2 weeks (*e.g.*, during weeks 1, 3, 5, 7) during each 8 week cycle, *e.g.*, up to 96 weeks.

Immune inhibitory molecules, *e.g.*, PD-1 and LAG-3, can regulate, *e.g.*, synergistically, T-cell function to promote tumoral immune escape. In another embodiment, the anti-LAG-3 antibody molecule is administered in combination with an anti-TIM-3 antibody molecule. In still another embodiment, the anti-LAG-3 antibody molecule is administered in combination with an anti-PD-L1 antibody molecule. In yet other embodiments, the anti-LAG-3 antibody molecule is administered in combination with an anti-PD-1 antibody and an anti-TIM-3 antibody. In certain embodiments, the anti-LAG-3 antibody molecule is administered in combination with an anti-PD-1 antibody and an anti-PD-L1 antibody. In certain embodiments, the anti-LAG-3 antibody molecule is administered in combination with an anti-TIM-3 antibody and an anti-PD-L1 antibody. The combination of antibodies recited herein can be administered separately, *e.g.*, as separate antibodies, or linked, *e.g.*, as a bispecific or trispecific antibody molecule. In another embodiment, the anti-LAG-3 antibody molecule is administered in combination with a CEACAM inhibitor (*e.g.*, CEACAM-1 and/or CEACAM-5 inhibitor), *e.g.*, an anti-CEACAM antibody molecule. In another embodiment, the anti-LAG-3 antibody molecule, is administered in combination with a CEACAM-1 inhibitor, *e.g.*, an anti-CEACAM-1 antibody molecule. In another embodiment, the anti-LAG-3 antibody molecule is administered in combination with a CEACAM-5 inhibitor, *e.g.*, an anti-CEACAM-5 antibody molecule. In one embodiment, a bispecific antibody that includes an anti-LAG-3 antibody molecule and an anti-PD-1 or anti-LAG-3 antibody is administered. In certain embodiments, the combination of antibodies recited herein is used to treat a cancer, *e.g.*, a cancer as described herein (*e.g.*, a solid tumor). The efficacy of the aforesaid combinations can be tested in animal models known in the art. For example, the animal models to test the synergistic effect of anti-LAG-3 and anti-PD-1 are described, *e.g.*, in Woo *et al.* (2012) *Cancer Res.* 72(4):917-27).

In one embodiment, the inhibitor of CEACAM (*e.g.*, CEACAM-1 and/or CEACAM-5) is an anti-CEACAM antibody molecule. Without wishing to be bound by theory, CEACAM-1 has been described as a ligand and partner of TIM-3 (see *e.g.*, WO 2014/022332). Synergistic *in vivo* effect of the combination of anti-TIM-3 and anti-CEACAM-1 antibodies have been

detected in xenograft cancer models (*see e.g.*, WO 2014/022332). Tumors are believed to use CEACAM-1 or CEACAM-5 to inhibit the immune system, as described in, *e.g.*, Markel *et al. J Immunol.* 2002 Mar 15;168(6):2803-10; Markel *et al. J Immunol.* 2006 Nov 1;177(9):6062-71; Markel *et al. Immunology.* 2009 Feb;126(2):186-200; Markel *et al. Cancer Immunol Immunother.* 2010 Feb;59(2):215-30; Ortenberg *et al. Mol Cancer Ther.* 2012 Jun;11(6):1300-10; Stern *et al. J Immunol.* 2005 Jun 1;174(11):6692-701; Zheng *et al. PLoS One.* 2010 Sep 2;5(9). pii: e12529. Thus, CEACAM inhibitors can be used with the other immunomodulators described herein (*e.g.*, anti-LAG-3, anti-PD-1, or anti-TIM-3 inhibitors) to enhance an immune response against a cancer, *e.g.*, melanoma, lung cancer (*e.g.*, NSCLC), bladder, colon or ovarian cancer, or other cancers as described herein. In one embodiment, the inhibitor of CEACAM is an anti-CEACAM-1 antibody as described in WO 2010/125571, WO 2013/82366 and WO 2014/022332, *e.g.*, a monoclonal antibody 34B1, 26H7, and 5F4 or a recombinant form thereof, as described in, *e.g.*, US 2004/0047858, US 7,132,255 and WO 99/52552. In other embodiments, the anti-CEACAM antibody is an anti-CEACAM-1 and/or anti-CEACAM-5 antibody molecule as described in, *e.g.*, WO 2010/125571, WO 2013/054331 and US 2014/0271618.

In some embodiments, the LAG-3 and PD-1 immune inhibitory molecules (*e.g.*, antibody molecules) are administered in combination with each other, *e.g.*, to treat cancer. In some embodiments, the patient is a patient who progressed (*e.g.*, experienced tumor growth) during therapy with a PD-1 inhibitor (*e.g.*, an antibody molecule as described herein) and/or a PD-L1 inhibitor (*e.g.*, antibody molecule). In some embodiments, therapy with the PD-1 antibody molecule and/or PDL1 antibody molecule is continued, and a LAG-3 immune inhibitory molecule (*e.g.*, antibody) is added to the therapy. In other embodiments, the anti-LAG-3 antibody molecule is administered in combination with a cytokine, *e.g.*, interleukin-21, interleukin-2, or interleukin 15. In certain embodiments, the combination of anti-LAG-3 antibody molecule and cytokine described herein is used to treat a cancer, *e.g.*, a cancer as described herein (*e.g.*, a solid tumor or melanoma).

Exemplary immunomodulators that can be used in combination with the anti-LAG-3 antibody molecules include, but are not limited to, *e.g.*, afutuzumab (available from Roche®); pegfilgrastim (Neulasta®); lenalidomide (CC-5013, Revlimid®); thalidomide (Thalomid®), actimid (CC4047); and cytokines, *e.g.*, IL-21 or IRX-2 (mixture of human cytokines including

interleukin 1, interleukin 2, and interferon γ , CAS 951209-71-5, available from IRX Therapeutics).

Another example of such a combination is an anti-LAG-3 antibody in combination with decarbazine for the treatment of melanoma. Another example of such a combination is an anti-LAG-3 antibody molecule in combination with interleukin-2 (IL-2) for the treatment of melanoma. In one embodiment the anti-LAG-3 antibody molecule can be combined with IL-21. Without being bound by theory, the combined use of LAG-3 blockade and chemotherapy is that cell death, is believed to be facilitated by cell death, that is a consequence of the cytotoxic action of most chemotherapeutic compounds, which can result in increased levels of tumor antigen in the antigen presentation pathway. Other combination therapies that may result in synergy with LAG-3 blockade through cell death are radiation, surgery, and hormone deprivation. Each of these protocols creates a source of tumor antigen in the host. Angiogenesis inhibitors may also be combined with LAG-3 blockade. Inhibition of angiogenesis leads to tumor cell death which may feed tumor antigen into host antigen presentation pathways.

Combinations that include LAG-3 blocking antibodies can also be used in combination with bispecific antibodies. Bispecific antibodies can be used to target two separate antigens. For example anti-Fc receptor/anti tumor antigen (*e.g.*, Her-2/neu) bispecific antibodies have been used to target macrophages to sites of tumor. This targeting may more effectively activate tumor specific responses. The T cell arm of these responses would be augmented by the use of LAG-3 blockade. Alternatively, antigen may be delivered directly to DCs by the use of bispecific antibodies which bind to tumor antigen and a dendritic cell specific cell surface marker.

Tumors evade host immune surveillance by a large variety of mechanisms. Many of these mechanisms may be overcome by the inactivation of proteins which are expressed by the tumors and which are immunosuppressive. These include among others TGF-beta (Kehrl, J. *et al.* (1986) *J. Exp. Med.* 163: 1037-1050), IL-10 (Howard, M. & O'Garra, A. (1992) *Immunology Today* 13: 198-200), and Fas ligand (Hahne, M. *et al.* (1996) *Science* 274: 1363-1365). Antibodies to each of these entities may be used in combination with anti-LAG-3 to counteract the effects of the immunosuppressive agent and favor tumor immune responses by the host.

Other antibodies which may be used to activate host immune responsiveness can be used in the combinations herein further in combination with an anti-LAG-3 antibody molecule, *e.g.*, an anti-LAG-3 antibody molecule as described herein. These include molecules on the surface

of dendritic cells which activate DC function and antigen presentation. Anti-CD40 antibodies are able to substitute effectively for T cell helper activity (Ridge, J. *et al.* (1998) *Nature* 393: 474-478) and can be used in conjunction with LAG-3 antibodies (Ito, N. *et al.* (2000) *Immunobiology* 201 (5) 527-40). Activating antibodies to T cell costimulatory molecules such as CTLA-4 (*e.g.*, U.S. Pat. No. 5,811,097), OX-40 (Weinberg, A. *et al.* (2000) *Immunol* 164: 2160-2169), 4-1BB (Melero, I. *et al.* (1997) *Nature Medicine* 3: 682-685 (1997), and ICOS (Hutloff, A. *et al.* (1999) *Nature* 397: 262-266) may also provide for increased levels of T cell activation.

Additional exemplary standard of care treatments are described in the section entitled "Combination Therapies" in US 2015/0259420 (USSN 14/657,260), entitled "Antibody Molecules to LAG-3 and Uses Thereof," incorporated by reference in its entirety, and below.

In all of the methods described herein, LAG-3 blockade can be combined with other forms of immunotherapy such as cytokine treatment (*e.g.*, interferons, GM-CSF, G-CSF, IL-2, IL-21), or bispecific antibody therapy, which provides for enhanced presentation of tumor antigens (*see, e.g.*, Holliger (1993) *Proc. Natl. Acad. Sci. USA* 90:6444-6448; Poljak (1994) *Structure* 2:1121-1123).

Methods of administering combination molecules (*e.g.*, the anti-LAG-3 antibody molecules) are known in the art and are described below. Suitable dosages of the molecules used will depend on the age and weight of the subject and the particular drug used. Dosages and therapeutic regimens of the anti-LAG-3 antibody molecule can be determined by a skilled artisan. In certain embodiments, the anti-LAG-3 antibody molecule is administered by injection (*e.g.*, subcutaneously or intravenously) at a dose of about 1 to 30 mg/kg, *e.g.*, about 5 to 25 mg/kg, about 10 to 20 mg/kg, about 1 to 5 mg/kg, or about 3 mg/kg, or about 10 mg/kg, about 20 mg/kg, about 30 mg/kg, or about 40 mg/kg. In some embodiments, the anti-LAG-3 antibody molecule is administered at a dose of about 1-3 mg/kg, or about 3-10 mg/kg. In some embodiments, the anti-LAG-3 antibody molecule is administered at a dose of about 0.5-2, 2-4, 2-5, 5-15, or 5-20 mg/kg. The dosing schedule can vary from *e.g.*, once a week to once every 2, 3, or 4 weeks. In one embodiment, the anti-LAG-3 antibody molecule is administered at a dose from about 10 to 20 mg/kg every other week.

The antibody molecule can be used in unconjugated forms or conjugated to a second agent, *e.g.*, a cytotoxic drug, radioisotope, or a protein, *e.g.*, a protein toxin or a viral protein. This method includes: administering the antibody molecule, alone or conjugated to a cytotoxic

drug, to a subject requiring such treatment. The antibody molecule can be used to deliver a variety of therapeutic agents, *e.g.*, a cytotoxic moiety, *e.g.*, a therapeutic drug, a radioisotope, molecules of plant, fungal, or bacterial origin, or biological proteins (*e.g.*, protein toxins) or particles (*e.g.*, a recombinant viral particles, *e.g.*; via a viral coat protein), or mixtures thereof.

Additional Combination Therapy

The combinations disclosed herein, *e.g.*, the combination comprising LAG-3 blocking agents, may also be combined with a standard cancer treatment, *e.g.*, chemotherapeutic regimens. In these instances, it may be possible to reduce the dose of chemotherapeutic reagent administered (Mokyr, M. *et al.* (1998) *Cancer Research* 58: 5301-5304). In certain embodiments, the methods and compositions described herein are administered in combination with one or more of other antibody molecules, chemotherapy, other anti-cancer therapy (*e.g.*, targeted anti-cancer therapies, or oncolytic drugs), cytotoxic agents, immune-based therapies (*e.g.*, cytokines), surgical and/or radiation procedures. Exemplary cytotoxic agents that can be administered in combination with include antimicrotubule agents, topoisomerase inhibitors, anti-metabolites, mitotic inhibitors, alkylating agents, anthracyclines, vinca alkaloids, intercalating agents, agents capable of interfering with a signal transduction pathway, agents that promote apoptosis, proteasome inhibitors, and radiation (*e.g.*, local or whole body irradiation).

Alternatively, or in combination with the aforesaid combinations, the methods and compositions described herein can be administered in combination with one or more of: an immunomodulator (*e.g.*, an activator of a costimulatory molecule or an inhibitor of an inhibitory molecule); a vaccine, *e.g.*, a therapeutic cancer vaccine; or other forms of cellular immunotherapy.

Exemplary combinations, *e.g.*, combinations comprising anti-LAG-3 antibody molecules and standard of care for cancer, are disclosed in US 2015/0259420 (USSN 14/657,260), entitled "Antibody Molecules to LAG-3 and Uses Thereof," incorporated by reference in its entirety, including, but not limited to, alkylating agents, anthracyclines, vinca alkaloids, proteasome inhibitors, and tyrosine kinase inhibitors (*e.g.*, a receptor tyrosine kinase (RTK) inhibitor).

Exemplary tyrosine kinase inhibitor include, but are not limited to, an epidermal growth factor (EGF) pathway inhibitor (*e.g.*, an epidermal growth factor receptor (EGFR) inhibitor), a vascular endothelial growth factor (VEGF) pathway inhibitor (*e.g.*, a vascular endothelial growth

factor receptor (VEGFR) inhibitor (*e.g.*, a VEGFR-1 inhibitor, a VEGFR-2 inhibitor, a VEGFR-3 inhibitor)), a platelet derived growth factor (PDGF) pathway inhibitor (*e.g.*, a platelet derived growth factor receptor (PDGFR) inhibitor (*e.g.*, a PDGFR- β inhibitor)), a RAF-1 inhibitor, a KIT inhibitor, and a RET inhibitor. Selected tyrosine kinase inhibitors are chosen from sunitinib, erlotinib, gefitinib, or sorafenib.

In certain embodiments, combinations include Vascular Endothelial Growth Factor (VEGF) receptor inhibitors, *e.g.*, a VEGFR inhibitor as described herein.

In some embodiments, the combination includes a PI3K inhibitor, *e.g.*, a PI3K inhibitor as described herein.

In some embodiments, the combination includes an mTOR inhibitor, *e.g.*, an mTOR inhibitor as described herein.

In some embodiments, the combination includes, *e.g.*, GSK2118436, RG7204, PLX4032, GDC-0879, PLX4720, and sorafenib tosylate (Bay 43-9006). In some embodiments, the combination includes a RAF inhibitor, *e.g.*, dabrafenib or N-{3-[5-(2-aminopyrimidin-4-yl)-2-tert-butyl-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide.

In some embodiments, the combination includes a MEK inhibitor. In some embodiments, the cancer treated with the combination is chosen from a melanoma, a colorectal cancer, a non-small cell lung cancer, an ovarian cancer, a breast cancer, a prostate cancer, a pancreatic cancer, a hematological malignancy or a renal cell carcinoma. In certain embodiments, the cancer includes a BRAF mutation (*e.g.*, a BRAF V600E mutation), a BRAF wildtype, a KRAS wildtype or an activating KRAS mutation. The cancer may be at an early, intermediate or late stage. Any MEK inhibitor can be used in combination including, but not limited to, ARRY-142886, G02442104 (also known as GSK1120212), RDEA436, RDEA119/BAY 869766, AS703026, G00039805 (also known as AZD6244 orselumetinib), BIX 02188, BIX 02189, CI-1040 (PD-184352), PD0325901, PD98059, U0126, GDC-0973 (Methanone, [3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl][3-hydroxy-3-(25)-2-piperidinyl-1-azetidiny]-), G-38963, G02443714 (also known as AS703206), or a pharmaceutically acceptable salt or solvate thereof. Additional examples of MEK inhibitors are disclosed in WO 2013/019906, WO 03/077914, WO 2005/121142, WO 2007/04415, WO 2008/024725 and WO 2009/085983, the contents of which are incorporated herein by reference. In some embodiments, the MEK inhibitor is trametinib or N-(3-{3-Cyclopropyl-5-[(2-fluoro-4-

iodophenyl)amino]-6,8-dimethyl-2,4,7-trioxo-3,4,6,7-tetrahydropyrido[4,3-d]pyrimidin-1(2H)-yl}phenyl)acetamide.

In some embodiments, the combination includes a JAK2 inhibitor, *e.g.*, CEP-701, INCB18424, CP-690550 (tasocitinib).

In some embodiments, the combination includes paclitaxel or a paclitaxel agent, *e.g.*, TAXOL®, protein-bound paclitaxel (*e.g.*, ABRAXANE®).

Radiation therapy can be administered through one of several methods, or a combination of methods, including without limitation external-beam therapy, internal radiation therapy, implant radiation, stereotactic radiosurgery, systemic radiation therapy, radiotherapy and permanent or temporary interstitial brachytherapy.

The combinations disclosed herein can be administered in combination with one or more of the existing modalities for treating cancers, including, but not limited to: surgery; radiation therapy (*e.g.*, external-beam therapy which involves three dimensional, conformal radiation therapy where the field of radiation is designed, local radiation (*e.g.*, radiation directed to a preselected target or organ), or focused radiation). Focused radiation can be selected from the group consisting of stereotactic radiosurgery, fractionated stereotactic radiosurgery, and intensity-modulated radiation therapy. The focused radiation can have a radiation source selected from the group consisting of a particle beam (proton), cobalt-60 (photon), and a linear accelerator (x-ray), *e.g.*, as described in WO 2012/177624.

In certain embodiments, the combination includes an antibody against a Killer-cell Immunoglobulin-like Receptor (also referred to herein as an “anti-KIR antibody”), a pan-KIR antibody, an anti-NKG2D antibody, and an anti-MICA antibody. In certain embodiments, the combination of anti-LAG-3 antibody molecule, anti-PD-1 antibody molecule and anti-KIR antibody, pan-KIR antibody, anti-MICA antibody, or anti-NKG2D antibody described herein is used to treat a cancer, *e.g.*, a cancer as described herein (*e.g.*, a solid tumor, *e.g.*, an advanced solid tumor).

In one embodiment, the combination includes a cellular immunotherapy (*e.g.*, Provenge (*e.g.*, Sipuleucel)), and optionally in combination with cyclophosphamide. In certain embodiments, the combination of anti-LAG-3 antibody molecule, anti-PD-1 antibody molecule, Provenge and/or cyclophosphamide is used to treat a cancer, *e.g.*, a cancer as described herein (*e.g.*, a prostate cancer, *e.g.*, an advanced prostate cancer).

In another embodiment, the combination includes a vaccine, *e.g.*, a dendritic cell renal carcinoma (DC-RCC) vaccine. In certain embodiments, the combination of anti-LAG-3 antibody molecule, anti-PD-1 antibody molecule and/or the DC-RCC vaccine is used to treat a cancer, *e.g.*, a cancer as described herein (*e.g.*, a renal carcinoma, *e.g.*, metastatic renal cell carcinoma (RCC)).

In one embodiment, the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), is used in combination with chemotherapy to treat a lung cancer, *e.g.*, non-small cell lung cancer. In one embodiment, the anti-LAG-3 antibody molecule is used with platinum doublet therapy to treat lung cancer.

In yet another embodiment, the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), is used to treat a renal cancer, *e.g.*, renal cell carcinoma (RCC) or metastatic RCC. The anti-LAG-3 antibody molecule can be administered in combination with one or more of: an immune-based strategy (*e.g.*, interleukin-2 or interferon- α), a targeted agent (*e.g.*, a VEGF inhibitor such as a monoclonal antibody to VEGF); a VEGF tyrosine kinase inhibitor such as sunitinib, sorafenib, axitinib and pazopanib; an RNAi inhibitor), or an inhibitor of a downstream mediator of VEGF signaling, *e.g.*, an inhibitor of the mammalian target of rapamycin (mTOR), *e.g.*, everolimus and temsirolimus.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecule described herein, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), described herein for treatment of pancreatic cancer includes, but is not limited to, a chemotherapeutic agent, *e.g.*, paclitaxel or a paclitaxel agent (*e.g.*, a paclitaxel formulation such as TAXOL, an albumin-stabilized nanoparticle paclitaxel formulation (*e.g.*, ABRAXANE) or a liposomal paclitaxel formulation); gemcitabine (*e.g.*, gemcitabine alone or in combination with AXP107-11); other chemotherapeutic agents such as oxaliplatin, 5-fluorouracil, capecitabine, rubitecan, epirubicin hydrochloride, NC-6004, cisplatin, docetaxel (*e.g.*, TAXOTERE), mitomycin C, ifosfamide; interferon; tyrosine kinase inhibitor (*e.g.*, EGFR inhibitor (*e.g.*, erlotinib, panitumumab, cetuximab, nimotuzumab); HER2/neu receptor inhibitor (*e.g.*, trastuzumab); dual kinase inhibitor (*e.g.*, bosutinib, saracatinib, lapatinib, vandetanib); multikinase inhibitor (*e.g.*, sorafenib,

sunitinib, XL184, pazopanib); VEGF inhibitor (*e.g.*, bevacizumab, AV-951, brivanib); radioimmunotherapy (*e.g.*, XR303); cancer vaccine (*e.g.*, GVAX, survivin peptide); COX-2 inhibitor (*e.g.*, celecoxib); IGF-1 receptor inhibitor (*e.g.*, AMG 479, MK-0646); mTOR inhibitor (*e.g.*, everolimus, temsirolimus); IL-6 inhibitor (*e.g.*, CNTO 328); cyclin-dependent kinase inhibitor (*e.g.*, P276-00, UCN-01); Altered Energy Metabolism-Directed (AEMD) compound (*e.g.*, CPI-613); HDAC inhibitor (*e.g.*, vorinostat); TRAIL receptor 2 (TR-2) agonist (*e.g.*, conatumumab); MEK inhibitor (*e.g.*, AS703026, selumetinib, GSK1120212); Raf/MEK dual kinase inhibitor (*e.g.*, RO5126766); Notch signaling inhibitor (*e.g.*, MK0752); monoclonal antibody-antibody fusion protein (*e.g.*, L19IL2); curcumin; HSP90 inhibitor (*e.g.*, tanespimycin, STA-9090); rIL-2; denileukin diftitox; topoisomerase 1 inhibitor (*e.g.*, irinotecan, PEP02); statin (*e.g.*, simvastatin); Factor VIIa inhibitor (*e.g.*, PCI-27483); AKT inhibitor (*e.g.*, RX-0201); hypoxia-activated prodrug (*e.g.*, TH-302); metformin hydrochloride, gamma-secretase inhibitor (*e.g.*, RO4929097); ribonucleotide reductase inhibitor (*e.g.*, 3-AP); immunotoxin (*e.g.*, HuC242-DM4); PARP inhibitor (*e.g.*, KU-0059436, veliparib); CTLA-4 inhibitor (*e.g.*, CP-675,206, ipilimumab); AdV-tk therapy; proteasome inhibitor (*e.g.*, bortezomib (Velcade), NPI-0052); thiazolidinedione (*e.g.*, pioglitazone); NPC-1C; Aurora kinase inhibitor (*e.g.*, R763/AS703569), CTGF inhibitor (*e.g.*, FG-3019); siG12D LODER; and radiation therapy (*e.g.*, tomotherapy, stereotactic radiation, proton therapy), surgery, and a combination thereof. In certain embodiments, a combination of paclitaxel or a paclitaxel agent, and gemcitabine can be used with the anti-PD-1 antibody molecules described herein.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of small cell lung cancer includes, but is not limited to, a chemotherapeutic agent, *e.g.*, etoposide, carboplatin, cisplatin, oxaliplatin, irinotecan, topotecan, gemcitabine, liposomal SN-38, bendamustine, temozolomide, belotecan, NK012, FR901228, flavopiridol); tyrosine kinase inhibitor (*e.g.*, EGFR inhibitor (*e.g.*, erlotinib, gefitinib, cetuximab, panitumumab); multikinase inhibitor (*e.g.*, sorafenib, sunitinib); VEGF inhibitor (*e.g.*, bevacizumab, vandetanib); cancer vaccine (*e.g.*, GVAX); Bcl-2 inhibitor (*e.g.*, oblimersen sodium, ABT-263); proteasome inhibitor (*e.g.*, bortezomib (Velcade), NPI-0052), paclitaxel or a paclitaxel agent; docetaxel; IGF-1 receptor inhibitor (*e.g.*, AMG 479); HGF/SF inhibitor (*e.g.*, AMG 102, MK-0646); chloroquine; Aurora kinase inhibitor (*e.g.*, MLN8237);

radioimmunotherapy (*e.g.*, TF2); HSP90 inhibitor (*e.g.*, tanespimycin, STA-9090); mTOR inhibitor (*e.g.*, everolimus); Ep-CAM-/CD3-bispecific antibody (*e.g.*, MT110); CK-2 inhibitor (*e.g.*, CX-4945); HDAC inhibitor (*e.g.*, belinostat); SMO antagonist (*e.g.*, BMS 833923); peptide cancer vaccine, and radiation therapy (*e.g.*, intensity-modulated radiation therapy (IMRT), hypofractionated radiotherapy, hypoxia-guided radiotherapy), surgery, and combinations thereof.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of non-small cell lung cancer includes, but is not limited to, a chemotherapeutic agent, *e.g.*, vinorelbine, cisplatin, docetaxel, pemetrexed disodium, etoposide, gemcitabine, carboplatin, liposomal SN-38, TLK286, temozolomide, topotecan, pemetrexed disodium, azacitidine, irinotecan, tegafur-gimeracil-oteracil potassium, sapacitabine); tyrosine kinase inhibitor (*e.g.*, EGFR inhibitor (*e.g.*, erlotinib, gefitinib, cetuximab, panitumumab, necitumumab, PF-00299804, nimotuzumab, RO5083945), MET inhibitor (*e.g.*, PF-02341066, ARQ 197), PI3K kinase inhibitor (*e.g.*, XL147, GDC-0941), Raf/MEK dual kinase inhibitor (*e.g.*, RO5126766), PI3K/mTOR dual kinase inhibitor (*e.g.*, XL765), SRC inhibitor (*e.g.*, dasatinib), dual inhibitor (*e.g.*, BIBW 2992, GSK1363089, ZD6474, AZD0530, AG-013736, lapatinib, MEHD7945A, linifanib), multikinase inhibitor (*e.g.*, sorafenib, sunitinib, pazopanib, AMG 706, XL184, MGCD265, BMS-690514, R935788), VEGF inhibitor (*e.g.*, endostar, endostatin, bevacizumab, cediranib, BIBF 1120, axitinib, tivozanib, AZD2171), cancer vaccine (*e.g.*, BLP25 liposome vaccine, GVAX, recombinant DNA and adenovirus expressing L523S protein), Bcl-2 inhibitor (*e.g.*, oblimersen sodium), proteasome inhibitor (*e.g.*, bortezomib, carfilzomib, NPI-0052, MLN9708), paclitaxel or a paclitaxel agent, docetaxel, IGF-1 receptor inhibitor (*e.g.*, cixutumumab, MK-0646, OSI 906, CP-751,871, BIIB022), hydroxychloroquine, HSP90 inhibitor (*e.g.*, tanespimycin, STA-9090, AUY922, XL888), mTOR inhibitor (*e.g.*, everolimus, temsirolimus, ridaforolimus), Ep-CAM-/CD3-bispecific antibody (*e.g.*, MT110), CK-2 inhibitor (*e.g.*, CX-4945), HDAC inhibitor (*e.g.*, MS 275, LBH589, vorinostat, valproic acid, FR901228), DHFR inhibitor (*e.g.*, pralatrexate), retinoid (*e.g.*, bexarotene, tretinoin), antibody-drug conjugate (*e.g.*, SGN-15), bisphosphonate (*e.g.*, zoledronic acid), cancer vaccine (*e.g.*, belagenpumatumucel-L), low molecular weight heparin (LMWH) (*e.g.*, tinzaparin, enoxaparin), GSK1572932A, melatonin, talactoferrin, dimesna, topoisomerase inhibitor (*e.g.*, amrubicin, etoposide, karenitecin), nelfinavir, cilengitide, ErbB3

inhibitor (*e.g.*, MM-121, U3-1287), survivin inhibitor (*e.g.*, YM155, LY2181308), eribulin mesylate, COX-2 inhibitor (*e.g.*, celecoxib), pegfilgrastim, Polo-like kinase 1 inhibitor (*e.g.*, BI 6727), TRAIL receptor 2 (TR-2) agonist (*e.g.*, CS-1008), CNGRC peptide (SEQ ID NO: 293)-TNF alpha conjugate, dichloroacetate (DCA), HGF inhibitor (*e.g.*, SCH 900105), SAR240550, PPAR-gamma agonist (*e.g.*, CS-7017), gamma-secretase inhibitor (*e.g.*, RO4929097), epigenetic therapy (*e.g.*, 5-azacitidine), nitroglycerin, MEK inhibitor (*e.g.*, AZD6244), cyclin-dependent kinase inhibitor (*e.g.*, UCN-01), cholesterol-Fus1, antitubulin agent (*e.g.*, E7389), farnesyl-OH-transferase inhibitor (*e.g.*, lonafarnib), immunotoxin (*e.g.*, BB-10901, SS1 (dsFv) PE38), fondaparinux, vascular-disrupting agent (*e.g.*, AVE8062), PD-L1 inhibitor (*e.g.*, MDX-1105, MDX-1106), beta-glucan, NGR-hTNF, EMD 521873, MEK inhibitor (*e.g.*, GSK1120212), epothilone analog (*e.g.*, ixabepilone), kinesin-spindle inhibitor (*e.g.*, 4SC-205), telomere targeting agent (*e.g.*, KML-001), P70 pathway inhibitor (*e.g.*, LY2584702), AKT inhibitor (*e.g.*, MK-2206), angiogenesis inhibitor (*e.g.*, lenalidomide), Notch signaling inhibitor (*e.g.*, OMP-21M18), radiation therapy, surgery, and combinations thereof.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of ovarian cancer includes, but is not limited to, a chemotherapeutic agent (*e.g.*, paclitaxel or a paclitaxel agent; docetaxel; carboplatin; gemcitabine; doxorubicin; topotecan; cisplatin; irinotecan, TLK286, ifosfamide, olaparib, oxaliplatin, melphalan, pemetrexed disodium, SJG-136, cyclophosphamide, etoposide, decitabine); ghrelin antagonist (*e.g.*, AEZS-130), immunotherapy (*e.g.*, APC8024, oregovomab, OPT-821), tyrosine kinase inhibitor (*e.g.*, EGFR inhibitor (*e.g.*, erlotinib), dual inhibitor (*e.g.*, E7080), multikinase inhibitor (*e.g.*, AZD0530, JI-101, sorafenib, sunitinib, pazopanib), ON 01910.Na), VEGF inhibitor (*e.g.*, bevacizumab, BIBF 1120, cediranib, AZD2171), PDGFR inhibitor (*e.g.*, IMC-3G3), paclitaxel, topoisomerase inhibitor (*e.g.*, karenitecin, Irinotecan), HDAC inhibitor (*e.g.*, valproate, vorinostat), folate receptor inhibitor (*e.g.*, farletuzumab), angiopoietin inhibitor (*e.g.*, AMG 386), epothilone analog (*e.g.*, ixabepilone), proteasome inhibitor (*e.g.*, carfilzomib), IGF-1 receptor inhibitor (*e.g.*, OSI 906, AMG 479), PARP inhibitor (*e.g.*, veliparib, AG014699, iniparib, MK-4827), Aurora kinase inhibitor (*e.g.*, MLN8237, ENMD-2076), angiogenesis inhibitor (*e.g.*, lenalidomide), DHFR inhibitor (*e.g.*, pralatrexate), radioimmunotherapeutic agent (*e.g.*, Hu3S193), statin (*e.g.*, lovastatin), topoisomerase 1

inhibitor (e.g., NKTR-102), cancer vaccine (e.g., p53 synthetic long peptides vaccine, autologous OC-DC vaccine), mTOR inhibitor (e.g., temsirolimus, everolimus), BCR/ABL inhibitor (e.g., imatinib), ET-A receptor antagonist (e.g., ZD4054), TRAIL receptor 2 (TR-2) agonist (e.g., CS-1008), HGF/SF inhibitor (e.g., AMG 102), EGEN-001, Polo-like kinase 1 inhibitor (e.g., BI 6727), gamma-secretase inhibitor (e.g., RO4929097), Wee-1 inhibitor (e.g., MK-1775), antitubulin agent (e.g., vinorelbine, E7389), immunotoxin (e.g., denileukin diftitox), SB-485232, vascular-disrupting agent (e.g., AVE8062), integrin inhibitor (e.g., EMD 525797), kinesin-spindle inhibitor (e.g., 4SC-205), revlimid, HER2 inhibitor (e.g., MGAH22), ErrB3 inhibitor (e.g., MM-121), radiation therapy; and combinations thereof.

In one exemplary embodiment, the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (e.g., an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), is used to treat a myeloma, alone or in combination with one or more of: chemotherapy or other anti-cancer agents (e.g., thalidomide analogs, e.g., lenalidomide), HSCT (Cook, R. (2008) *J Manag Care Pharm.* 14(7 Suppl):19-25), an anti-TIM3 antibody (Hallett, WHD *et al.* (2011) *J of American Society for Blood and Marrow Transplantation* 17(8):1133-145), tumor antigen-pulsed dendritic cells, fusions (e.g., electrofusions) of tumor cells and dendritic cells, or vaccination with immunoglobulin idiotype produced by malignant plasma cells (reviewed in Yi, Q. (2009) *Cancer J.* 15(6):502-10).

In yet another embodiment, the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (e.g., an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), is used to treat a renal cancer, e.g., renal cell carcinoma (RCC) or metastatic RCC. The anti-PD-1 antibody molecule can be administered in combination with one or more of: an immune-based strategy (e.g., interleukin-2 or interferon- α), a targeted agent (e.g., a VEGF inhibitor such as a monoclonal antibody to VEGF, e.g., bevacizumab (Rini, B.I. *et al.* (2010) *J. Clin. Oncol.* 28(13):2137-2143)); a VEGF tyrosine kinase inhibitor such as sunitinib, sorafenib, axitinib and pazopanib (reviewed in Pal, S.K. *et al.* (2014) *Clin. Advances in Hematology & Oncology* 12(2):90-99)); an RNAi inhibitor), or an inhibitor of a downstream mediator of VEGF signaling, e.g., an inhibitor of the mammalian target of rapamycin (mTOR), e.g., everolimus and temsirolimus (Hudes, G. *et al.* (2007) *N. Engl. J. Med.* 356(22):2271-2281, Motzer, R.J. *et al.* (2008) *Lancet* 372: 449-456).

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of chronic myelogenous leukemia (AML) according to the invention includes, but is not limited to, a chemotherapeutic (*e.g.*, cytarabine, hydroxyurea, clofarabine, melphalan, thiotepa, fludarabine, busulfan, etoposide, cordycepin, pentostatin, capecitabine, azacitidine, cyclophosphamide, cladribine, topotecan), tyrosine kinase inhibitor (*e.g.*, BCR/ABL inhibitor (*e.g.*, imatinib, nilotinib), ON 01910.Na, dual inhibitor (*e.g.*, dasatinib, bosutinib), multikinase inhibitor (*e.g.*, DCC-2036, ponatinib, sorafenib, sunitinib, RGB-286638)), interferon alfa, steroids, apoptotic agent (*e.g.*, omacetaxine mepesuccinat), immunotherapy (*e.g.*, allogeneic CD4+ memory Th1-like T cells/microparticle-bound anti-CD3/anti-CD28, autologous cytokine induced killer cells (CIK), AHN-12), CD52 targeting agent (*e.g.*, alemtuzumab), HSP90 inhibitor (*e.g.*, tanesprimycin, STA-9090, AUY922, XL888), mTOR inhibitor (*e.g.*, everolimus), SMO antagonist (*e.g.*, BMS 833923), ribonucleotide reductase inhibitor (*e.g.*, 3-AP), JAK-2 inhibitor (*e.g.*, INCB018424), Hydroxychloroquine, retinoid (*e.g.*, fenretinide), cyclin-dependent kinase inhibitor (*e.g.*, UCN-01), HDAC inhibitor (*e.g.*, belinostat, vorinostat, JNJ-26481585), PARP inhibitor (*e.g.*, veliparib), MDM2 antagonist (*e.g.*, RO5045337), Aurora B kinase inhibitor (*e.g.*, TAK-901), radioimmunotherapy (*e.g.*, actinium-225-labeled anti-CD33 antibody HuM195), Hedgehog inhibitor (*e.g.*, PF-04449913), STAT3 inhibitor (*e.g.*, OPB-31121), KB004, cancer vaccine (*e.g.*, AG858), bone marrow transplantation, stem cell transplantation, radiation therapy, and combinations thereof.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of chronic lymphocytic leukemia (CLL) includes, but is not limited to, a chemotherapeutic agent (*e.g.*, fludarabine, cyclophosphamide, doxorubicin, vincristine, chlorambucil, bendamustine, chlorambucil, busulfan, gemcitabine, melphalan, pentostatin, mitoxantrone, 5-azacytidine, pemetrexed disodium), tyrosine kinase inhibitor (*e.g.*, EGFR inhibitor (*e.g.*, erlotinib), BTK inhibitor (*e.g.*, PCI-32765), multikinase inhibitor (*e.g.*, MGCD265, RGB-286638), CD-20 targeting agent (*e.g.*, rituximab, ofatumumab, RO5072759, LFB-R603), CD52 targeting agent (*e.g.*, alemtuzumab), prednisolone, darbepoetin alfa, lenalidomide, Bcl-2 inhibitor (*e.g.*, ABT-263), immunotherapy (*e.g.*, allogeneic CD4+ memory Th1-like T cells/microparticle-bound anti-CD3/anti-CD28, autologous cytokine induced

killer cells (CIK)), HDAC inhibitor (*e.g.*, vorinostat, valproic acid, LBH589, JNJ-26481585, AR-42), XIAP inhibitor (*e.g.*, AEG35156), CD-74 targeting agent (*e.g.*, milatuzumab), mTOR inhibitor (*e.g.*, everolimus), AT-101, immunotoxin (*e.g.*, CAT-8015, anti-Tac(Fv)-PE38 (LMB-2)), CD37 targeting agent (*e.g.*, TRU-016), radioimmunotherapy (*e.g.*, 131-tositumomab), hydroxychloroquine, perifosine, SRC inhibitor (*e.g.*, dasatinib), thalidomide, PI3K delta inhibitor (*e.g.*, CAL-101), retinoid (*e.g.*, fenretinide), MDM2 antagonist (*e.g.*, RO5045337), plerixafor, Aurora kinase inhibitor (*e.g.*, MLN8237, TAK-901), proteasome inhibitor (*e.g.*, bortezomib), CD-19 targeting agent (*e.g.*, MEDI-551, MOR208), MEK inhibitor (*e.g.*, ABT-348), JAK-2 inhibitor (*e.g.*, INCB018424), hypoxia-activated prodrug (*e.g.*, TH-302), paclitaxel or a paclitaxel agent, HSP90 inhibitor, AKT inhibitor (*e.g.*, MK2206), HMG-CoA inhibitor (*e.g.*, simvastatin), GNKG186, radiation therapy, bone marrow transplantation, stem cell transplantation, and a combination thereof.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of acute lymphocytic leukemia (ALL) includes, but is not limited to, a chemotherapeutic agent (*e.g.*, prednisolone, dexamethasone, vincristine, asparaginase, daunorubicin, cyclophosphamide, cytarabine, etoposide, thioguanine, mercaptopurine, clofarabine, liposomal anthracycline, busulfan, etoposide, capecitabine, decitabine, azacitidine, topotecan, temozolomide), tyrosine kinase inhibitor (*e.g.*, BCR/ABL inhibitor (*e.g.*, imatinib, nilotinib), ON 01910.Na, multikinase inhibitor (*e.g.*, sorafenib)), CD-20 targeting agent (*e.g.*, rituximab), CD52 targeting agent (*e.g.*, alemtuzumab), HSP90 inhibitor (*e.g.*, STA-9090), mTOR inhibitor (*e.g.*, everolimus, rapamycin), JAK-2 inhibitor (*e.g.*, INCB018424), HER2/neu receptor inhibitor (*e.g.*, trastuzumab), proteasome inhibitor (*e.g.*, bortezomib), methotrexate, asparaginase, CD-22 targeting agent (*e.g.*, epratuzumab, inotuzumab), immunotherapy (*e.g.*, autologous cytokine induced killer cells (CIK), AHN-12), blinatumomab, cyclin-dependent kinase inhibitor (*e.g.*, UCN-01), CD45 targeting agent (*e.g.*, BC8), MDM2 antagonist (*e.g.*, RO5045337), immunotoxin (*e.g.*, CAT-8015, DT2219ARL), HDAC inhibitor (*e.g.*, JNJ-26481585), JVRS-100, paclitaxel or a paclitaxel agent, STAT3 inhibitor (*e.g.*, OPB-31121), PARP inhibitor (*e.g.*, veliparib), EZN-2285, radiation therapy, steroid, bone marrow transplantation, stem cell transplantation, or a combination thereof.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of acute myeloid leukemia (AML) includes, but is not limited to, a chemotherapeutic agent (*e.g.*, cytarabine, daunorubicin, idarubicin, clofarabine, decitabine, vosaroxin, azacitidine, clofarabine, ribavirin, CPX-351, treosulfan, elacytarabine, azacitidine), tyrosine kinase inhibitor (*e.g.*, BCR/ABL inhibitor (*e.g.*, imatinib, nilotinib), ON 01910.Na, multikinase inhibitor (*e.g.*, midostaurin, SU 11248, quizartinib, sorafenib)), immunotoxin (*e.g.*, gemtuzumab ozogamicin), DT388IL3 fusion protein, HDAC inhibitor (*e.g.*, vorinostat, LBH589), plerixafor, mTOR inhibitor (*e.g.*, everolimus), SRC inhibitor (*e.g.*, dasatinib), HSP90 inhibitor (*e.g.*, STA-9090), retinoid (*e.g.*, bexarotene, Aurora kinase inhibitor (*e.g.*, BI 811283), JAK-2 inhibitor (*e.g.*, INCB018424), Polo-like kinase inhibitor (*e.g.*, BI 6727), cenersen, CD45 targeting agent (*e.g.*, BC8), cyclin-dependent kinase inhibitor (*e.g.*, UCN-01), MDM2 antagonist (*e.g.*, RO5045337), mTOR inhibitor (*e.g.*, everolimus), LY573636-sodium, ZRx-101, MLN4924, lenalidomide, immunotherapy (*e.g.*, AHN-12), histamine dihydrochloride, radiation therapy, bone marrow transplantation, stem cell transplantation, and a combination thereof.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of multiple myeloma (MM) includes, but is not limited to, a chemotherapeutic agent (*e.g.*, melphalan, amifostine, cyclophosphamide, doxorubicin, clofarabine, bendamustine, fludarabine, adriamycin, SyB L-0501), thalidomide, lenalidomide, dexamethasone, prednisone, pomalidomide, proteasome inhibitor (*e.g.*, bortezomib, carfilzomib, MLN9708), cancer vaccine (*e.g.*, GVAX), CD-40 targeting agent (*e.g.*, SGN-40, CHIR-12.12), perifosine, zoledronic acid, Immunotherapy (*e.g.*, MAGE-A3, NY-ESO-1, HuMax-CD38), HDAC inhibitor (*e.g.*, vorinostat, LBH589, AR-42), aplidin, cyclin-dependent kinase inhibitor (*e.g.*, PD-0332991, dinaciclib), arsenic trioxide, CB3304, HSP90 inhibitor (*e.g.*, KW-2478), tyrosine kinase inhibitor (*e.g.*, EGFR inhibitor (*e.g.*, cetuximab), multikinase inhibitor (*e.g.*, AT9283)), VEGF inhibitor (*e.g.*, bevacizumab), plerixafor, MEK inhibitor (*e.g.*, AZD6244), IPH2101, atorvastatin, immunotoxin (*e.g.*, BB-10901), NPI-0052, radioimmunotherapeutic (*e.g.*, yttrium Y 90 ibritumomab tiuxetan), STAT3 inhibitor (*e.g.*, OPB-31121), MLN4924, Aurora kinase inhibitor (*e.g.*, ENMD-2076), IMGN901, ACE-041, CK-2

inhibitor (*e.g.*, CX-4945), radiation therapy, bone marrow transplantation, stem cell transplantation, and a combination thereof.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecule, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of prostate cancer includes, but is not limited to, a chemotherapeutic agent (*e.g.*, docetaxel, carboplatin, fludarabine), abiraterone, hormonal therapy (*e.g.*, flutamide, bicalutamide, nilutamide, cyproterone acetate, ketoconazole, aminoglutethimide, abarelix, degarelix, leuprolide, goserelin, triptorelin, buserelin), tyrosine kinase inhibitor (*e.g.*, dual kinase inhibitor (*e.g.*, lapatanib), multikinase inhibitor (*e.g.*, sorafenib, sunitinib)), VEGF inhibitor (*e.g.*, bevacizumab), TAK-700, cancer vaccine (*e.g.*, BPX-101, PEP223), lenalidomide, TOK-001, IGF-1 receptor inhibitor (*e.g.*, cixutumumab), TRC105, Aurora A kinase inhibitor (*e.g.*, MLN8237), proteasome inhibitor (*e.g.*, bortezomib), OGX-011, radioimmunotherapy (*e.g.*, HuJ591-GS), HDAC inhibitor (*e.g.*, valproic acid, SB939, LBH589), hydroxychloroquine, mTOR inhibitor (*e.g.*, everolimus), dovitinib lactate, diindolylmethane, efavirenz, OGX-427, genistein, IMC-3G3, bafetinib, CP-675,206, radiation therapy, surgery, or a combination thereof.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecules, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of HNSCC includes, but is not limited to, one or both of Compound A8 as described herein (or a compound described in PCT Publication No. WO2010/029082) and cetuximab (*e.g.*, Erbitux, marketed by BMS). In some embodiments, the therapeutic (*e.g.*, the Compound A8 or compound related to A8) is a PI3K modulator, *e.g.*, a PI3K inhibitor. In some embodiments, the therapeutic (*e.g.*, cetuximab) modulates, *e.g.*, inhibits, EGFR. In some embodiments, the cancer has, or is identified as having, elevated levels or activity of PI3K or EGFR compared to a control cell or reference value.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecules, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of gastric cancer, *e.g.*, MSI-high and/or EBV+ gastric cancer, includes, but is not limited to, Compound A8 as described herein (or a compound described in PCT Publication No. WO2010/029082). In some embodiments, the therapeutic (*e.g.*, the Compound A8 or compound related to A8) is a PI3K modulator, *e.g.*, a

PI3K inhibitor. In some embodiments, the cancer has, or is identified as having, elevated levels or activity of PI3K compared to a control cell or reference value.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecules, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of gastric cancer, *e.g.*, MSI-high and/or RNF43-inactivated gastric cancer, includes, but is not limited to, Compound A28 as described herein (or a compound described in PCT Publication No. WO2010/101849). In some embodiments, the therapeutic (*e.g.*, the Compound A28 or compound related to A28) is a modulator, *e.g.*, inhibitor, of porcupine. In some embodiments, the cancer has, or is identified as having, elevated levels or activity of porcupine compared to a control cell or reference value.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecules, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of GI stromal tumor (GIST), includes, but is not limited to, Compound A16 as described herein (or a compound described in PCT Publication No. WO1999/003854). In some embodiments, the therapeutic (*e.g.*, the Compound A16 or compound related to A16) is a modulator, *e.g.*, inhibitor, of a tyrosine kinase. In some embodiments, the cancer has, or is determined to have, elevated levels or activity of a tyrosine kinase compared to a control cell or reference value.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecules, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of NSCLC, *e.g.*, squamous or adenocarcinoma, includes, but is not limited to, one or both of Compound A17 as described herein (or a compound described in US Patent No. 7,767,675 and 8,420,645) and Compound A23 as described herein (or a compound described in PCT Publication No. WO2003/077914). In some embodiments, the compound (*e.g.*, the Compound A17 or compound related to A17) modulates, *e.g.*, inhibits, c-MET. In some embodiments, the compound (*e.g.*, the Compound A23 or compound related to A23) modulates, *e.g.*, inhibits, Alk. In some embodiments, the cancer has, or is determined to have, elevated levels or activity of one or both of c-MET or Alk compared to a control cell or reference value. In some embodiments, the cancer has, or is identified as having, a mutation in EGFR.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecules, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of melanoma (*e.g.*, NRAS melanoma) includes, but is not limited to, one or both of Compound A24 as described herein (or a compound described in US Patent Nos. 8,415,355 and 8,685,980) and Compound A34 as described herein (or a compound described in PCT Publication No. WO2003/077914). In some embodiments, the compound (*e.g.*, the Compound A24 or compound related to A24) modulates, *e.g.*, inhibits, one or more of JAK and CDK4/6. In some embodiments, the compound (*e.g.*, the Compound A34 or compound related to A34) modulates, *e.g.*, inhibits, MEK. In some embodiments, the cancer has, or is identified as having, elevated levels or activity of one or more of JAK, CDK4/6, and MEK compared to a control cell or reference value.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecules, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of melanoma (*e.g.*, NRAS melanoma) includes, but is not limited to, one or both of Compound A29 as described herein (or a compound described in PCT Publication No. WO2011/025927) and Compound A34 as described herein (or a compound described in PCT Publication No. WO2003/077914). In some embodiments, the compound (*e.g.*, the Compound A29 or compound related to A29) modulates, *e.g.*, inhibits, BRAF. In some embodiments, the compound (*e.g.*, the Compound A34 or compound related to A34) modulates, *e.g.*, inhibits, MEK. In some embodiments, the cancer has, or is identified as having, elevated levels or activity of one or both of BRAF and MEK compared to a control cell or reference value.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecules, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), for treatment of squamous NSCLC includes, but is not limited to, Compound A5 as described herein (or a compound described in US Patent No. 8,552,002). In some embodiments, the compound (*e.g.*, the Compound A5 or compound related to A5) modulates, *e.g.*, inhibits, FGFR. In some embodiments, the cancer has, or is identified as having, elevated levels or activity of FGFR compared to a control cell or reference value.

An example of suitable therapeutics for use in combination with the anti-LAG-3 antibody molecules, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-

L1 or anti-TIM-3 antibody molecule), for treatment of colorectal cancer includes, but is not limited to, one or both of Compound A29 as described herein (or a compound PCT Publication No. WO2011/025927) and cetuximab (*e.g.*, Erbitux, marketed by BMS). In some embodiments, the therapeutic (*e.g.*, the Compound A29 or compound related to A29) modulates, *e.g.*, inhibits, BRAF. In some embodiments, the therapeutic (*e.g.*, cetuximab) modulates, *e.g.*, inhibits EGFR. In some embodiments, the cancer has, or is identified as having, elevated levels or activity of BRAF or EGFR compared to a control cell or reference value.

This disclosure also provides a method of treating cancer with Compound A8, cetuximab, and a LAG-3 antibody molecule (optionally in combination with a PD-1 antibody molecule or TIM-3 antibody molecule). In some embodiments, the patient is first treated with Compound A8 and cetuximab. This treatment continues for an amount of time, *e.g.*, a predetermined amount of time, *e.g.*, about 1, 2, 4, 6, 8, 10, or 12 months. Next, the LAG-3 antibody molecule (optionally in combination with a PD-1 antibody molecule or TIM-3 antibody molecule) is administered. The LAG-3 antibody can optionally be administered in combination with cetuximab.

In some embodiments, the patient is first treated with all three of Compound A8, cetuximab, and a LAG-3 antibody molecule (optionally in combination with a PD-1 antibody molecule or TIM-3 antibody molecule). This treatment continues for an amount of time, *e.g.*, a predetermined amount of time, *e.g.*, about 6, 8, 10, or 12 months. Next, the Compound A8 and/or cetuximab can be tapered off, so that the maintenance phase involves treatment with the LAG-3 antibody molecule (*e.g.*, as a monotherapy, or in combination with a PD-1 antibody molecule or TIM-3 antibody molecule) but not Compound A8 or cetuximab.

In other embodiments, the three compounds (Compound A8, cetuximab, and a LAG-3 antibody molecule, optionally in combination with a PD-1 antibody molecule or TIM-3 antibody molecule) are given sequentially at the outset of the treatment. For instance, Compound A8 and cetuximab can be given first, as described above. Next, the LAG-3 antibody molecule (optionally in combination with a PD-1 antibody molecule or TIM-3 antibody molecule) is added to the regimen. Next, the Compound A8 and/or cetuximab can be tapered off as described above.

Exemplary doses for the three (or more) agent regimens are as follows. The LAG-3 antibody molecule can be administered, *e.g.*, at a dose of about 1 to 40 mg/kg, *e.g.*, 1 to 30 mg/kg, *e.g.*, about 5 to 25 mg/kg, about 10 to 20 mg/kg, about 1 to 5 mg/kg, or about 3 mg/kg.

In some embodiments, the Compound A8 is administered at a dose of approximately 200-300, 300-400, or 200-400 mg. In some embodiments, the cetuximab is administered at a 400 mg/m² initial dose as a 120-minute intravenous infusion followed by 250 mg/m² weekly infused over 60 minutes. In embodiments, one or more of the Compound A8, cetuximab, and LAG-3 antibody molecule is administered at a dose that is lower than the dose at which that agent is typically administered as a monotherapy, *e.g.*, about 0-10%, 10-20%, 20-30%, 30-40%, 40-50%, 50-60%, 60-70%, 70-80%, or 80-90% lower than the dose at which that agent is typically administered as a monotherapy. In embodiments, the one or more of the Compound A8, cetuximab, and LAG-3 antibody molecule is administered at a dose that is lower than the dose of that agent recited in this paragraph, *e.g.*, about 0-10%, 10-20%, 20-30%, 30-40%, 40-50%, 50-60%, 60-70%, 70-80%, or 80-90% lower than the dose of that agent recited in this paragraph. In certain embodiments, the concentration of the Compound A8 that is required to achieve inhibition, *e.g.*, growth inhibition, is lower when the Compound A8 is administered in combination with one or both of the cetuximab and LAG-3 antibody molecule than when the Compound A8 is administered individually. In certain embodiments, the concentration of the cetuximab that is required to achieve inhibition, *e.g.*, growth inhibition, is lower when the cetuximab is administered in combination with one or both of the Compound A8 and LAG-3 antibody molecule than when the cetuximab is administered individually. In certain embodiments, the concentration of the LAG-3 antibody molecule that is required to achieve inhibition, *e.g.*, growth inhibition, is lower when the LAG-3 antibody molecule is administered in combination with one or both of the cetuximab and Compound A8 than when the LAG-3 antibody molecule is administered individually.

Additionally disclosed herein is a method of treating cancer with the anti-LAG-3 antibody molecules, alone or in combination with another immunomodulator (*e.g.*, an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule), and a targeted anti-cancer agent, *e.g.*, an agent that targets one or more proteins. In some embodiments, the anti-LAG-3 antibody molecule (and optionally other immunomodulator(s)) are administered first, and the targeted anti-cancer agent is administered second. The length of time between administration of the anti-LAG-3 antibody molecule and the targeted anti-cancer agent can be, *e.g.*, 10, 20, or 30 minutes, 1, 2, 4, 6, or 12 hours, or 1, 2, 3, 4, 5, 6, or 7 days, or any span of time within this range. In certain embodiments, the anti-LAG-3 antibody molecule is administered repeatedly over a period of

time (*e.g.*, 1, 2, 3, 4, 5, or 6 days, or 1, 2, 4, 8, 12, 16, or 20 weeks, or any span of time within this range) before the targeted anti-cancer agent is administered. In other embodiments, the anti-LAG-3 antibody molecule and the targeted anti-cancer agent are administered at substantially the same time.

Infectious Diseases

Other methods of the invention are used to treat patients that have been exposed to particular toxins or pathogens. Accordingly, another aspect of the invention provides a method of treating an infectious disease in a subject comprising administering to the subject a combination as disclosed herein, *e.g.*, a combination including an anti-LAG-3 antibody molecule, such that the subject is treated for the infectious disease.

In the treatment of infection (*e.g.*, acute and/or chronic), administration of the anti-LAG-3 antibody molecules (alone or in combination with an anti-PD-1, anti-PD-L1 or anti-TIM-3 antibody molecule) can be combined with conventional treatments in addition to or in lieu of stimulating natural host immune defenses to infection. Natural host immune defenses to infection include, but are not limited to inflammation, fever, antibody-mediated host defense, T-lymphocyte-mediated host defenses, including lymphokine secretion and cytotoxic T-cells (especially during viral infection), complement mediated lysis and opsonization (facilitated phagocytosis), and phagocytosis. The ability of the anti-LAG-3 antibody molecules to reactivate dysfunctional T-cells would be useful to treat chronic infections, in particular those in which cell-mediated immunity is important for complete recovery.

Similar to its application to tumors as discussed above, antibody mediated LAG-3 blockade can be used alone, or as an adjuvant, in combination with vaccines, to stimulate the immune response to pathogens, toxins, and self-antigens. Examples of pathogens for which this therapeutic approach may be particularly useful, include pathogens for which there is currently no effective vaccine, or pathogens for which conventional vaccines are less than completely effective. These include, but are not limited to Hepatitis (A, B, and C), Influenza, HIV, Herpes, Giardia, Malaria, Leishmania, Staphylococcus aureus, Pseudomonas Aeruginosa. LAG-3 blockade is particularly useful against established infections by agents such as HIV that present altered antigens over the course of the infections. These novel epitopes are recognized as foreign

at the time of anti-human LAG-3 administration, thus provoking a strong T cell response that is not dampened by negative signals through LAG-3.

Additional Combination Therapies

Combinations disclosed herein, *e.g.*, combination of anti-LAG-3 antibody molecules with one or more second therapeutics are provided herein. Many of the combinations in this section are useful in treating cancer, but other indications are also described. This section focuses on combinations of anti-LAG-3 antibody molecules, optionally in combination with one or more immunomodulators (*e.g.*, an anti-PD-1 antibody molecule, an anti-TIM-3 antibody molecule, or an anti-PD-L1 antibody molecule), with one or more of the agents described in Table 7. In the combinations herein below, in one embodiment, the anti-LAG-3 antibody molecule comprises (i) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence chosen from SEQ ID NO: 1, SEQ ID NO: 4 or SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and (ii) a light chain variable region (VL) comprising a VLCDR amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12.

In one embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a PKC inhibitor, Sotrastaurin (Compound A1), or a compound disclosed in PCT Publication No. WO 2005/039549, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PKC inhibitor is Sotrastaurin (Compound A1) or a compound disclosed in PCT Publication No. WO 2005/039549. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Sotrastaurin (Compound A1), or a compound as described in PCT Publication No. WO 2005/039549, to treat a disorder such as a cancer, a melanoma, a non-Hodgkin lymphoma, an inflammatory bowel disease, transplant rejection, an ophthalmic disorder, or psoriasis.

In certain embodiments, Sotrastaurin (Compound A1) is administered at a dose of about 20 to 600 mg, *e.g.*, about 200 to about 600 mg, about 50 mg to about 450 mg, about 100 mg to 400 mg, about 150 mg to 350 mg, or about 200 mg to 300 mg, *e.g.*, about 50 mg, 100 mg, 150mg, 200 mg, 300 mg, 400 mg, 500 mg, or 600 mg. The dosing schedule can vary from *e.g.*, every other day to daily, twice or three times a day.

In one embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a BCR-ABL inhibitor, TASIGNA (Compound A2, or a compound disclosed in PCT Publication No. WO 2004/005281, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the BCR-ABL inhibitor is TASIGNA, or a compound disclosed in PCT Publication No. WO 2004/005281. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with TASIGNA (Compound A2), or a compound as described in PCT Publication No. WO 2004/005281, to treat a disorder such as a lymphocytic leukemia, Parkinson's Disease, a neurologic cancer, a melanoma, a digestive/gastrointestinal cancer, a colorectal cancer, a myeloid leukemia, a head and neck cancer, or pulmonary hypertension.

In one embodiment, the BCR-ABL inhibitor or TASIGNA is administered at a dose of about 300 mg (*e.g.*, twice daily, *e.g.*, for newly diagnosed Ph+ CML-CP), or about 400 mg, *e.g.*, twice daily, *e.g.*, for resistant or intolerant Ph+ CML-CP and CML-AP). BCR-ABL inhibitor or a Compound A2 is administered at a dose of about 300-400 mg.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an HSP90 inhibitor, such as 5-(2,4-dihydroxy-5-isopropylphenyl)-N-ethyl-4-(4-(morpholinomethyl)phenyl)isoxazole-3-carboxamide (Compound A3), or a compound disclosed in PCT Publication No. WO 2010/060937 or WO 2004/072051, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the HSP90 inhibitor is 5-(2,4-dihydroxy-5-isopropylphenyl)-N-ethyl-4-(4-(morpholinomethyl)phenyl)isoxazole-3-carboxamide (Compound A3), or a compound disclosed in PCT Publication No. WO 2010/060937 or WO 2004/072051. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with 5-(2,4-dihydroxy-5-isopropylphenyl)-N-ethyl-4-(4-(morpholinomethyl)phenyl)isoxazole-3-carboxamide (Compound A3), or a compound as described in PCT Publication No. WO 2010/060937 or WO 2004/072051, to treat a disorder such as a cancer, a multiple myeloma, a non-small cell lung cancer, a lymphoma, a gastric cancer, a breast cancer, a digestive/gastrointestinal cancer, a pancreatic cancer, a colorectal cancer, a solid tumor, or a hematopoiesis disorder.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an inhibitor of PI3K and/or mTOR, Dactolisib (Compound A4) or 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-

3-trifluoromethyl-phenyl)-1,3-dihydro-imidazo[4,5-c]quinolin-2-one (Compound A41), or a compound disclosed in PCT Publication No. WO 2006/122806, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PI3K and/or mTOR inhibitor is Dactolisib (Compound A4), 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydro-imidazo[4,5-c]quinolin-2-one (Compound A41), or a compound disclosed in PCT Publication No. WO 2006/122806. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Dactolisib (Compound A4), 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydro-imidazo[4,5-c]quinolin-2-one (Compound A41), or a compound described in PCT Publication No. WO 2006/122806, to treat a disorder such as a cancer, a prostate cancer, a leukemia (*e.g.*, lymphocytic leukemia), a breast cancer, a brain cancer, a bladder cancer, a pancreatic cancer, a renal cancer, a solid tumor, or a liver cancer.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an FGFR inhibitor, 3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-(6-((4-(4-ethylpiperazin-1-yl)phenyl)amino)pyrimidin-4-yl)-1-methylurea (Compound A5) or a compound disclosed in US Patent 8,552,002, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the FGFR inhibitor is 3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-(6-((4-(4-ethylpiperazin-1-yl)phenyl)amino)pyrimidin-4-yl)-1-methylurea (Compound A5) or a compound disclosed in US Patent 8,552,002. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Compound A5, or a compound as described in US 8,552,002, to treat a disorder such as a digestive/gastrointestinal cancer, a hematological cancer, or a solid tumor.

In one embodiment, the FGFR inhibitor or 3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-(6-((4-(4-ethylpiperazin-1-yl)phenyl)amino)pyrimidin-4-yl)-1-methylurea (Compound A5) is administered at a dose of about 100-125 mg (*e.g.*, per day), *e.g.*, about 100 mg or about 125 mg.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a PI3K inhibitor, Buparlisib (Compound A6), or a compound disclosed in PCT Publication No. WO 2007/084786, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PI3K inhibitor is Buparlisib (Compound A6) or a compound disclosed in PCT Publication No. WO 2007/084786. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Buparlisib

(Compound A6), or a compound disclosed in PCT Publication No. WO 2007/084786, to treat a disorder such as, a prostate cancer, a non-small cell lung cancer, an endocrine cancer, a leukemia, an ovarian cancer, a melanoma, a bladder cancer, a breast cancer, a female reproductive system cancer, a digestive/gastrointestinal cancer, a colorectal cancer, a glioblastoma multiforme, a solid tumor, a non-Hodgkin lymphoma, a hematopoiesis disorder, or a head and neck cancer.

In one embodiment, the PI3K inhibitor or Buparlisib (Compound A6) is administered at a dose of about 100 mg (*e.g.*, per day).

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an FGFR inhibitor, 8-(2,6-difluoro-3,5-dimethoxyphenyl)-N-(4-((dimethylamino)methyl)-1H-imidazol-2-yl)quinoxaline-5-carboxamide (Compound A7) or a compound disclosed in PCT Publication No. WO 2009/141386 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the FGFR inhibitor is 8-(2,6-difluoro-3,5-dimethoxyphenyl)-N-(4-((dimethylamino)methyl)-1H-imidazol-2-yl)quinoxaline-5-carboxamide(Compound A7) or a compound disclosed in a PCT Publication No. WO 2009/141386. In one embodiment, the FGFR inhibitor is 8-(2,6-difluoro-3,5-dimethoxyphenyl)-N-(4-((dimethylamino)methyl)-1H-imidazol-2-yl)quinoxaline-5-carboxamide(Compound A7). In one embodiment, an anti-LAG-3 antibody molecule is used in combination with 8-(2,6-difluoro-3,5-dimethoxyphenyl)-N-(4-((dimethylamino)methyl)-1H-imidazol-2-yl)quinoxaline-5-carboxamide(Compound A7), or a compound disclosed in PCT Publication No. WO 2009/141386, to treat a disorder such as a cancer characterized by angiogenesis.

In one embodiment, the FGFR inhibitor or 8-(2,6-difluoro-3,5-dimethoxyphenyl)-N-(4-((dimethylamino)methyl)-1H-imidazol-2-yl)quinoxaline-5-carboxamide (Compound A7) is administered at a dose of *e.g.*, from approximately 3 mg to approximately 5 g, more preferably from approximately 10 mg to approximately 1.5 g per person per day, optionally divided into 1 to 3 single doses which may, for example, be of the same size.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a PI3K inhibitor, (S)-N1-(4-methyl-5-(2-(1,1,1-trifluoro-2-methylpropan-2-yl)pyridin-4-yl)thiazol-2-yl)pyrrolidine-1,2-dicarboxamide (Compound A8) or a compound disclosed PCT Publication No. WO

2010/029082 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PI3K inhibitor is (S)-N1-(4-methyl-5-(2-(1,1,1-trifluoro-2-methylpropan-2-yl)pyridin-4-yl)thiazol-2-yl)pyrrolidine-1,2-dicarboxamide (Compound A8) or a compound disclosed PCT Publication No. WO 2010/029082. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with (S)-N1-(4-methyl-5-(2-(1,1,1-trifluoro-2-methylpropan-2-yl)pyridin-4-yl)thiazol-2-yl)pyrrolidine-1,2-dicarboxamide (Compound A8), or a compound disclosed PCT Publication No. WO 2010/029082, to treat a disorder such as a gastric cancer, a breast cancer, a pancreatic cancer, a digestive/ gastrointestinal cancer, a solid tumor, and a head and neck cancer.

In one embodiment, the PI3K inhibitor or (S)-N1-(4-methyl-5-(2-(1,1,1-trifluoro-2-methylpropan-2-yl)pyridin-4-yl)thiazol-2-yl)pyrrolidine-1,2-dicarboxamide (Compound A8) is administered at a dose of about 150-300, 200-300, 200-400, or 300-400 mg (*e.g.*, per day), *e.g.*, about 200, 300, or 400 mg.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an inhibitor of cytochrome P450 (*e.g.*, a CYP17 inhibitor) or a compound disclosed in PCT Publication No. WO 2010/149755, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the cytochrome P450 inhibitor (*e.g.*, the CYP17 inhibitor) is a compound disclosed in PCT Publication No. WO 2010/149755. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with a compound disclosed in PCT Publication No. WO 2010/149755, to treat prostate cancer.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an HDM2 inhibitor, (S)-1-(4-chlorophenyl)-7-isopropoxy-6-methoxy-2-(4-(methyl(((1*r*,4*S*)-4-(4-methyl-3-oxopiperazin-1-yl)cyclohexyl)methyl)amino)phenyl)-1,2-dihydroisoquinolin-3(4*H*)-one (Compound A10) or a compound disclosed in PCT Publication No. WO 2011/076786 to treat a disorder, *e.g.*, a disorder described herein). In one embodiment, the HDM2 inhibitor is (S)-1-(4-chlorophenyl)-7-isopropoxy-6-methoxy-2-(4-(methyl(((1*r*,4*S*)-4-(4-methyl-3-oxopiperazin-1-yl)cyclohexyl)methyl)amino)phenyl)-1,2-dihydroisoquinolin-3(4*H*)-one (Compound A10) or a compound disclosed in PCT Publication No. WO 2011/076786. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with (S)-1-(4-chlorophenyl)-7-isopropoxy-6-methoxy-2-(4-(methyl(((1*r*,4*S*)-4-(4-methyl-3-oxopiperazin-1-

yl)cyclohexyl)methyl)amino)phenyl)-1,2-dihydroisoquinolin-3(4H)-one (Compound A10), or a compound disclosed in PCT Publication No. WO 2011/076786, to treat a disorder such as a solid tumor.

In one embodiment, the HDM2 inhibitor or (S)-1-(4-chlorophenyl)-7-isopropoxy-6-methoxy-2-(4-(methyl(((1r,4S)-4-(4-methyl-3-oxopiperazin-1-yl)cyclohexyl)methyl)amino)phenyl)-1,2-dihydroisoquinolin-3(4H)-one (Compound A10) is administered at a dose of about 400 to 700 mg, *e.g.*, administered three times weekly, 2 weeks on and one week off. In some embodiments, the dose is about 400, 500, 600, or 700 mg; about 400-500, 500-600, or 600-700 mg, *e.g.*, administered three times weekly.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an iron chelating agent, Deferasirox (also known as EXJADE; Compound A11), or a compound disclosed in PCT Publication No. WO 1997/049395 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the iron chelating agent is Deferasirox or a compound disclosed in PCT Publication No. WO 1997/049395. In one embodiment, the iron chelating agent is Deferasirox (Compound A11). In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Deferasirox (Compound A11), or a compound disclosed in PCT Publication No. WO 1997/049395, to treat iron overload, hemochromatosis, or myelodysplasia.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an aromatase inhibitor, Letrozole (also known as FEMARA; Compound A12), or a compound disclosed in US 4,978,672 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the aromatase inhibitor is Letrozole (Compound A12) or a compound disclosed in US Patent 4,978,672. In one embodiment, an LAG-3 antibody molecule is used in combination with Letrozole (Compound A12), or a compound disclosed in US Patent 4,978,672, to treat a disorder such as a cancer, a leiomyosarcoma, an endometrium cancer, a breast cancer, a female reproductive system cancer, or a hormone deficiency.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a PI3K inhibitor, *e.g.*, a pan-PI3K inhibitor, (4S,5R)-3-(2'-amino-2-morpholino-4'-(trifluoromethyl)-[4,5'-bipyrimidin]-6-yl)-4-(hydroxymethyl)-5-methyloxazolidin-2-one (Compound A13) or a compound disclosed in

PCT Publication No. WO2013/124826 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PI3K inhibitor is (4S,5R)-3-(2'-amino-2-morpholino-4'-(trifluoromethyl)-[4,5'-bipyrimidin]-6-yl)-4-(hydroxymethyl)-5-methyloxazolidin-2-one (Compound A13) or a compound disclosed in PCT Publication No. WO2013/124826. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with (4S,5R)-3-(2'-amino-2-morpholino-4'-(trifluoromethyl)-[4,5'-bipyrimidin]-6-yl)-4-(hydroxymethyl)-5-methyloxazolidin-2-one (Compound A13), or a compound disclosed in PCT Publication No. WO2013/124826, to treat a disorder such as a cancer or an advanced solid tumor.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an inhibitor of p53 and/or a p53/Mdm2 interaction, (S)-5-(5-chloro-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-6-(4-chlorophenyl)-2-(2,4-dimethoxypyrimidin-5-yl)-1-isopropyl-5,6-dihydropyrrolo[3,4-d]imidazol-4(1H)-one (Compound A14), or a compound disclosed in PCT Publication No.

WO2013/111105 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the p53 and/or a p53/Mdm2 interaction inhibitor is (S)-5-(5-chloro-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-6-(4-chlorophenyl)-2-(2,4-dimethoxypyrimidin-5-yl)-1-isopropyl-5,6-dihydropyrrolo[3,4-d]imidazol-4(1H)-one (Compound A14) or a compound disclosed in PCT Publication No. WO2013/111105. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with (S)-5-(5-chloro-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-6-(4-chlorophenyl)-2-(2,4-dimethoxypyrimidin-5-yl)-1-isopropyl-5,6-dihydropyrrolo[3,4-d]imidazol-4(1H)-one (Compound A14), or a compound disclosed in PCT Publication No. WO2013/111105, to treat a disorder such as a cancer or a soft tissue sarcoma.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a CSF-1R tyrosine kinase inhibitor, 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-methylpicolinamide (Compound A15), or a compound disclosed in PCT Publication No. WO 2005/073224 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the CSF-1R tyrosine kinase inhibitor is 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-methylpicolinamide (Compound A15) or a compound disclosed in PCT Publication No. WO 2005/073224. In one embodiment, a LAG-3 antibody molecule is used in combination with 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-

methylpicolinamide (Compound A15) or a compound disclosed in PCT Publication No. WO 2005/073224, to treat a disorder such as cancer.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an apoptosis inducer and/or an angiogenesis inhibitor, such as Imatinib mesylate (also known as GLEEVEC; Compound A16) or a compound disclosed in PCT Publication No. WO1999/003854 to treat a disorder, *e.g.*, a disorder described. In one embodiment, the apoptosis inducer and/or an angiogenesis inhibitor is Imatinib mesylate (Compound A16) or a compound disclosed in PCT Publication No. WO1999/003854. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Imatinib mesylate (Compound A16), or a compound disclosed in PCT Publication No. WO1999/003854, to treat a disorder such as a cancer, a multiple myeloma, a prostate cancer, a non-small cell lung cancer, a lymphoma, a gastric cancer, a melanoma, a breast cancer, a pancreatic cancer, a digestive/gastrointestinal cancer, a colorectal cancer, a glioblastoma multiforme, a liver cancer, a head and neck cancer, asthma, multiple sclerosis, allergy, Alzheimer's dementia, amyotrophic lateral sclerosis, or rheumatoid arthritis.

In certain embodiments, Imatinib mesylate (Compound A16) is administered at a dose of about 100 to 1000 mg, *e.g.*, about 200 mg to 800 mg, about 300 mg to 700 mg, or about 400 mg to 600 mg, *e.g.*, about 200 mg, 300 mg, 400 mg, 500 mg, 600 mg, or 700 mg. The dosing schedule can vary from *e.g.*, every other day to daily, twice or three times a day. In one embodiment, Imatinib mesylate is administered at an oral dose from about 100 mg to 600 mg daily, *e.g.*, about 100 mg, 200 mg, 260 mg, 300 mg, 400 mg, or 600 mg daily.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a JAK inhibitor, 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof, or a compound disclosed in PCT Publication No. WO 2007/070514, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the JAK inhibitor is 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof, or a compound disclosed in PCT Publication No. WO 2007/070514. In one embodiment, an LAG-3 antibody molecule is used in combination with 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof, or a

compound disclosed in PCT Publication No. WO 2007/070514, to treat a disorder such as colorectal cancer, myeloid leukemia, hematological cancer, autoimmune disease, non-Hodgkin lymphoma, or thrombocytopenia.

In one embodiment, the JAK inhibitor or a 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof is administered at a dose of about 400-600 mg (*e.g.*, per day), *e.g.*, about 400, 500, or 600 mg, or about 400-500 or 500-600 mg.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a JAK inhibitor, Ruxolitinib Phosphate (also known as JAKAFI; Compound A18) or a compound disclosed in PCT Publication No. WO 2007/070514 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the JAK inhibitor is Ruxolitinib Phosphate (Compound A18) or a compound disclosed in PCT Publication No. WO 2007/070514. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Ruxolitinib Phosphate (Compound A18), or a compound disclosed in PCT Publication No. WO 2007/070514, to treat a disorder such as a prostate cancer, a lymphocytic leukemia, a multiple myeloma, a lymphoma, a lung cancer, a leukemia, cachexia, a breast cancer, a pancreatic cancer, rheumatoid arthritis, psoriasis, a colorectal cancer, a myeloid leukemia, a hematological cancer, an autoimmune disease, a non-Hodgkin lymphoma, or thrombocytopenia.

In one embodiment, the JAK inhibitor or Ruxolitinib Phosphate (Compound A18) is administered at a dose of about 15-25 mg, *e.g.*, twice daily. In some embodiments, the dose is about 15, 20, or 25 mg, or about 15-20 or 20-25 mg.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a deacetylase (DAC) inhibitor, Panobinostat (Compound A19), or a compound disclosed in PCT Publication No. WO 2014/072493 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the DAC inhibitor is Panobinostat (Compound A19) or a compound disclosed in PCT Publication No. WO 2014/072493. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Panobinostat (Compound A19), a compound disclosed in PCT Publication No. WO 2014/072493, to treat a disorder such as a small cell lung cancer, a respiratory/thoracic cancer, a prostate cancer, a multiple myeloma, myelodysplastic syndrome, a bone cancer, a non-small cell

lung cancer, an endocrine cancer, a lymphoma, a neurologic cancer, a leukemia, HIV/AIDS, an immune disorder, transplant rejection, a gastric cancer, a melanoma, a breast cancer, a pancreatic cancer, a colorectal cancer, a glioblastoma multiforme, a myeloid leukemia, a hematological cancer, a renal cancer, a non-Hodgkin lymphoma, a head and neck cancer, a hematopoiesis disorders, or a liver cancer.

In one embodiment, the DAC inhibitor or Panobinostat (Compound A19) is administered at a dose of about 20 mg (*e.g.*, per day).

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an inhibitor of one or more of cytochrome P450 (*e.g.*, 11B2), aldosterone or angiogenesis, Osilodrostat (Compound A20), or a compound disclosed in PCT Publication No. WO2007/024945 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the inhibitor of one or more of cytochrome P450 (*e.g.*, 11B2), aldosterone or angiogenesis is Osilodrostat (Compound A20) or a compound disclosed in PCT Publication No. WO2007/024945. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Osilodrostat (Compound A20), or a compound disclosed in PCT Publication No. WO2007/024945, to treat a disorder such as Cushing's syndrome, hypertension, or heart failure therapy.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a IAP inhibitor, (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide (Compound A21) or a compound disclosed in US 8,552,003 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the IAP inhibitor is (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide (Compound A21) or a compound disclosed in US Patent 8,552,003. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide (Compound A21), or a compound disclosed in US Patent 8,552,003, to treat a disorder such as a multiple myeloma, a breast cancer, an ovarian cancer, a pancreatic cancer, or a hematopoiesis disorder.

In one embodiment, the IAP inhibitor or (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide

(Compound A21) or a compound disclosed in US 8,552,003 is administered at a dose of approximately 1800 mg, *e.g.*, once weekly.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination a Smoothened (SMO) inhibitor, Sonidegib phosphate (Compound A22), (R)-2-(5-(4-(6-benzyl-4,5-dimethylpyridazin-3-yl)-2-methylpiperazin-1-yl)pyrazin-2-yl)propan-2-ol (Compound A25), or a compound disclosed in PCT Publication No. WO 2007/131201 or WO 2010/007120 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the SMO inhibitor is Sonidegib phosphate (Compound A22), (R)-2-(5-(4-(6-benzyl-4,5-dimethylpyridazin-3-yl)-2-methylpiperazin-1-yl)pyrazin-2-yl)propan-2-ol (Compound A25), or a compound disclosed in PCT Publication No. WO 2007/131201 or WO 2010/007120. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Sonidegib phosphate (Compound A22), (R)-2-(5-(4-(6-benzyl-4,5-dimethylpyridazin-3-yl)-2-methylpiperazin-1-yl)pyrazin-2-yl)propan-2-ol (Compound A25), or a compound disclosed in PCT Publication No. WO 2007/131201 or WO 2010/007120 to treat a disorder such as a cancer, a medulloblastoma, a small cell lung cancer, a prostate cancer, a basal cell carcinoma, a pancreatic cancer, or an inflammation.

In certain embodiments, Sonidegib phosphate (Compound A22) is administered at a dose of about 20 to 500 mg, *e.g.*, about 40 mg to 400 mg, about 50 mg to 300 mg, or about 100 mg to 200 mg, *e.g.*, about 50 mg, 100 mg, 150 mg, 200 mg, 250 mg, or 300 mg. The dosing schedule can vary from *e.g.*, every other day to daily, twice or three times a day.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an Alk inhibitor, ceritinib (also known as ZYKADIA; Compound A23) or a compound disclosed in PCT Publication No. WO 2007/131201 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the Alk inhibitor is ceritinib (Compound A23) or a compound disclosed in PCT Publication No. WO 2007/131201. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with ceritinib (Compound A23), or a compound disclosed in PCT Publication No. WO 2007/131201, to treat a disorder such as non-small cell lung cancer or solid tumors.

In one embodiment, the Alk inhibitor or ceritinib (Compound A23) is administered at a dose of approximately 750 mg, *e.g.*, once daily.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a JAK and/or CDK4/6 inhibitor, 7-cyclopentyl-N,N-dimethyl-2-((5-(piperazin-1-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A24), or a compound disclosed in US Patent 8,415,355 or US Patent 8,685,980 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the JAK and/or CDK4/6 inhibitor is 7-cyclopentyl-N,N-dimethyl-2-((5-(piperazin-1-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A24) or a compound disclosed in US Patent 8,415,355 or US Patent 8,685,980. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with 7-cyclopentyl-N,N-dimethyl-2-((5-(piperazin-1-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A24), or a compound disclosed in US 8,415,355 or US 8,685,980, to treat a disorder such as a lymphoma, a neurologic cancer, a melanoma, a breast cancer, or a solid tumor.

In one embodiment, the JAK and/or CDK4/6 inhibitor or 7-cyclopentyl-N,N-dimethyl-2-((5-(piperazin-1-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A24) is administered at a dose of approximately 200-600 mg, *e.g.*, per day. In one embodiment, the compound is administered at a dose of about 200, 300, 400, 500, or 600 mg, or about 200-300, 300-400, 400-500, or 500-600 mg.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination a prolactin receptor (PRLR) inhibitor, a human monoclonal antibody molecule (Compound A26) as disclosed in US Patent 7,867,493), to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PRLR inhibitor is a human monoclonal antibody (Compound A26) disclosed in US 7,867,493. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with human monoclonal antibody molecule (Compound A26) described in US Patent 7,867,493 to treat a disorder such as, a cancer, a prostate cancer, or a breast cancer.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a PIM Kinase inhibitor, N-(4-((1R,3S,5S)-3-amino-5-methylcyclohexyl)pyridin-3-yl)-6-(2,6-difluorophenyl)-5-fluoropicolinamide (Compound A27) or a compound disclosed in PCT Publication No. WO 2010/026124 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PIM Kinase inhibitor is N-(4-((1R,3S,5S)-3-amino-5-methylcyclohexyl)pyridin-3-yl)-6-(2,6-

difluorophenyl)-5-fluoropicolinamide (Compound A27) or a compound disclosed in PCT Publication No. WO 2010/026124. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with N-(4-((1R,3S,5S)-3-amino-5-methylcyclohexyl)pyridin-3-yl)-6-(2,6-difluorophenyl)-5-fluoropicolinamide (Compound A27), or a compound disclosed in PCT Publication No. WO 2010/026124, to treat a disorder such as a multiple myeloma, myelodysplastic syndrome, a myeloid leukemia, or a non-Hodgkin lymphoma.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination a Wnt signaling inhibitor, 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28) or a compound disclosed in PCT publication No. WO 2010/101849 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the Wnt signaling inhibitor is 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28) or a compound disclosed in PCT publication No. WO 2010/101849. In one embodiment, the Wnt signaling inhibitor is 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28). In one embodiment, an anti-LAG-3 antibody molecule is used in combination with 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28), or a compound disclosed in PCT publication No. WO 2010/101849, to treat a disorder such as a solid tumor (*e.g.*, a head and neck cancer, a squamous cell carcinoma, a breast cancer, a pancreatic cancer, or a colon cancer).

In certain embodiments, 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28) is administered at a dose of about 1 to 50 mg, *e.g.*, about 2 mg to 45 mg, about 3 mg to 40 mg, about 5 mg to 35 mg, 5 mg to 10 mg, or about 10 mg to 30 mg, *e.g.*, about 2 mg, 5 mg, 10 mg, 20 mg, 30 mg, or 40 mg. The dosing schedule can vary from *e.g.*, every other day to daily, twice or three times a day.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a BRAF inhibitor, Encorafenib (Compound A29), or a compound disclosed in PCT Publication No. WO 2011/025927 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the BRAF inhibitor is Encorafenib (Compound A29) or a compound disclosed in PCT Publication No. WO 2011/025927. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Encorafenib (Compound A29), or a compound disclosed in PCT Publication No. WO

2011/025927, to treat a disorder such as a non-small cell lung cancer, a melanoma, or a colorectal cancer.

In one embodiment, the BRAF inhibitor or Encorafenib (Compound A29) is administered at a dose of about 200-300, 200-400, or 300-400 mg, *e.g.*, per day. In one embodiment, the compound is administered at a dose of about 200, about 300 or about 400 mg.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a CDK4/6 inhibitor, 7-cyclopentyl-N,N-dimethyl-2-((5-((1R,6S)-9-methyl-4-oxo-3,9-diazabicyclo[4.2.1]nonan-3-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A30), or a compound disclosed in PCT publication No. WO 2011/101409 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the CDK4/6 inhibitor is 7-cyclopentyl-N,N-dimethyl-2-((5-((1R,6S)-9-methyl-4-oxo-3,9-diazabicyclo[4.2.1]nonan-3-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A30) or a compound disclosed in PCT publication No. WO 2011/101409. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with 7-cyclopentyl-N,N-dimethyl-2-((5-((1R,6S)-9-methyl-4-oxo-3,9-diazabicyclo[4.2.1]nonan-3-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A30), or a compound disclosed in PCT publication No. WO 2011/101409, to treat a disorder such as a cancer, a mantle cell lymphoma, a liposarcoma, a non-small cell lung cancer, a melanoma, a squamous cell esophageal cancer, or a breast cancer.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a HER3 inhibitor, Compound A31, or a compound disclosed in PCT Publication No. WO 2012/022814, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the HER3 inhibitor is Compound A31 or a compound disclosed in PCT Publication WO 2012/022814. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Compound A31, or a compound disclosed in PCT Publication WO 2012/022814, to treat a disorder such as a gastric cancer, an esophageal cancer, a head and neck cancer, a squamous cell carcinoma, a stomach cancer, a breast cancer (*e.g.*, metastatic breast cancer), or a digestive/gastrointestinal cancer.

In some embodiments, Compound A31 is a human monoclonal antibody molecule.

In one embodiment, the HER3 inhibitor or Compound A31 is administered at a dose of about 3, 10, 20, or 40 mg/kg, *e.g.*, once weekly (QW). In one embodiment, the compound is administered at a dose of about 3-10, 10-20, or 20-40 mg/kg.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination an FGFR2 and/or FGFR4 inhibitor, Compound A32, or a compound disclosed in a publication PCT Publication No. WO 2014/160160 (*e.g.*, an antibody molecule drug conjugate against an FGFR2 and/or FGFR4, *e.g.*, mAb 12425), to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the FGFR2 and/or FGFR4 inhibitor is Compound A32 or a compound disclosed in a publication PCT Publication No. WO 2014/160160. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Compound A32, or a compound as described in Table 7, to treat a disorder such as a cancer, a gastric cancer, a breast cancer, a rhabdomyosarcoma, a liver cancer, an adrenal cancer, a lung cancer, an esophageal cancer, a colon cancer, or an endometrial cancer.

In some embodiments, Compound A32 is an antibody molecule drug conjugate against an FGFR2 and/or FGFR4, *e.g.*, mAb 12425.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination an M-CSF inhibitor, Compound A33, or a compound disclosed in PCT Publication No. WO 2004/045532 (*e.g.*, an antibody molecule or Fab fragment against M-CSF), to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the M-CSF inhibitor is Compound A33 or a compound disclosed in PCT Publication No. WO 2004/045532. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Compound A33, or a compound as described in PCT Publication No. WO 2004/045532, to treat a disorder such as a cancer, a prostate cancer, a breast cancer, or pigmented villonodular synovitis (PVNS).

In embodiments, Compound A33 is a monoclonal antibody molecule against M-CSF or a fragment (*e.g.*, Fab fragment) thereof. In embodiments, the M-CSF inhibitor or Compound A33 is administered at an average dose of about 10mg/kg.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a MEK inhibitor, Binimetinib (Compound A34), or a compound disclosed in PCT Publication No. WO 2003/077914 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the MEK inhibitor is Binimetinib

(Compound A34), or a compound disclosed in PCT Publication No. WO 2003/077914. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Binimetinib (Compound A34), or a compound disclosed in PCT Publication No. WO 2003/077914, to treat a disorder such as a non-small cell lung cancer, a multisystem genetic disorder, a melanoma, an ovarian cancer, a digestive/gastrointestinal cancer, a rheumatoid arthritis, or a colorectal cancer.

In one embodiment, the MEK inhibitor or Binimetinib (Compound A34) is administered at a dose of about 45 mg, *e.g.*, twice daily.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination an inhibitor of one or more of c-KIT, histamine release, Flt3 (*e.g.*, FLK2/STK1) or PKC, Midostaurin (Compound A35) or a compound disclosed in PCT Publication No. WO 2003/037347 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the inhibitor is Midostaurin (Compound A35) or compound disclosed in PCT Publication No. WO 2003/037347. In one embodiment, the inhibitor of one or more of c-KIT, histamine release, Flt3 (*e.g.*, FLK2/STK1) or PKC is Midostaurin. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Midostaurin (Compound A35), or compound disclosed in PCT Publication No. WO 2003/037347, to treat a disorder such as a cancer, a colorectal cancer, a myeloid leukemia, myelodysplastic syndrome, an age-related muscular degeneration, a diabetic complication, or a dermatologic disorder.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a TOR inhibitor (*e.g.*, mTOR inhibitor), Everolimus (also known as AFINITOR; Compound A36) or a Compound disclosed in PCT Publication No. WO 2014/085318 to treat a disorder, *e.g.*, a disorder described herein). In one embodiment, the TOR inhibitor is Everolimus (Compound A36) or a Compound disclosed in PCT Publication No. WO 2014/085318. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Everolimus (Compound A36) to treat a disorder such as an interstitial lung disease, a small cell lung cancer, a respiratory/thoracic cancer, a prostate cancer, a multiple myeloma, a sarcoma, an age-related macular degeneration, a bone cancer, tuberous sclerosis, a non-small cell lung cancer, an endocrine cancer (*e.g.*, an atypical pulmonary carcinoid tumor), a lymphoma, a neurologic disorders, an astrocytoma, a cervical cancer, a

neurologic cancer, a leukemia, an immune disorders, transplant rejection, a gastric cancer, a melanoma, epilepsy, a breast cancer, or a bladder cancer.

In one embodiment, the TOR inhibitor or Everolimus (Compound A36) administered at a dose of about 2.5-20 mg/day. In one embodiment, the compound is administered at a dose of about 2.5, 5, 10, or 20 mg/day, *e.g.*, about 2.5-5, 5-10, or 10-20 mg/day.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination an inhibitor of one or more of VEGFR-2, PDGFRbeta, KIT or Raf kinase C, 1-methyl-5-((2-(5-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-4-yl)oxy)-N-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazol-2-amine (Compound A37) or a compound disclosed in PCT Publication No. WO 2007/030377 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the inhibitor of one or more of VEGFR-2, PDGFRbeta, KIT or Raf kinase C is 1-methyl-5-((2-(5-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-4-yl)oxy)-N-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazol-2-amine (Compound A37) or a compound disclosed in PCT Publication No. WO 2007/030377. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with 1-methyl-5-((2-(5-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-4-yl)oxy)-N-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazol-2-amine (Compound A37), or a compound disclosed in PCT Publication No. WO 2007/030377, to treat a disorder such as a cancer, a melanoma, or a solid tumor.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination a somatostatin agonist and/or growth hormone release inhibitor, Pasireotide diaspartate (also known as SIGNIFOR; Compound A38) or a compound disclosed in PCT Publication No. WO2002/010192 or US Patent No. 7,473,761 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the somatostatin agonist and/or growth hormone release inhibitor is Pasireotide diaspartate (Compound A38) or a compound disclosed in PCT Publication No. WO2002/010192 or US Patent No. 7,473,761. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Pasireotide diaspartate (Compound A38), or a compound disclosed in PCT Publication No. WO2002/010192 or US Patent No. 7,473,761, to treat a disorder such as a prostate cancer, an endocrine cancer, a neurologic cancer, a skin cancer (*e.g.*, a melanoma), a pancreatic cancer, a liver cancer, Cushing's syndrome, a gastrointestinal disorder, acromegaly, a liver and biliary tract disorder, or liver cirrhosis.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a signal transduction modulator and/or angiogenesis inhibitor, Dovitinib (Compound A39) or a compound disclosed in PCT Publication No. WO 2009/115562 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the signal transduction modulator and/or angiogenesis inhibitor is Dovitinib (Compound A39) or a compound disclosed in PCT Publication No. WO 2009/115562. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Dovitinib (Compound A39), or a compound disclosed in PCT Publication No. WO 2009/115562, to treat a disorder such as a cancer, a respiratory/thoracic cancer, a multiple myeloma, a prostate cancer, a non-small cell lung cancer, an endocrine cancer, or a neurological genetic disorder.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an EGFR inhibitor, (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication No. WO 2013/184757 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the EGFR inhibitor is (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication No. WO 2013/184757. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40), or a compound disclosed in PCT Publication No. WO 2013/184757, to treat a disorder such as a cancer, *e.g.*, a solid tumor.

In one embodiment, the EGFR inhibitor or (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) is administered at a dose of 150-250 mg, *e.g.*, per day. In one embodiment, the compound is administered at a dose of about 150, 200, or 250 mg, or about 150-200 or 200-250 mg.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an ALK inhibitor, N⁶-(2-isopropoxy-5-methyl-4-(1-methylpiperidin-4-yl)phenyl)-N⁴-(2-(isopropylsulfonyl)phenyl)-1H-pyrazolo[3,4-d]pyrimidine-4,6-diamine (Compound A42) or a compound disclosed in PCT

Publication No. WO 2008/073687 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the ALK inhibitor is N⁶-(2-isopropoxy-5-methyl-4-(1-methylpiperidin-4-yl)phenyl)-N⁴-(2-(isopropylsulfonyl)phenyl)-1H-pyrazolo[3,4-d]pyrimidine-4,6-diamine (Compound A42) or a compound disclosed in PCT Publication No. WO 2008/073687. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with N⁶-(2-isopropoxy-5-methyl-4-(1-methylpiperidin-4-yl)phenyl)-N⁴-(2-(isopropylsulfonyl)phenyl)-1H-pyrazolo[3,4-d]pyrimidine-4,6-diamine (Compound A42), or a compound disclosed in PCT Publication No. WO 2008/073687, to treat a disorder such as a cancer, an anaplastic large-cell lymphoma (ALCL), a non-small cell lung carcinoma (NSCLC), or a neuroblastoma.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination an IGF-1R inhibitor, 3-(4-(4-((5-chloro-4-((5-methyl-1H-pyrazol-3-yl)amino)pyrimidin-2-yl)amino)-5-fluoro-2-methylphenyl)piperidin-1-yl)thietane 1,1-dioxide (Compound A43), 5-chloro-N²-(2-fluoro-5-methyl-4-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)phenyl)-N⁴-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A44), or 5-chloro-N²-(4-(1-ethylpiperidin-4-yl)-2-fluoro-5-methylphenyl)-N⁴-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A45) or a compound disclosed in PCT Publication No. WO 2010/002655 to treat a disorder, *e.g.*, a disorder described. In one embodiment, the IGF-1R inhibitor is 3-(4-(4-((5-chloro-4-((5-methyl-1H-pyrazol-3-yl)amino)pyrimidin-2-yl)amino)-5-fluoro-2-methylphenyl)piperidin-1-yl)thietane 1,1-dioxide (Compound A43), 5-chloro-N²-(2-fluoro-5-methyl-4-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)phenyl)-N⁴-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A44), 5-chloro-N²-(4-(1-ethylpiperidin-4-yl)-2-fluoro-5-methylphenyl)-N⁴-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A45), or a compound disclosed in PCT Publication No. WO 2010/002655. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with 3-(4-(4-((5-chloro-4-((5-methyl-1H-pyrazol-3-yl)amino)pyrimidin-2-yl)amino)-5-fluoro-2-methylphenyl)piperidin-1-yl)thietane 1,1-dioxide (Compound A43), 5-chloro-N²-(2-fluoro-5-methyl-4-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)phenyl)-N⁴-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A44), 5-chloro-N²-(4-(1-ethylpiperidin-4-yl)-2-fluoro-5-methylphenyl)-N⁴-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A45), or a compound disclosed in PCT Publication No. WO 2010/002655, to treat a disorder such as a cancer or a sarcoma.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a P-Glycoprotein 1 inhibitor, Valspodar (also known as AMDRAY; Compound A46) or a compound disclosed in EP 296122 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the P-Glycoprotein 1 inhibitor is Valspodar (Compound A46) or a compound disclosed in EP 296122. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Valspodar (Compound A46), or a compound disclosed in EP 296122, to treat a disorder such as a cancer or a drug-resistant tumor.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with one or more of a VEGFR inhibitor, Vatalanib succinate (Compound A47) or a compound disclosed in EP 296122 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the VEGFR inhibitor is Vatalanib succinate (Compound A47) or a compound disclosed in EP 296122. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Vatalanib succinate (Compound A47), or a compound disclosed in EP 296122, to treat cancer.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an IDH inhibitor or a compound disclosed in WO2014/141104 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the IDH inhibitor is a compound disclosed in PCT Publication No. WO2014/141104. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with a compound disclosed in WO2014/141104 to treat a disorder such as a cancer.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a BCL-ABL inhibitor or a compound disclosed in PCT Publication No. WO2013/171639, WO2013/171640, WO2013/171641, or WO2013/171642 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the BCL-ABL inhibitor is a compound disclosed in PCT Publication No. WO2013/171639, WO2013/171640, WO2013/171641, or WO2013/171642. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with a compound disclosed in PCT Publication No. WO2013/171639, WO2013/171640, WO2013/171641, or WO2013/171642 to treat a disorder such as a cancer.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a c-RAF inhibitor or a compound disclosed in PCT Publication No. WO2014/151616 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the c-RAF inhibitor is Compound A50 or a compound disclosed in PCT Publication No. WO2014/151616. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with a compound disclosed in PCT Publication No. WO2014/151616 to treat a disorder such as a cancer.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with an ERK1/2 ATP competitive inhibitor or a compound disclosed in PCT Publication No. WO2015/066188 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the ERK1/2 ATP competitive inhibitor is a compound disclosed in PCT Publication No. WO2015/066188. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with Compound A51 or a compound disclosed in PCT Publication No. WO2015/066188 to treat a disorder such as a cancer.

In another embodiment, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is used in combination with a tyrosine kinase inhibitor, (Compound A52) or a compound disclosed in PCT Publication No. WO2005/073224 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the tyrosine kinase inhibitor is 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-methylpicolinamide (Compound A52) or a compound disclosed in PCT Publication No. WO2005/073224. In one embodiment, an anti-LAG-3 antibody molecule is used in combination with 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-methylpicolinamide (Compound A52), or a compound disclosed in PCT Publication No. WO2005/073224, to treat a disorder such as a cancer.

In some embodiments, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is administered in combination with one or more agents selected from, Compound A8, Compound A17, Compound A23, Compound A24, Compound A27, Compound A29, and Compound A33.

In some embodiments, the combination, *e.g.*, a combination comprising an anti-LAG-3 antibody molecule as described herein, is administered in combination with an anti-cancer agent having a known activity in an immune cell assay, *e.g.*, in one or more of a huMLR assay, a T cell

proliferation assay, and a B-cell proliferation assay. Exemplary assays are described below. Based on the assay, an IC₅₀ for can be calculated for each test agent. In embodiments, the anti-cancer agent has an IC₅₀ of, *e.g.*, 0-1 μ M, 1-4 μ M, or greater than 4 μ M, *e.g.*, 4-10 μ M or 4-20 μ M. In embodiments, the second therapeutic agent is chosen from one or more of: Compound A9, Compound A16, Compound A17, Compound A21, Compound A22, Compound A25, Compound A28, Compound A48, and Compound 49.

In some embodiments, the Compound A28 (or a compound related to Compound A28) is administered at a dose of approximately 5-10 or 10-30 mg. In some embodiments, the Compound A22 (or compound related to Compound A22) is administered at a dose of about 200 mg. In some embodiments, the Compound A17 (or compound related to Compound A17) is administered at a dose of approximately 400-600 mg. In some embodiments, the Compound A16 (or compound related to Compound A16) is administered at a dose of approximately 400-600 mg PO qDay. In some embodiments, the Compound A29 (or compound related to Compound A29) is administered at a dose of approximately 200-400 or 300-400 mg. In some embodiments, the Compound A24 (or compound related to Compound A24) is administered at a dose of approximately 200-600 mg. In some embodiments, the Compound A23 (ceritinib) (or compound related to ceritinib) is administered at a dose of approximately 750 mg once daily. In some embodiments, the Compound A8 (or compound related to Compound A8) is administered at a dose of approximately 200-400 or 300-400 mg. In some embodiments, the Compound A5 (or compound related to Compound A5) is administered at a dose of approximately 100-125 mg. In some embodiments, the Compound A6 (or compound related to Compound A6) is administered at a dose of about 100 mg. In some embodiments, the Compound A1 (or compound related to Compound A1) is administered at a dose of approximately 200-300 or 200-600 mg. In some embodiments, the Compound A40 (or compound related to Compound A40) is administered at a dose of approximately 150-250 mg. In some embodiments, the Compound A10 (or compound related to Compound A10) is administered at a dose of approximately 400 to 700 mg, *e.g.*, administered three times weekly, 2 weeks on and one week off. In some embodiments, the BCR-ABL inhibitor is administered at a dose of approximately 20 mg bid-80 mg bid.

Exemplary huMLR assay and B or T cell proliferation assays are provided below.

Human mixed lymphocyte reaction

The Mixed Lymphocyte Reaction (MLR) is a functional assay which measures the proliferative response of lymphocytes from one individual (the responder) to lymphocytes from another individual (the stimulator). To perform an allogeneic MLR, peripheral blood mononuclear cells (PBMC) from three donors were isolated from buffy-coats of unknown HLA type (Kantonspital Blutspendezentrum from Bern and Aarau, Switzerland). The cells were prepared at 2×10^5 in 0.2mL of culture medium containing RPMI 1640 GlutaMAX™ with 10% fetal calf serum (FCS), 100U penicillin/ 100µg streptomycin, 50µM 2-Mercaptoethanol. Individual 2-way reactions were set up by mixing PBMC from two different donors at a 1:1 ratio and co-cultures were done in triplicates in flat-bottomed 96-well tissue culture plates for 6 days at 37°C, 5% CO₂, in presence or not of an 8-point concentration range of test compounds. Cells were pulsed with 3H-TdR (1 µCi/0.2mL) for the last 16h of culture and incorporated radioactivity was used as a measure of cell proliferation. The concentration that inhibited 50% of the maximal huMLR response (IC₅₀) was calculated for each compound. Cyclosporine was used as a positive control of huMLR inhibition.

Human B cell proliferation assay

PBMC were freshly isolated by Ficoll-Paque density gradient from human blood and subjected to negative B-cell isolation. B cells were resuspended in culture medium (RPMI 1640, HEPES, 10% FCS, 50µg/mL gentamicine, 50µM 2-Mercaptoethanol, 1x ITS (Insulin, Transferrin and Sodium Selenite), 1x Non-Essential Amino-Acids) at a concentration of 9.104 per well in a flat-bottom 96-well culture plate. B cell stimulation was performed by human anti-IgM antibody molecule (30ug/mL) and IL-4 (75ng/mL) or by CD40 ligand (3ug/mL) and IL-4 (75ng/mL) in presence or not of a 7-point concentration range of test compounds. After 72h of culture at 37°C, 10% CO₂, cells were pulsed with 3H-TdR (1 µCi/well) for the last 6h of culture. B cells were then harvested and the incorporation of thymidine was measured using a scintillation counter. Of each duplicate treatment, the mean was calculated and these data were plotted in XLfit 4 to determine the respective IC₅₀ values.

Human T cell proliferation assay

PBMC were freshly isolated by Ficoll-Paque density gradient from human blood and subjected to negative isolation of T cells. T cells were prepared in culture medium (RPMI 1640, HEPES, 10% FCS, 50µg/mL gentamicine, 50µM 2-Mercaptoethanol, 1x ITS (Insulin, Transferrin and Sodium Selenite), 1x Non-Essential Amino-Acids) at a concentration of 8.104 per well in a flat-bottom 96-well culture plate. T cell stimulation was performed by human anti-CD3 antibody molecule (10ug/mL) or by human anti-CD3 antibody molecule (5µg/mL) and anti-CD28 antibody molecule (1µg/mL) in presence or not of a 7-point concentration range of test compounds. After 72h of culture at 37°C, 10% CO₂, cells were pulsed with 3H-TdR (1 µCi/well) for the last 6h of culture. Cell proliferation was measured by the incorporation of thymidine allowing IC50 determination for each tested compound.

Nucleic Acids

The invention also features nucleic acids comprising nucleotide sequences that encode heavy and light chain variable regions and CDRs of the anti-LAG-3 antibody molecules, as described herein. For example, the invention features a first and second nucleic acid encoding heavy and light chain variable regions, respectively, of an anti-LAG-3 antibody molecule chosen from one or more of the antibody molecules disclosed herein. The nucleic acid can comprise a nucleotide sequence as set forth in the tables herein, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 3, 6, 15, 30, or 45 nucleotides from the sequences shown in the tables herein).

In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs from a heavy chain variable region having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, *e.g.*, conserved substitutions). In other embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs from a light chain variable region having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, *e.g.*, conserved substitutions). In yet another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one,

two, three, four, five, or six CDRs from heavy and light chain variable regions having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, *e.g.*, conserved substitutions).

In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs from a heavy chain variable region having the nucleotide sequence as set forth in the tables herein, a sequence substantially homologous thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs from a light chain variable region having the nucleotide sequence as set forth in the tables herein, or a sequence substantially homologous thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In yet another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, three, four, five, or six CDRs from heavy and light chain variable regions having the nucleotide sequence as set forth in the tables herein, or a sequence substantially homologous thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein).

In another aspect, the application features host cells and vectors containing the nucleic acids described herein. The nucleic acids may be present in a single vector or separate vectors present in the same host cell or separate host cell, as described in more detail hereinbelow.

Vectors

Further provided herein are vectors comprising nucleotide sequences encoding an antibody molecule described herein. In one embodiment, the vectors comprise nucleotides encoding an antibody molecule described herein. In one embodiment, the vectors comprise the nucleotide sequences described herein. The vectors include, but are not limited to, a virus, plasmid, cosmid, lambda phage or a yeast artificial chromosome (YAC).

Numerous vector systems can be employed. For example, one class of vectors utilizes DNA elements which are derived from animal viruses such as, for example, bovine papilloma

virus, polyoma virus, adenovirus, vaccinia virus, baculovirus, retroviruses (Rous Sarcoma Virus, MMTV or MOMLV) or SV40 virus. Another class of vectors utilizes RNA elements derived from RNA viruses such as Semliki Forest virus, Eastern Equine Encephalitis virus and Flaviviruses.

Additionally, cells which have stably integrated the DNA into their chromosomes may be selected by introducing one or more markers which allow for the selection of transfected host cells. The marker may provide, for example, prototrophy to an auxotrophic host, biocide resistance, (*e.g.*, antibiotics), or resistance to heavy metals such as copper, or the like. The selectable marker gene can be either directly linked to the DNA sequences to be expressed, or introduced into the same cell by cotransformation. Additional elements may also be needed for optimal synthesis of mRNA. These elements may include splice signals, as well as transcriptional promoters, enhancers, and termination signals.

Once the expression vector or DNA sequence containing the constructs has been prepared for expression, the expression vectors may be transfected or introduced into an appropriate host cell. Various techniques may be employed to achieve this, such as, for example, protoplast fusion, calcium phosphate precipitation, electroporation, retroviral transduction, viral transfection, gene gun, lipid based transfection or other conventional techniques. In the case of protoplast fusion, the cells are grown in media and screened for the appropriate activity.

Methods and conditions for culturing the resulting transfected cells and for recovering the antibody molecule produced are known to those skilled in the art, and may be varied or optimized depending upon the specific expression vector and mammalian host cell employed, based upon the present description.

Cells

The invention also provides host cells comprising a nucleic acid encoding an antibody molecule as described herein.

In one embodiment, the host cells are genetically engineered to comprise nucleic acids encoding the antibody molecule.

In one embodiment, the host cells are genetically engineered by using an expression cassette. The phrase "expression cassette," refers to nucleotide sequences, which are capable of affecting expression of a gene in hosts compatible with such sequences. Such cassettes may

include a promoter, an open reading frame with or without introns, and a termination signal. Additional factors necessary or helpful in effecting expression may also be used, such as, for example, an inducible promoter.

The invention also provides host cells comprising the vectors described herein.

The cell can be, but is not limited to, a eukaryotic cell, a bacterial cell, an insect cell, or a human cell. Suitable eukaryotic cells include, but are not limited to, Vero cells, HeLa cells, COS cells, CHO cells, HEK293 cells, BHK cells, MDCKII cells and Per C6 cell line (*e.g.*, PER C6 cells from Crucell). Suitable insect cells include, but are not limited to, Sf9 cells.

In some embodiments, the host cell is an eukaryotic cell, *e.g.*, a mammalian cell, an insect cell, a yeast cell, or a prokaryotic cell, *e.g.*, *E. coli*. For example, the mammalian cell can be a cultured cell or a cell line. Exemplary mammalian cells include lymphocytic cell lines (*e.g.*, NSO), Chinese hamster ovary cells (CHO), COS cells, oocyte cells, and cells from a transgenic animal, *e.g.*, mammary epithelial cell.

Table 1. Amino acid and nucleotide sequences for murine, chimeric and humanized antibody molecules. The antibody molecules include murine mAb BAP050, chimeric mAbs BAP050-chi, humanized mAbs BAP050-hum01 to BAP050-hum20, humanized mAbs BAP050-hum01-Ser to BAP050-hum15-Ser, BAP050-hum18-Ser to BAP050-hum20-Ser, and humanized mAbs BAP050-Clone-F to BAP050-Clone-J. The amino acid and nucleotide sequences of the heavy and light chain CDRs, the heavy and light chain variable regions, and the heavy and light chains are shown.

BAP050 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 6	VH	QIQLVQSGPELKKPGETVKISCKASGFLLTNYGMN WVRQTPGKGLKWMGWINTDTGEPYADDFKGRFAF SLETSASTASLQINNLKNADTATYFCARNPPYYYG TNNAEAMDYWGQGTAVTVSS
SEQ ID NO: 7	DNA VH	CAGATCCAGTTGGTGCAGTCTGGACCTGAGCTGAA GAAGCCTGGAGAGACAGTCAAGATCTCCTGCAAGG CTTCTGGATTTACCCTCACAAACTATGGAATGAAC TGGGTGAGGCAGACTCCAGGAAAGGGTTTAAAGTG GATGGGCTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGACGGTTTGCCTTC TCTTTGGAGACCTCTGCCAGCACTGCCTCTTTGCA GATCAACAACCTCAAAAATGCCGACACGGCTACAT ATTTCTGTGCAAGAAACCCCTTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGTCA AGGAACCGCAGTCACCGTCTCCTCA
BAP050 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 16	VL	DIQMTQTTSSLSASLGDRVTISCSQQDISNYLNW YQQKPDGTVKVLIIYTTSTLHLGVPSRFSGSGSGTD YSLTISNLELEDIATYYCQQYYNLPWTFGGGTKLE IK
SEQ ID NO: 17	DNA VL	GATATCCAGATGACACAGACTACATCCTCCCTGTC TGCCTCTCTGGGAGACAGAGTCACCATCAGTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG

		TATCAGCAGAAACCAGATGGAACCTGTTAAAGTCCT GATCTATTACACATCAACCTTACACTTAGGAGTCC CATCAAGGTTTCAGTGGCAGTGGGTCTGGGACAGAT TATTCTCTCACCATCAGCAACCTGGAACCTCGAAGA TATTGCCACATACTATTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGTGGAGGCACCAAGTTGGAA ATCAAA
BAP050-chi HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 20	VH	QIQLVQSGPELKKPGETVKISCKASGFTLTNYGMN WVRQTPGKGLKWMGWINTDTGEPYADDFKGRFAF SLETSASTASLQINNLLKNADTATYFCARNPPYYYG TNNAEAMDYWGQGTTVTVSS
SEQ ID NO: 21	DNA VH	CAGATCCAGTTGGTGCAGTCTGGACCTGAGCTGAA GAAGCCTGGAGAGACAGTCAAGATCTCCTGCAAGG CTTCTGGATTTACCTCACAACCTATGGAATGAAC TGGGTGAGGCAGACTCCAGGAAAGGGTTTAAAGTG GATGGGCTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGACGGTTTGCCTTC TCTTTGGAGACCTCTGCCAGCACTGCCTCTTTGCA GATCAACAACCTCAAAAATGCGGACACGGCTACAT ATTTCTGTGCAAGAAACCCCTTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCTCC
SEQ ID NO: 22	HC	QIQLVQSGPELKKPGETVKISCKASGFTLTNYGMN WVRQTPGKGLKWMGWINTDTGEPYADDFKGRFAF SLETSASTASLQINNLLKNADTATYFCARNPPYYYG TNNAEAMDYWGQGTTVTVSSASTKGPSVFPPLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGTKTYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSV FLFPPKPKDTLMI SRTPVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
SEQ ID NO: 23	DNA HC	CAGATCCAGTTGGTGCAGTCTGGACCTGAGCTGAA GAAGCCTGGAGAGACAGTCAAGATCTCCTGCAAGG CTTCTGGATTTACCTCACAACCTATGGAATGAAC TGGGTGAGGCAGACTCCAGGAAAGGGTTTAAAGTG GATGGGCTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGACGGTTTGCCTTC TCTTTGGAGACCTCTGCCAGCACTGCCTCTTTGCA GATCAACAACCTCAAAAATGCGGACACGGCTACAT ATTTCTGTGCAAGAAACCCCTTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC

		<p>AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCCCCAAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACAGTGCCTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCGTCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AAGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA</p>
BAP050-chi LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 24	VL	<p>DIQMTQTTSSLSASLGDRVTISCSSSQDISNYLNW YQQKPDGTVKVLIIYYTSTLHLGVP SRFSGSGSGTD YSLTISNLELEDIATYYCQYYNLPWTFGQGTKVE IK</p>
SEQ ID NO: 25	DNA VL	<p>GATATCCAGATGACACAGACTACATCCTCCCTGTC TGCCCTCTCTGGGAGACAGAGTCACCATCAGTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGATGGAACGT TAAAGTCTT GATCTATTACACATCAACCTTACACTTAGGAGTCC CATCAAGGTTT CAGTGGCAGTGGGTCTGGGACAGAT TATTCTCTCACCATCAGCAACCTGGAAC TCGAAGA TATTGCCACATACTATTGT CAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA</p>
SEQ ID NO: 26	LC	<p>DIQMTQTTSSLSASLGDRVTISCSSSQDISNYLNW YQQKPDGTVKVLIIYYTSTLHLGVP SRFSGSGSGTD YSLTISNLELEDIATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHOGLSSPVTKSFN</p>

		RGEC
SEQ ID NO: 27	DNA LC	GATATCCAGATGACACAGACTACATCCTCCCTGTC TGCCTCTCTGGGAGACAGAGTCACCATCAGTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGATGGAACGTGTTAAAGTCCT GATCTATTACACATCAACCTTACACTTAGGAGTCC CATCAAGGTTTCAGTGGCAGTGGGTCTGGGACAGAT TATTCTCTCACCATCAGCAACCTGGAACCTCGAAGA TATTGCCACATACTATTGTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCCTGCCAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum01 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 28	VH	EVQLVQSGAEVKKPGATVKISCKVSGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 29	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG TTTCTGGATTACCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATACTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 30	HC	EVQLVQSGAEVKKPGATVKISCKVSGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSKV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQF NWFYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVHLH QDNLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE

		WESNGQPENNYKTTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLGLGK
		GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGTCTC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCCT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCCTGTCCCCCAAACCAAGGACACTCTCAT GATCTCCCGACCCCTGAGGTACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTACGCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAATACTAA GACCACGCCTCCCGTGTCTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
SEQ ID NO: 31	DNA HC	
BAP050-hum01 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
		DIQMTQSPSSLSASVGRVITTCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGVP SRFSGSGGTD FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 32	VL	
SEQ ID NO: 33	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCACTGTAGGAGACAGAGTACCATCACTTGCA

		GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTACAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAAA
SEQ ID NO: 34	LC	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGVPSPRFSGSGSDT FTFTISSLEAEDAATYYCQQYYNLPWTFGGQTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNRFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSYSTLS SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEK
SEQ ID NO: 35	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTACAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum02 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 28	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVIVSS
SEQ ID NO: 29	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT

		ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCC
SEQ ID NO: 30	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSKV HTFPAVLQSSGLYSLSSVTVTPSSSLGTKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPPVLDSDGSAFLYRSLTVDKSK RWQEGNVFSCSVMEALHNHYTQKSLSLSLGK
SEQ ID NO: 31	DNA HC	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACGTCGCTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCGTCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCTTGCCCCCATCCAGGAGGA GATGACCAAGAACCAGGTACGCTGACCTGCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum02 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN

SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 36	VL	DIQMTQSPSSLSASVGDRTITCASSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGT FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 37	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATTTCAGTGGCAGCGGGTATGGAACAGAT TTTACCCTCACAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 38	LC	DIQMTQSPSSLSASVGDRTITCASSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGT FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKDYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEN
SEQ ID NO: 39	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATTTCAGTGGCAGCGGGTATGGAACAGAT TTTACCCTCACAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum03 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY

SEQ ID NO: 28	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 29	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCC
SEQ ID NO: 30	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVDVSDQEDPEVQF NWFYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLSLGK
SEQ ID NO: 31	DNA HC	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCCCTACAGTCCCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCAGCACCTGAGTTCCCTGGGGGGACCATCAGTC TTCCTGTTCCCCCAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA

		GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCGTCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTCAGCCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTTAA
BAP050-hum03 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 40	VL	EIVLTQSPATLPVTLGQPASISCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 41	DNA VL	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTCACCCTTGGACAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTTCAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 42	LC	EIVLTQSPATLPVTLGQPASISCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY BREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEN
SEQ ID NO: 43	DNA LC	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTCACCCTTGGACAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTTCAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCGTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC

		AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCCTGCCAAGTCACCCATC AGGGCCTGAGCTCGCCCCTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum04 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 28	VH	EVQLVQSGAEVKKPGATVKISCKVSGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 29	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGACGACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCCGCTTCCACCA
SEQ ID NO: 30	HC	EVQLVQSGAEVKKPGATVKISCKVSGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHPKSNKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRPEVTCVVVDVSDQEDPEVQF NWFYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLGLK
SEQ ID NO: 31	DNA HC	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGACGACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCCGCTTCCACCA AGGGCCCATCCGCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG

		CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCACCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCGTCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTCAGCCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAATACTAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum04 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 44	VL	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGIPDRFSGSGSGTD FTLTISRLEPEDFAVYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 45	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CAGACAGGTTTCAAGTGGCAGTGGGTCTGGGACAGAC TTCACCTCTACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 46	LC	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGIPDRFSGSGSGTD FTLTISRLEPEDFAVYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE
SEQ ID NO: 47	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA

		GTTCAAGTCAGGACATCAGCAATTTAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CAGACAGGTTTACAGTGGCAGTGGGTCTGGGACAGAC TTCCTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCAGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum05 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 28	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 29	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGACACCTCTGTCTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 30	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSKV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCVMHEALHNYTQKSLSLSLGK
SEQ ID NO: 31	DNA HC	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG

		<p>TTTCTGGATTACCCCTCACAAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGACGACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTGCTGGAACCTCAGGCGCCCTGACCAGCGGGCTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCCTGTTCCCCCAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCGTCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTACGCTGACCTGCCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAACACTAAA GACCACGCCCTCCCGTGTGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA</p>
BAP050-hum05 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 48	VL	<p>EIVLTQSPATLSLSPGERATLSCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGVPSRFSGSGSGTD FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IK</p>
SEQ ID NO: 49	DNA VL	<p>GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTC TTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTCAGTGGCAGTGGATCTGGGACAGAT</p>

		TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTGAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAA
SEQ ID NO: 50	LC	EIVLTQSPATLSLSPGERATLSCSSSQDISNYLNW YQQKPKAPKLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQQYINLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEN
SEQ ID NO: 51	DNA LC	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTC TTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGTCC CCTCGAGGTTTCAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTGAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCAAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum06 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 28	VH	EVQLVQSGAEVKKPGATVKISCKVSGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 29	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAAAATATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGAGCAGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAAACCTCCCTATTACTACGGT ACTAATAACCGGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 30	HC	EVQLVQSGAEVKKPGATVKISCKVSGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF

		<p>SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQGTIVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSV FLFPKPKDLMISRTPVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNYHQKSLSLSLGK</p>
<p>SEQ ID NO: 31</p>	<p>DNA HC</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG TTTCTGGATTTACCCTCACAAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTGGACACCTCTGTTCAGCACGGCATACTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTGCTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGACCATCAGTC TTCTGTTCCCCCAAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTACGCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCCTACACACAGA AGAGCCTTCCCTGTCTCTGGGTAAA</p>
<p>BAP050-hum06 LC</p>		
<p>SEQ ID NO: 10 (Kabat)</p>	<p>LCDR1</p>	<p>SSSQDISNYLN</p>
<p>SEQ ID NO: 11 (Kabat)</p>	<p>LCDR2</p>	<p>YTSTLHL</p>
<p>SEQ ID NO: 12 (Kabat)</p>	<p>LCDR3</p>	<p>QYYNLPWT</p>
<p>SEQ ID NO: 13 (Chothia)</p>	<p>LCDR1</p>	<p>SQDISNY</p>

SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 52	VL	DIVMTQTPLSLPVTGPGEPAISCSSSQDISNYLNLW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQYYNLPWTFGGQGTKVE IK
SEQ ID NO: 53	DNA VL	GATATTGTGATGACCCAGACTCCACTCTCCCTGCC CGTCACCCCTGGAGAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAA TTCACTCTCACCATCAGCAGCCTGCAGCCTGATGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 54	LC	DIVMTQTPLSLPVTGPGEPAISCSSSQDISNYLNLW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQYYNLPWTFGGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 55	DNA LC	GATATTGTGATGACCCAGACTCCACTCTCCCTGCC CGTCACCCCTGGAGAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAA TTCACTCTCACCATCAGCAGCCTGCAGCCTGATGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum07 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 28	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLITNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS

<p>SEQ ID NO: 29</p>	<p>DNA VH</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACCGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC</p>
<p>SEQ ID NO: 30</p>	<p>HC</p>	<p>EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFP LPPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK</p>
<p>SEQ ID NO: 31</p>	<p>DNA HC</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACCGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCACCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACCGTGCCTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCTGCCCCCATCCAGGAGGA GATGACCAAGAACCAGGTGACCGTGCCTGG</p>

		TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAA GACCACGCCTCCCCTGGTGGACTCCGACGGCTCCT TCTTCCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCCTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum07 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 56	VL	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 57	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACTATCACTTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAA TTCACCTCACCATCAGCAGCCTGCAGCCTGATGA TTTTGCAACTTATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 58	LC	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE
SEQ ID NO: 59	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACTATCACTTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAA TTCACCTCACCATCAGCAGCCTGCAGCCTGATGA TTTTGCAACTTATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT

BAP050-hum08 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 28	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 29	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGA AAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA
SEQ ID NO: 30	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMI SRTPEVTCVVDVVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMEALHNHYTQKSLSLSLGK
SEQ ID NO: 31	DNA HC	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGA AAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG

		<p>AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCCTGTTCCCCCAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCGTACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAATAACAA GACCACGCCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA</p>
BAP050-hum08 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 60	VL	<p>EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQYYNLPWTFGQGTKVE IK</p>
SEQ ID NO: 61	DNA VL	<p>GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTACGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA</p>
SEQ ID NO: 62	LC	<p>EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC</p>
SEQ ID NO: 63	DNA LC	<p>GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTACGCGGCAGTGGATCTGGGACAGAT</p>

		TTCACCTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCCTCTGTTGTGTGCCTGTCTGAATAACTTCTAT CCCAGAGAGGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCCTGCCAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum09 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 64	VH	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVSS
SEQ ID NO: 65	DNA VH	CAGGTTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCTCAGCACGGCATACTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 66	HC	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPPEVTCVVVDVSDPEVQF NWIYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLGLK
SEQ ID NO: 67	DNA HC	CAGGTTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC

		TCCTTGGACACCTCTGTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAATAAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCCTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum09 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 36	VL	DIQMTQSPSSLSASVGDRTVITCSSSQDISNYLNW YQKPKAPKLLIYYTSTLHLGIPPRFSGSGYGTD FTLTINNIESEDAAYYFCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 37	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATTGAGTGGCAGCGGTATGGAACAGAT TTTACCCTCACAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGCCAAGGGACCAAGGTGGAA ATCAAA

SEQ ID NO: 38	LC	DIQMTQSPSSLSASVGDRTVITTCSSSQDISNYLNW YQQKPKAPKLLIYYTSTLHLGIPPRFSGSGYGT FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEN
SEQ ID NO: 39	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATTTCAGTGGCAGCGGGTATGGAACAGAT TTTACCCTCACAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGTGTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCACCCATC AGGGCTGAGCTCGCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum10 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 64	VH	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 65	DNA VH	CAGGTTGAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTACCTCACAACATATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCTCC
SEQ ID NO: 66	HC	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV

		<p>DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK</p>
<p>SEQ ID NO: 67</p>	<p>DNA HC</p>	<p>CAGGTCAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTCTGGATTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGACACCTCTGTGACGACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTACCGTGCCCTCCA GCAGCTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCCCCAAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACCGTGCCTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCCATCCAGGAGGA GATGACCAAGAACCAGGTACCGCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCCTCCCGTGTCTGGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA</p>
BAP050-hum10 LC		
<p>SEQ ID NO: 10 (Kabat)</p>	<p>LCDR1</p>	<p>SSSQDISNYLN</p>
<p>SEQ ID NO: 11 (Kabat)</p>	<p>LCDR2</p>	<p>YTSTLHL</p>
<p>SEQ ID NO: 12 (Kabat)</p>	<p>LCDR3</p>	<p>QQYINLPWT</p>
<p>SEQ ID NO: 13 (Chothia)</p>	<p>LCDR1</p>	<p>SQDISNY</p>
<p>SEQ ID NO: 14 (Chothia)</p>	<p>LCDR2</p>	<p>YTS</p>
<p>SEQ ID NO: 15 (Chothia)</p>	<p>LCDR3</p>	<p>YYNLPW</p>

SEQ ID NO: 40	VL	EIVLTQSPATLPVTLGQPASISCSSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 41	DNA VL	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTCACCCTTGGACAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTACAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTGACAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 42	LC	EIVLTQSPATLPVTLGQPASISCSSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY BREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEK
SEQ ID NO: 43	DNA LC	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTCACCCTTGGACAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTACAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTGACAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGGAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum11 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 64	VH	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTIVVSS
SEQ ID NO: 65	DNA VH	CAGGTTTACGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC

		TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 66	HC	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGTKTYTCNV DHKPNTKVDKRVESKYGPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLGLK
SEQ ID NO: 67	DNA HC	CAGGTTGAGTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCGCTGGCGCCCTGCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCGAACCAGGTGACGG TGTGCTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCTCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCTTCCAGGAGGA GATGACCAAGAACCAGGTACGCTGACCTGCCTGG TCAAAGGCTTCTACCCCGAGGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAATACTCAA GACCACGCCTCCCGTGTGACTCCGACGGCTCCT

		TCTTCCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum11 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 56	VL	DIQMTQSPSSLSASVGDRTVITTCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGVP SRFSGSGSGTE FTLTISLQPDFFATYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 57	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACTATCACTTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAA TTCACTCTCACCATCAGCAGCCTGCAGCCTGATGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 58	LC	DIQMTQSPSSLSASVGDRTVITTCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGVP SRFSGSGSGTE FTLTISLQPDFFATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE
SEQ ID NO: 59	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACTATCACTTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAA TTCACTCTCACCATCAGCAGCCTGCAGCCTGATGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum12 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN

SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 64	VH	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 65	DNA VH	CAGGTTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA
SEQ ID NO: 66	HC	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWIYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVHL QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYRSLTVDKS RWQEGNVFSCSVMEALHNHYTQKSLSLSLGK
SEQ ID NO: 67	DNA HC	CAGGTTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC

		TTCCTGTTCCCCC AAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCCCTACCGTCCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTTCCAAACAAAGGCCCTCCCGTCCCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCC TGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGT CAGCCTGACCTGCCTGG TCAAAGGCTTCTACCC CAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCCT TCTTCCCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum12 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 60	VL	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTLTISSLQPEDFATYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 61	DNA VL	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTT CAGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGT CAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 62	LC	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTLTISSLQPEDFATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNRFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 63	DNA LC	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTT CAGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGT CAGCAGTATTATAACC

		<p>TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCAAAAAGAGCTTCAAC AGGGGAGAGTGT</p>
BAP050-hum13 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 68	VH	<p>QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS</p>
SEQ ID NO: 69	DNA VH	<p>CAGGTTCAGCTGGTGCAGTCCGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTGGATAAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC</p>
SEQ ID NO: 70	HC	<p>QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NQYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLGLK</p>
SEQ ID NO: 71	DNA HC	<p>CAGGTTCAGCTGGTGCAGTCCGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTGGATAAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT</p>

		ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGACCATCAGTC TTCTGTCCCCC AAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTCAGCCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAATAACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCCTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum13 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 36	VL	DIQMTQSPSSLSASVGDRTTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGT FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 37	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATTTCAGTGGCAGCGGGTATGGAACAGAT TTTACCCTCACAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGCCAAGGGACCAAGGTGGAA ATCAA
SEQ ID NO: 38	LC	DIQMTQSPSSLSASVGDRTTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGT

		FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEN
SEQ ID NO: 39	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCAGTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATTTCAGTGGCAGCGGGTATGGAACAGAT TTTACCCTCACAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGTGTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum14 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 72	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WIRQSPSRGLEWLGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 73	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG TTTCTGGATTTACCCTCACAACCTATGGAATGAAC TGGATCAGGCAGTCCCCATCGAGAGGCCTTGAGTG GCTGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCTCC
SEQ ID NO: 74	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WIRQSPSRGLEWLGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFPPLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHPKSNITKVDKRVESKYGPPCPPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDPEVQF

		NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGLK
		GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAAAATCTCCTGCAAGG TTTCTGGATTACCCCTCACAAACTATGGAATGAAC TGGATCAGGCAGTCCCCATCGAGAGGCCTTGAGTG GCTGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTGGACACCTCTGTGACGACGGCATACTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCACCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCGTCTGAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
SEQ ID NO: 75	DNA HC	
BAP050-hum14 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYINLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
		EIVLTQSPATLPVTLGQPASISCSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSTRFSGSGSDT FTFTISSLEAEDAATYYCQQYINLPWTFGGQTKVE
SEQ ID NO: 40	VL	

		IK
SEQ ID NO: 41	DNA VL	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTCACCCTTGGACAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTCAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAA
SEQ ID NO: 42	LC	EIVLTQSPATLPVTLGQPASISCSQQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSDT FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE
SEQ ID NO: 43	DNA LC	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTCACCCTTGGACAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTCAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCTGCGAAGTCACCCATC AGGGCTGAGCTCGCCCGTCAAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum15 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 72	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLNTNYGMN WIRQSPSRGLEWLGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVIVSS
SEQ ID NO: 73	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAAACTATGGAATGAAC TGGATCAGGCAGTCCCCATCGAGAGGCTTGAGTG GCTGGGTTGGATAAACACCGACACTGGAGAGCCAA

		<p>CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC</p>
<p>SEQ ID NO: 74</p>	<p>HC</p>	<p>EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WIRQSPSRGLEWLGWINTDTGPEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQTTVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVNF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSK RWQEGNVFSCSVMHEALHNHYTQKSLSLGLK</p>
<p>SEQ ID NO: 75</p>	<p>DNA HC</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGATCAGGCAGTCCCATCGAGAGGCCTTGAGTG GCTGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCGAACCGGTGACGG TGTCTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCCTG GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCCTGTCCCCCAAACCAAGGACACTCTCAT GATCTCCCGACCCCTGAGGTACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT</p>

		GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum15 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 60	VL	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTLTISLQPEDFATYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 61	DNA VL	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTACGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAAA
SEQ ID NO: 62	LC	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTLTISLQPEDFATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 63	DNA LC	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTACGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCAGCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTGTGTGCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum16 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG

SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLLNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 76	VH	EVQLVQSGAEVKKPGESLRISCKGSGFTLLTNYGMN WVRQATGQGLEWMGWINTDTGEPYADDFKGRVTI SADKSI STAYLQWSSLKASDTAMYICARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 77	DNA VH	GAAGTGCAGCTGGTGCAGTCTGGAGCAGAGGTGAA AAAGCCCGGGGAGTCTCTGAGGATCTCCTGTAAGG GTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCACTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGAGTCACCATC TCAGCCGACAAGTCCATCAGCACCGCCTACCTGCA GTGGAGCAGCCTGAAGGCCCTCGGACACCGCCATGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 78	HC	EVQLVQSGAEVKKPGESLRISCKGSGFTLLTNYGMN WVRQATGQGLEWMGWINTDTGEPYADDFKGRVTI SADKSI STAYLQWSSLKASDTAMYICARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTISWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPAPEFLGGPSV FLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMEALHNHYTQKSLSLSLGK
SEQ ID NO: 79	DNA HC	GAAGTGCAGCTGGTGCAGTCTGGAGCAGAGGTGAA AAAGCCCGGGGAGTCTCTGAGGATCTCCTGTAAGG GTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCACTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGAGTCACCATC TCAGCCGACAAGTCCATCAGCACCGCCTACCTGCA GTGGAGCAGCCTGAAGGCCCTCGGACACCGCCATGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCTCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG

		TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCCCTACCGTCCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCCCTCCATCGAGA AAACCATCTCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCC TGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGT CAGCCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACA ACTACAA GACCACGCCTCCCGTGCTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum16 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 60	VL	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQQYYNLPWTFGGGTKVE IK
SEQ ID NO: 61	DNA VL	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTT CAGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGT CAGCAGTATTATAACC TTCCGTGGACGTTCCGCCAAGGGACCAAGGTGGAA ATCAAAA
SEQ ID NO: 62	LC	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQQYYNLPWTFGGGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEN
SEQ ID NO: 63	DNA LC	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTT CAGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGT CAGCAGTATTATAACC TTCCGTGGACGTTCCGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT

		CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum17 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 80	VH	QVQLVQSGSELKPKGASVKVSKASGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISTLKAEDTATYFCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 81	DNA VH	CAGGTGCAGCTGGTGCAATCTGGGTCTGAGTTGAA GAAGCCTGGGGCCTCAGTGAAGGTTTCCCTGCAAGG CTTCTGGATTACCCCTGACTAACTATGGCATGAAT TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGATGGATCAACACCGACACTGGGGAGCCAA CGTATGCCGATGACTTCAAGGGACGGTTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCACGCTAAAGGCTGAGGACACTGCTACAT ATTTCTGTGCAAGAAACCCCTTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 82	HC	QVQLVQSGSELKPKGASVKVSKASGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISTLKAEDTATYFCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYPPCPPAPEFLGGPSV FLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMEALHNHYTQKLSLSLGLK
SEQ ID NO: 83	DNA HC	CAGGTGCAGCTGGTGCAATCTGGGTCTGAGTTGAA GAAGCCTGGGGCCTCAGTGAAGGTTTCCCTGCAAGG CTTCTGGATTACCCCTGACTAACTATGGCATGAAT TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGATGGATCAACACCGACACTGGGGAGCCAA CGTATGCCGATGACTTCAAGGGACGGTTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCACGCTAAAGGCTGAGGACACTGCTACAT ATTTCTGTGCAAGAAACCCCTTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA

		GGGCACCACCGTGACCGTGTCCCTCCGCTTCCACCA AGGGCCCATCCGCTTTCCTCCCGCCCTGGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCCCTACAGTCCCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GACCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCCTGTTCCCCCAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCCCTACCGTCCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCCCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCCATCCAGGAGGA GATGACCAAGAACCAGGTGACCGTGCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCCTCCCGTGGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum17 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 84	VL	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLQPEDIAITYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 85	DNA VL	GACATCCAGATGACCCAGTCTCCATCCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCT CCTCTAGTCAGGACATTAGCAACTATTTAAATTGG TATCAGCAGAAACCAGGGAAAGCCCCCTAAGCTCCT GATCTACTATACATCCACTTTGCACCTGGGGTCC CATCAAGGTTTCAGTGGAAAGTGGATCTGGGACAGAT TTTACTTTTACCATCAGCAGCCTGCAGCCTGAAGA TATTGCAACATATTACTGTCAACAGTATTATAATC TCCCTTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 86	LC	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLQPEDIAITYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY

		PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE
SEQ ID NO: 87	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTACCATCACTTGCT CCTCTAGTCAGGACATTAGCAACTATTTAAATTGG TATCAGCAGAAACCAGGGAAAGCCCCCTAAGCTCCT GATCTACTATACATCCACTTTGCACCTGGGGGTCC CATCAAGGTTTCAGTGGAAAGTGGATCTGGGACAGAT TTTACTTTTACCATCAGCAGCCTGCAGCCTGAAGA TATTGCAACATATTACTGTCAACAGTATTATAATC TCCCTTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCCTGCCAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum18 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 28	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 29	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGACACCTCTGTGACGACGGCATACTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACCGGAGGCTATGGACTACTGGGGCCA GGGACCACCGTGACCGTGCCTCC
SEQ ID NO: 30	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHPKSNITKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQF NHWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDNLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE

		PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
		GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGACGACGGCATACTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACCGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCCCCAAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACGTCGCTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACA ACTACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
SEQ ID NO: 31	DNA HC	
BAP050-hum18 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
		AIQLTQSPSSLSASVGDVRTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGGTD FTLTISLQPEDFATYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 88	VL	

SEQ ID NO: 89	DNA VL	GCCATCCAGTTGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 90	LC	AIQLTQSPSSLSASVGDVRTITCSSSQDISNYLW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTLTISSLQPEDFATYYCQQYYNLPWTFGGGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 91	DNA LC	GCCATCCAGTTGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCAACCATC AGGGCCTGAGCTCGCCCGTCAAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum19 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTN
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 28	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 29	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCTCAGCAGGCATATCTGCA

		<p>GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC</p>
<p>SEQ ID NO: 30</p>	<p>HC</p>	<p>EVQLVQSGAEVKKPGATVKISKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQTTVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSKV HTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQF NWFYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHLEALHNHYTQKLSLSLSLGK</p>
<p>SEQ ID NO: 31</p>	<p>DNA HC</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAAAATCTCCTGCAAGG TTTCTGGATTACCCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCTGGGGGGACCATCAGTC TTCCTGTCCCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTACCGTACCTGCCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA</p>

BAP050-hum19 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 92	VL	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 93	DNA VL	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTTCAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAAA
SEQ ID NO: 94	LC	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNMFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLS SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 95	DNA LC	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTTCAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCCTGCTGAATAACTTCTAT CCCAGAGAGGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCAAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum20 HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY

SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 64	VH	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 65	DNA VH	CAGGTT CAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCCTCACAAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 66	HC	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQIAVE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPPVLDSGDGSFFLYRSLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLGLK
SEQ ID NO: 67	DNA HC	CAGGTT CAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCCTCACAAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCTGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACCGTGCCTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA

		CGTACCGTGTGGTCAGCGTCCCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCCATCGAGA AAACCATCTCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTACAGCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCCTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum20 LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 96	VL	DIVMTQTPLSLPVTTPGEPASISCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGIPDRFSGSGSGTD FTLTISRLEPEDFAVYYCQYYNLPWTFGGQTKVE IK
SEQ ID NO: 97	DNA VL	GATATTGTGATGACCCAGACTCCACTCTCCCTGCC CGTACCCCTGGAGAGCCGGCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGATCC CAGACAGGTTTCAGTGGCAGTGGGTCTGGGACAGAC TTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAA
SEQ ID NO: 98	LC	DIVMTQTPLSLPVTTPGEPASISCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGIPDRFSGSGSGTD FTLTISRLEPEDFAVYYCQYYNLPWTFGGQTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 99	DNA LC	GATATTGTGATGACCCAGACTCCACTCTCCCTGCC CGTACCCCTGGAGAGCCGGCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGATCC CAGACAGGTTTCAGTGGCAGTGGGTCTGGGACAGAC TTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA

		CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum01-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 101	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 102	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHPKSNKVDKRVESKYGPPCPPAPEFLGGPSV FLFPPKPKDITLMISRTPVTCVVVDVSDQEDPEVQF NWFYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDNLNGKEYKCKVSNKGLPSSIEKTIKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK
SEQ ID NO: 103	DNA HC	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGGCTG

		CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCCCTACAGTCCCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCCT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCACCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACAGTGCCTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCCTGTGGTACAGCGTCCCTACCCTCCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGCCAACAAAGGCCTCCCGTCCCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTACAGCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGGCTCTGCACAACCCTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum01-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYINLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYINLPW
SEQ ID NO: 32	VL	DIQMTQSPSSLSASVGDRTITCASSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQQYINLPWTFGQGTKVE IK
SEQ ID NO: 33	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGTCC CCTCGAGGTTTCAAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTGAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAAA
SEQ ID NO: 34	LC	DIQMTQSPSSLSASVGDRTITCASSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQQYINLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE

SEQ ID NO: 35	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTCAAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAAACAAAAGTCTACGCCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum02-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISCKVSGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 101	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGA AAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAAACCCCTCCCTATTACTACGGT ACTAATAACCGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 102	HC	EVQLVQSGAEVKKPGATVKISCKVSGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFPLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDPEVQF NWFYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMEALHNHYTQKLSLSLSLGK

		GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCTAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGTCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCCT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCCTGTTCCCCCAAACCAAGGACACTCTCAT GATCTCCCGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAAGCCAAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
SEQ ID NO: 103	DNA HC	
BAP050-hum02-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 36	VL	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSYGTD FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 37	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT

		GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATTTCAGTGGCAGCGGGTATGGAACAGAT TTTACCCTCACAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGTTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAA
SEQ ID NO: 38	LC	DIQMTQSPSSLSASVGDRTTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGT FTLTINNIESEDAAYYFCQQYYNLPWTFGQGT IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFF PREAKVQWKVDNALQSGNSQESVTEQDSKDSST SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEN
SEQ ID NO: 39	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATTTCAGTGGCAGCGGGTATGGAACAGAT TTTACCCTCACAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGTTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCGTACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum03-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFV SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 101	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATACTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC

<p>SEQ ID NO: 102</p>	<p>HC</p>	<p>EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGPEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQGTTVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPPVLDSGSEFFLYSRLTVDKS RWQEGNVFSCSMHEALHNHYTQKSLSLSLGK</p>
<p>SEQ ID NO: 103</p>	<p>DNA HC</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGACGACGGCATACTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACGTCGCTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAAACAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTACGCTGACCTGCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAACACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCCTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA</p>
<p>BAP050-hum03-Ser LC</p>		
<p>SEQ ID NO: 10 (Kabat)</p>	<p>LCDR1</p>	<p>SSSQDISNYLN</p>
<p>SEQ ID NO: 11 (Kabat)</p>	<p>LCDR2</p>	<p>YTSTLHL</p>

SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 40	VL	EIVLTQSPATLPVTLGQPASISCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 41	DNA VL	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTCACCCCTGGACAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTCAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAAA
SEQ ID NO: 42	LC	EIVLTQSPATLPVTLGQPASISCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNRFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSYSTLS SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEK
SEQ ID NO: 43	DNA LC	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTCACCCCTGGACAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTCAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCCTGCTGAATAACTTCTAT CCCAGAGAGGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum04-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISKVSGFTLTNYGMN

		<p>WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTTVTVSS</p>
<p>SEQ ID NO: 101</p>	<p>DNA VH</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCC</p>
<p>SEQ ID NO: 102</p>	<p>HC</p>	<p>EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTTVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSKV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYPPCPPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLSLGK</p>
<p>SEQ ID NO: 103</p>	<p>DNA HC</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCCGCTTCCACCA AGGGCCCATCCGCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTGGGACACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA</p>

		AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCGTCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum04-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYINLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 44	VL	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGIPDRFSGSGSDT FTLTISRLEPEDFAVYYCQQYINLPWTFGQGTKVE IK
SEQ ID NO: 45	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CAGACAGGTTTTCAGTGGCAGTGGGTCTGGGACAGAC TTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 46	LC	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGIPDRFSGSGSDT FTLTISRLEPEDFAVYYCQQYINLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 47	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CAGACAGGTTTTCAGTGGCAGTGGGTCTGGGACAGAC TTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTCCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGTCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA

		GAAACACAAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum05-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 101	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACCGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA
SEQ ID NO: 102	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQF NWFYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLSLGK
SEQ ID NO: 103	DNA HC	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACCGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT

		CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCCT GCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCTCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCGTCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTCAGCCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACA ACTACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum05-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 48	VL	EIVLTQSPATLSLSPGERATLSCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 49	DNA VL	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTC TTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCA GTTCAAGTCAGGACATCAGCAATTTTAAACTGG TATCAGCAGAAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACTTAGGGGTCC CCTCGAGGTTTCAAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTGACAGTATTATAACC TTCCGTGGACGTTCCGGCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 50	LC	EIVLTQSPATLSLSPGERATLSCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 51	DNA LC	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTC TTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCA GTTCAAGTCAGGACATCAGCAATTTTAAACTGG

		TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTACAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum06-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTN
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQTTVTVSS
SEQ ID NO: 101	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 102	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQTTVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGTKYTCNV DHKPSNTKVDKRVESKYGPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMEALHNHYTQKSLSLSLGK
SEQ ID NO: 103	DNA HC	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC

		TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGACGACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCATGCCACCCTG GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCCTGTTCCCCCAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTTACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCACAAAGGGCTTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAACATAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCCTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum06-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 52	VL	DIVMTQTPLSLPVTGPEPASISCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTE FTLTISSLQPDDEFATYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 53	DNA VL	GATATTGTGATGACCCAGACTCCACTCTCCCTGCC CGTCACCCCTGGAGAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTGAGCGGAGTGGATCTGGGACAGAA TTCACTCTCACCATCAGCAGCCTGCAGCCTGATGA

		TTTTGCAACTTATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 54	LC	DIVMTQTPLSLPVTPEPASICSSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSTRFSGSGSGTE FTLTISSLQPDFATYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEK
SEQ ID NO: 55	DNA LC	GATATTGTGATGACCCAGACTCCACTCTCCCTGCC CGTCACCCCTGGAGAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGTCC CATCAAGGTTTCCAGCGGCAGTGGATCTGGGACAGAA TTCCTCTCACCATCAGCAGCCTGCAGCCTGATGA TTTTGCAACTTATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCAAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum07-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 101	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 102	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG

		<p>TNNAEAMDYWGQGTTVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQF NWFYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLSLGK</p>
<p>SEQ ID NO: 103</p>	<p>DNA HC</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGT CAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCATCCGCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAAC T CAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGACCATCAGTC TTCTGTCCCCCCCCAAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGT CAGCCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCC TCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCCTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCAC TACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA</p>
<p>BAP050-hum07-Ser LC</p>		
<p>SEQ ID NO: 10 (Kabat)</p>	<p>LCDR1</p>	<p>SSSQDISNYLN</p>
<p>SEQ ID NO: 11 (Kabat)</p>	<p>LCDR2</p>	<p>YTSTLHL</p>
<p>SEQ ID NO: 12 (Kabat)</p>	<p>LCDR3</p>	<p>QQYYNLPWT</p>
<p>SEQ ID NO: 13 (Chothia)</p>	<p>LCDR1</p>	<p>SQDISNY</p>

SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 56	VL	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGVP SRFSGSGSGTE FTLTISSLQPDDFATYYCQQYYNLPWTFGGQGTKVE IK
SEQ ID NO: 57	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACTATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAA TTCACTCTCACCATCAGCAGCCTGCAGCCTGATGA TTTTGCAACTTATTACTGTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 58	LC	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGVP SRFSGSGSGTE FTLTISSLQPDDFATYYCQQYYNLPWTFGGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 59	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACTATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAA TTCACTCTCACCATCAGCAGCCTGCAGCCTGATGA TTTTGCAACTTATTACTGTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum08-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISKVSGFTLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS

<p>SEQ ID NO: 101</p>	<p>DNA VH</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATAATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACCGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC</p>
<p>SEQ ID NO: 102</p>	<p>HC</p>	<p>EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFP LPPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK</p>
<p>SEQ ID NO: 103</p>	<p>DNA HC</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATAATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACCGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCACCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACCGTGCCTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCTGCCCCCATCCAGGAGGA GATGACCAAGAACCAGGTGACCGTGCCTGG</p>

		TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAA GACCACGCCTCCCGTGGTGGACTCCGACGGCTCCT TCTTCCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCCTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum08-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 60	VL	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 61	DNA VL	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 62	LC	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTLTISSLQPEDFATYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE
SEQ ID NO: 63	DNA LC	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCAAAAGAGCTTCAAC AGGGGAGAGTGT

BAP050-hum09-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKGF
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 104	VH	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 105	DNA VH	CAGGTT CAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA
SEQ ID NO: 106	HC	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMI SRTPEVTCVVDVVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMEALHNHYTQKSLSLSLGK
SEQ ID NO: 107	DNA HC	CAGGTT CAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG

		AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCCTGTTCCCCCAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCGTACCTGCCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum09-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 36	VL	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGTD FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 37	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATTGAGTGGCAGCGGGTATGGAACAGAT TTTACCCTCACAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGTGAGCAGTATTATAACC TTCCGTGGACGTTCCGGCAAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 38	LC	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGTD FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 39	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATTGAGTGGCAGCGGGTATGGAACAGAT

		TTTACCCCTCACAAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGTGCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCCTCTGTTGTGTGCCTGTGAATAACTTCTAT CCCAGAGAGGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCCTGCCAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum10-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 104	VH	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVSS
SEQ ID NO: 105	DNA VH	CAGGTTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGCAGCACGGCATACTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 106	HC	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWIYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMEALHNHYTQKSLSLSLGK
SEQ ID NO: 107	DNA HC	CAGGTTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC

		TCCTTGGACACCTCTGTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAATAACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCCTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum10-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 40	VL	EIVLTQSPATLPVTLGQPASISCSQQDISNYLNW YQKPGQAPRLLIYYTSTLHLGVP SRFSGSGGTD FTFTISSLEAEDAATYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 41	DNA VL	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTCACCCTTGGACAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTTCAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGCCAAGGGACCAAGGTGGAA ATCAAA

SEQ ID NO: 42	LC	EIVLTQSPATLPVTLGQPASISCSSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTFTISSLEAEDAATYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNIFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEN
SEQ ID NO: 43	DNA LC	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTCACCCTTGGACAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTACAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTGGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTGAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCACCCATC AGGGCTGAGCTCGCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum11-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 104	VH	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 105	DNA VH	CAGGTTGAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTACCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGACGACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCTC
SEQ ID NO: 106	HC	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV

		<p>DHKPSNFKVDRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK</p>
<p>SEQ ID NO: 107</p>	<p>DNA HC</p>	<p>CAGGTCAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTCTGGATTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTACCGTGCCCTCCA GCAGCTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCCT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTCCCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACCGTGCCTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTACCGTACCTGCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAACAACACTACAA GACCACGCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA</p>
BAP050-hum11-Ser LC		
<p>SEQ ID NO: 10 (Kabat)</p>	<p>LCDR1</p>	<p>SSSQDISNYLN</p>
<p>SEQ ID NO: 11 (Kabat)</p>	<p>LCDR2</p>	<p>YTSTLHL</p>
<p>SEQ ID NO: 12 (Kabat)</p>	<p>LCDR3</p>	<p>QQYINLPWT</p>
<p>SEQ ID NO: 13 (Chothia)</p>	<p>LCDR1</p>	<p>SQDISNY</p>
<p>SEQ ID NO: 14 (Chothia)</p>	<p>LCDR2</p>	<p>YTS</p>
<p>SEQ ID NO: 15 (Chothia)</p>	<p>LCDR3</p>	<p>YYNLPW</p>

SEQ ID NO: 56	VL	DIQMTQSPSSLSASVGDRTVITTCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGVP SRFSGSGSGTE FTLTISLQPD FAYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 57	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACTATCACTTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTT CAGCGGCAGTGGATCTGGGACAGAA TTC ACTCTCACCATCAGCAGCCTGCAGCCTGATGA TTTTGCAACTTATTACTGT CAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 58	LC	DIQMTQSPSSLSASVGDRTVITTCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGVP SRFSGSGSGTE FTLTISLQPD FAYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE C
SEQ ID NO: 59	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACTATCACTTGCA GTTCAAGTCAGGACATCAGCAATTTAAACTGG TACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTT CAGCGGCAGTGGATCTGGGACAGAA TTC ACTCTCACCATCAGCAGCCTGCAGCCTGATGA TTTTGCAACTTATTACTGT CAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCC TGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCC TGC GAAGTCACCCATC AGGGCCTGAGCTCGCCCGT CACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum12-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 104	VH	QVQLVQSGAEVKKPGASVKV SCKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTIVVSS
SEQ ID NO: 105	DNA VH	CAGGTT CAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC

		<p>TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC</p>
<p>SEQ ID NO: 106</p>	<p>HC</p>	<p>QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGTKTYTCNV DHKPSNTKVDKRVESKYGPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLGLK</p>
<p>SEQ ID NO: 107</p>	<p>DNA HC</p>	<p>CAGGTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCGAACCAGGTGACGG TGTGCTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCTCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTACGCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACA ACTACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT</p>

		TCTTCCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum12-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 60	VL	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTLTISLQPEDFATYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 61	DNA VL	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTACAGCGGAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAA
SEQ ID NO: 62	LC	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTLTISLQPEDFATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE
SEQ ID NO: 63	DNA LC	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTACAGCGGAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum13-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN

SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 108	VH	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 109	DNA VH	CAGGTTCAGCTGGTGCAGTCCGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA
SEQ ID NO: 110	HC	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWKVDGVEVHNAKTKPREEQFNSTYRVVSVLTVHL QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHREALHNYTQKLSLSLGLK
SEQ ID NO: 111	DNA HC	CAGGTTCAGCTGGTGCAGTCCGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC

		TTCCTGTTCCCCC AAAACCCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCCCTACCGTCCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTTCCAAACAAAGGCCCTCCCGTCCCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCC TGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGT CAGCCTGACCTGCCTGG TCAAAGGCTTCTACCC CAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCCT TCTTCCCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum13-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 36	VL	DIQMTQSPSSLSASVGD RVTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGTD FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 37	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATT CAGTGGCAGCGGTATGGAACAGAT TTTACCCTCACAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGT CAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 38	LC	DIQMTQSPSSLSASVGD RVTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGTD FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNRFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 39	DNA LC	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TATCAGCAGAAACCAGGGAAAGCTCCTAAGCTCCT GATCTATTACACATCAACCTTACACTTAGGGATCC CACCTCGATT CAGTGGCAGCGGTATGGAACAGAT TTTACCCTCACAATTAATAACATAGAATCTGAGGA TGCTGCATATTACTTCTGT CAGCAGTATTATAACC

		TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCAAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum14-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 8	VH	EVQLVQSGAEVKKPGATVKISCKVSGFLLTNYGMN WIRQSPSRGLEWLGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 9	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAAACTATGGAATGAAC TGGATCAGGCAGTCCCCATCGAGAGGCCTTGAGTG GCTGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 18	HC	EVQLVQSGAEVKKPGATVKISCKVSGFLLTNYGMN WIRQSPSRGLEWLGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLGLK
SEQ ID NO: 19	DNA HC	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAAACTATGGAATGAAC TGGATCAGGCAGTCCCCATCGAGAGGCCTTGAGTG GCTGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT

		ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTCCCCCCTAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTACGCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAATAACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCCTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum14-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 40	VL	EIVLTQSPATLPVTLGQPASISCSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSTRFSGSGSGTD FTFTISSLEAEDAATYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 41	DNA VL	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTACCCCTTGGACAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTCAAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTGACAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAA
SEQ ID NO: 42	LC	EIVLTQSPATLPVTLGQPASISCSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSTRFSGSGSGTD

		FTFTISSLEAEDAATYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNLFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLS SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEN
SEQ ID NO: 43	DNA LC	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTACCCTTGGACAGCCGGCCTCCATCTCCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTTTACAGTGGCAGTGGATCTGGGACAGAT TTCACCTTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum15-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 8	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLLTNYGMN WIRQSPSRGLEWLGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 9	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGATCAGGCAGTCCCCATCGAGAGGCCTTGAGTG GCTGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGCACCACCGTGACCGTGTCTCTCC
SEQ ID NO: 18	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLLTNYGMN WIRQSPSRGLEWLGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFPPLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDPEVQF

		NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLGLGK
		GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAAAATCTCCTGCAAGG TTTCTGGATTACCCCTCACAAACTATGGAATGAAC TGGATCAGGCAGTCCCCATCGAGAGGCCTTGAGTG GCTGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGACGACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCACCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAAGCCGCGGGAGGAGCAGTTCAACAGCA CGTACCGTGTGGTCAGCGTCTCACCGTCTGAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGCCAACAAAGGCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCGCCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAATACTAA GACCACGCCTCCCGTGTGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
SEQ ID NO: 19	DNA HC	
BAP050-hum15-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 60	VL	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSGTD FTLTISSLQPEDFATYYCQYYNLPWTFGGQTKVE

		IK
SEQ ID NO: 61	DNA VL	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGCCAAGGGACCAAGGTGGAA ATCAA
SEQ ID NO: 62	LC	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLW YQQKPGQAPRLLIYYTSTLHLGVP SRFSGSGSDT FTLTISSLQPEDFATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNIFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE
SEQ ID NO: 63	DNA LC	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTCAGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCTGCGAAGTCACCCATC AGGGCTGAGCTCGCCCGTCAAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum18-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTIVVSS
SEQ ID NO: 101	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA

		<p>CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC</p>
<p>SEQ ID NO: 102</p>	<p>HC</p>	<p>EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGPEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQTTVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVNF NWFYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSK RWQEGNVFSCSVMHEALHNHYTQKSLSLGLGK</p>
<p>SEQ ID NO: 103</p>	<p>DNA HC</p>	<p>GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATACTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCGCTTCCACCA AGGGCCCATCCGCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGTG CCTGGTCAAGGACTACTTCCCGAACCGGTGACGG TGTCTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCCT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCCTGTCCCCCAAACCAAGGACACTCTCAT GATCTCCCGACCCCTGAGGTACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCTCACCCTCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCTCCATCGAGA AAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGTGACCTGACCTGCCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT</p>

		GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum18-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 88	VL	AIQLTQSPSSLSASVGDRVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTLTISLQPEDFATYYCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 89	DNA VL	GCCATCCAGTTGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTACGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAAA
SEQ ID NO: 90	LC	AIQLTQSPSSLSASVGDRVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTLTISLQPEDFATYYCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 91	DNA LC	GCCATCCAGTTGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTCACCATCACTTGCA GTTCAAGTCAGGACATCAGCAATTATTTAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CATCAAGGTTTACGCGGCAGTGGATCTGGGACAGAT TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGA TTTTGCAACTTATTACTGTCAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCAGCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTGTGTGCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum19-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG

SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLLNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 101	DNA VH	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 102	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMEALHNHYTQKSLSLSLGK
SEQ ID NO: 103	DNA HC	GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTAAAAATCTCCTGCAAGG TTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTGTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCCCTCCGCTTCCACCA AGGGCCCATCCGTCTTCCCCCTGGCGCCCTGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG TGTGCGTGGAACTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCTTACAGTCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCTGTTCCCCCAAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG

		TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCCCTACCGTCCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCTCCCGTCCCTCCATCGAGA AAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCC TGCCCCATCCCAGGAGGA GATGACCAAGAACCAGGT CAGCCTGACCTGCCTGG TCAAAGGCTTCTACCCCAGCGACATCGCCGTGGAG TGGGAGAGCAATGGGCAGCCGGAGAACA ACTACAA GACCACGCCTCCCGTGTGGACTCCGACGGCTCCT TCTTCTCTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum19-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 92	VL	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTFTISSLEAEDAATYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 93	DNA VL	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTT CAGTGGCAGTGGATCTGGGACAGAT TTCACCTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGT CAGCAGTATTATAACC TTCCGTGGACGTTCCGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 94	LC	EIVLTQSPDFQSVTPKEKVTITCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGVPSRFSGSGSGTD FTFTISSLEAEDAATYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSL SSLTTLTKADYEEKHKVYACEVTHQGLSSPVTKSFN RGEN
SEQ ID NO: 95	DNA LC	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGGTCC CCTCGAGGTT CAGTGGCAGTGGATCTGGGACAGAT TTCACCTTACCATCAGTAGCCTGGAAGCTGAAGA TGCTGCAACATATTACTGT CAGCAGTATTATAACC TTCCGTGGACGTTCCGCCAAGGGACCAAGGTGGAA ATCAACGTTACGGTGGCTGCACCATCTGTCTTCAT

		CTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGAAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCAAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-hum20-Ser HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 104	VH	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 105	DNA VH	CAGGTTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA GGGCACCACCGTGACCGTGTCTCC
SEQ ID NO: 106	HC	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMEALHNHYTQKLSLSLSLGK
SEQ ID NO: 107	DNA HC	CAGGTTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCTGGATTTACCCTCACAACTATGGAATGAAC TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGTTGGATAAACACCGACACTGGAGAGCCAA CATATGCTGATGACTTCAAGGGAAGATTTGTCTTC TCCTTGGACACCTCTGTTCAGCACGGCATATCTGCA GATCAGCAGCCTAAAGGCTGAGGACACTGCCGTGT ATTACTGTGCAAGAAACCCCTCCCTATTACTACGGT ACTAATAACGCGGAGGCTATGGACTACTGGGGCCA

		GGGCACCACCGTGACCGTGTCCCTCCGCTTCCACCA AGGGCCCATCCGCTTTCCTCCCGCCCTGGCTCC AGGAGCACCTCCGAGAGCACAGCCGCCCTGGGCTG CCTGGTCAAGGACTACTTCCCGAACCGGTGACGG TGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGTG CACACCTTCCCGGCTGTCCCTACAGTCCCTCAGGACT CTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCA GCAGCTTGGGCACGAAGACCTACACCTGCAACGTA GATCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTTGAGTCCAAATATGGTCCCCCATGCCACCGT GCCAGCACCTGAGTTCCTGGGGGGACCATCAGTC TTCCTGTTCCCCCAAACCAAGGACACTCTCAT GATCTCCCGGACCCCTGAGGTCACGTGCGTGGTGG TGGACGTGAGCCAGGAAGACCCCGAGGTCCAGTTC AACTGGTACGTGGATGGCGTGGAGGTGCATAATGC CAAGACAAAGCCGCGGGAGGAGCAGTTC AACAGCA CGTACCGTGTGGTCAGCGTCCCTACCGTCCCTGCAC CAGGACTGGCTGAACGGCAAGGAGTACAAGTGCAA GGTGTCCAACAAAGGCCCTCCCGTCCCTCCATCGAGA AAACCATCTCAAAGCCAAAGGGCAGCCCCGAGAG CCACAGGTGTACACCCTGCCCCCATCCAGGAGGA GATGACCAAGAACCAGGTGACCGTGCCTGG TCAAAGGCTTCTACCCAGCGACATCGCCGTGGAG TGGAGAGCAATGGGCAGCCGGAGAACAAC TACAA GACCACGCCCTCCCGTGGTGGACTCCGACGGCTCCT TCTTCTTACAGCAGGCTAACCGTGGACAAGAGC AGGTGGCAGGAGGGGAATGTCTTCTCATGCTCCGT GATGCATGAGGCTCTGCACAACCACTACACACAGA AGAGCCTCTCCCTGTCTCTGGGTAAA
BAP050-hum20-Ser LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 96	VL	DIVMTQTPLSLPVTTPGEPASISCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGIPDRFSGSGSGTD FTLTISRLEPEDFAVYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 97	DNA VL	GATATTGTGATGACCCAGACTCCACTCTCCCTGCC CGTACCCCTGGAGAGCCGCCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGATCC CAGACAGGTTTCAAGTGGCAGTGGGTCTGGGACAGAC TTCACTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTGAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAA
SEQ ID NO: 98	LC	DIVMTQTPLSLPVTTPGEPASISCSSSQDISNYLNW YQQKPGQAPRLLIYYTSTLHLGIPDRFSGSGSGTD FTLTISRLEPEDFAVYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFFY

		PREAKVQWKVDNALQSGNSQESVTEQDSKDYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE
SEQ ID NO: 99	DNA LC	GATATTGTGATGACCCAGACTCCACTCTCCCTGCC CGTACCCCTGGAGAGCCGGCCTCCATCTCCTGCA GTTCAAGTCAGGACATCAGCAATTATTTAAACTGG TACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCT CATCTATTACACATCAACCTTACACTTAGGGATCC CAGACAGGTTTCAAGTGGCAGTGGGTCTGGGACAGAC TTCCTCTCACCATCAGCAGACTGGAGCCTGAAGA TTTTGCAGTGTATTACTGTGAGCAGTATTATAACC TTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAA ATCAAACGTACGGTGGCTGCACCATCTGTCTTCAT CTTCCCAGCATCTGATGAGCAGTTGAAATCTGGAA CTGCCTCTGTTGTGTGCCTGTGAATAACTTCTAT CCCAGAGAGGCCAAAGTACAGTGGGAAGGTGGATAA CGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCA CAGAGCAGGACAGCAAGGACAGCACCTACAGCCTC AGCAGCACCCCTGACGCTGAGCAAAGCAGACTACGA GAAACACAAAGTCTACGCTGCGAAGTCACCCATC AGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAAC AGGGGAGAGTGT
BAP050-Clone-F HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 112	DNA VH	GAAGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCCGGCGCTACCGTGAAGATCTCCTGCAAGG TGTCCGGCTTACCCTGACCAACTACGGCATGAAC TGGGTGCGACAGGCCCTGGACAGGGCCTGGAATG GATGGGCTGGATCAACACCGACACCGGCGAGCCTA CCTACGCCGACGACTTCAAGGGCAGATTCTGTGTTT TCCCTGGACACCTCCGTGTCCACCGCCTACCTGCA GATCTCCAGCCTGAAGGCCGAGGATACCGCCGTGT ACTACTGCGCCCGGAACCCCTTACTACTACGGC ACCAACAACGCCGAGGCCATGGACTATTGGGGCCA GGGACCACCGTGACCGTGTCTCT
SEQ ID NO: 113	HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFPPLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQF NHWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDNLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE

		PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSLG
		GAAGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCCGGCGCTACCGTGAAGATCTCCTGCAAGG TGTCCGGCTTACCCCTGACCAACTACGGCATGAAC TGGGTGCGACAGGCCCTGGACAGGGCCTGGAATG GATGGGCTGGATCAACACCGACACCGGCGAGCCTA CCTACGCCGACGACTTCAAGGGCAGATTCTGTGTTT TCCCTGGACACCTCCGTGTCCACCGCCTACCTGCA GATCTCCAGCCTGAAGGCCGAGGATAACCGCGTGT ACTACTGCGCCCGGAACCCCTTACTACTACGGC ACCAACAACGCCGAGGCCATGGACTATTGGGGCCA GGGCACCACCGTGACCGTGTCTCTGCTTCTACCA AGGGGCCAGCGTGTTCCTCCCGCCCTGCTGCC AGAAGCACCCAGCGAGAGCACAGCCGCCCTGGGCTG CCTGGTGAAGGACTACTTCCCGAGCCCGTGACCG TGTCTGGAACAGCGGAGCCCTGACCAGCGGCGTG CACACCTTCCCGCCGTGCTGCAGAGCAGCGGCCT GTACAGCCTGAGCAGCGTGGTGACCGTGCCAGCA GCAGCCTGGGCACCAAGACCTACACCTGTAACGTG GACCACAAGCCCAGCAACACCAAGGTGGACAAGAG GGTGGAGAGCAAGTACGGCCACCCCTGCCCCCT GCCAGCCCCGAGTTCCTGGGCGGACCCAGCGTG TTCTGTTCCTCCCAAGCCCAAGGACACCCCTGAT GATCAGCAGAACCCCGAGGTGACCTGTGTGGTGG TGGACGTGTCCCAGGAGGACCCCGAGGTCCAGTTC AACTGGTACGTGGACGGCGTGGAGGTGCACAACGC CAAGACCAAGCCCAGAGAGGAGCAGTTTAAACAGCA CCTACCGGGTGGTGTCCGTGCTGACCGTGTGTCAC CAGGACTGGCTGAACGGCAAAGAGTACAAGTGTA GGTCTCCAACAAGGGCCTGCCAAGCAGCATCGAAA AGACCATCAGCAAGGCCAAGGGCCAGCCTAGAGAG CCCCAGGTCTACACCTGCCACCCAGCCAAGAGGA GATGACCAAGAACCAGGTGTCCCTGACCTGTCTGG TGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAG TGGGAGAGCAACGGCCAGCCCGAGAACAATAAA GACCACCCCCAGTGTGGACAGCGACGGCAGCT TCTTCTGTACAGCAGGCTGACCGTGGACAAGTCC AGATGGCAGGAGGGCAACGTCTTTAGCTGCTCCGT GATGCACGAGGCCCTGCACAACCACTACACCCAGA AGAGCCTGAGCCTGTCCCTGGGC
SEQ ID NO: 114	DNA HC	
BAP050-Clone-F LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
		DIQMTQSPSSLSASVGRVITTCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGVPSTRFSGSGGTD FTFTISSLEAEDAATYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 32	VL	

SEQ ID NO: 115	DNA VL	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTC TGCTTCCGTGGGCGACAGAGTGACCATCACCTGTT CCTCCAGCCAGGACATCTCCAACCTGAACTGG TATCAGCAGAAGCCCGGCAAGGCCCAAGCTGCT GATCTACTACACCTCCACCCTGCACCTGGGCGTGC CCTCCAGATTTTCCGGCTCTGGCTCTGGCACCGAC TTTACCTTCACCATCAGCTCCCTGGAAGCCGAGGA CGCCGCCACCTACTACTGCCAGCAGTACTACAACC TGCCCTGGACCTTCGGCCAGGGCACCAAGGTGGAA ATCAAG
SEQ ID NO: 34	LC	DIQMTQSPSSLSASVGRVTITCSSSQDISNYLNW YQQKPKGKAPKLLIYYTSTLHLGVP SRFSGSGSDT FTFTISSLEAEDAATYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 117	DNA LC	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTC TGCTTCCGTGGGCGACAGAGTGACCATCACCTGTT CCTCCAGCCAGGACATCTCCAACCTGAACTGG TATCAGCAGAAGCCCGGCAAGGCCCAAGCTGCT GATCTACTACACCTCCACCCTGCACCTGGGCGTGC CCTCCAGATTTTCCGGCTCTGGCTCTGGCACCGAC TTTACCTTCACCATCAGCTCCCTGGAAGCCGAGGA CGCCGCCACCTACTACTGCCAGCAGTACTACAACC TGCCCTGGACCTTCGGCCAGGGCACCAAGGTGGAA ATCAAGCGTACGGTGGCCGCTCCCAGCGTGTTTCAT CTTCCCCCAAGCGACGAGCAGCTGAAGAGCGGCA CCGCCAGCGTGGTGTGTCTGCTGAACAACCTTCTAC CCCAGGGAGGCCAAGGTGCAGTGGAAAGGTGGACAA CGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCA CCGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCCCTGACCCTGAGCAAGGCCGACTACGA GAAGCACAAAGGTGTACGCTGTGAGGTGACCCACC AGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAAC AGGGGCGAGTGC
BAP050-Clone-G HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 100	VH	EVQLVQSGAEVKKPGATVKISCKVSGFLLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 112	DNA VH	GAAGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCCGGCGCTACCGTGAAGATCTCCTGCAAGG TGTCGGCTTCACCCTGACCAACTACGGCATGAAC TGGGTGCGACAGGCCCTGGACAGGGCCTGGAATG GATGGGCTGGATCAACACCGACACCGGCGAGCCTA CCTACGCCGACGACTTCAAGGGCAGATTCTGTGTTT TCCCTGGACACCTCCGTGTCCACCGCTACCTGCA

		<p>GATCTCCAGCCTGAAGGCCGAGGATACCGCCGTGT ACTACTGCGCCCGGAACCCCTTACTACTACGGC ACCAACAACGCCGAGGCCATGGACTATTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCT</p>
<p>SEQ ID NO: 113</p>	<p>HC</p>	<p>EVQLVQSGAEVKKPGATVKISKVSGFTLTNYGMN WVRQAPGQGLEWMGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQTTVTVSSASTKGPSVFP LAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSKV HTFPAVLQSSGLYSLSSVTVTPSSSLGKTYTCNV DHKPSTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWFYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLSLG</p>
<p>SEQ ID NO: 114</p>	<p>DNA HC</p>	<p>GAAGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCCGGCGCTACCGTGAAGATCTCCTGCAAGG TGTCCGGCTTCACCCTGACCAACTACGGCATGAAC TGGGTGCGACAGGCCCTGGACAGGGCCTGGAATG GATGGGCTGGATCAACACCGACACCGGCGAGCCTA CCTACGCCGACGACTTCAAGGGCAGATTCTGTGTTT TCCCTGGACACCTCCGTGTCCACCGCCTACCTGCA GATCTCCAGCCTGAAGGCCGAGGATACCGCCGTGT ACTACTGCGCCCGGAACCCCTTACTACTACGGC ACCAACAACGCCGAGGCCATGGACTATTGGGGCCA GGGCACCACCGTGACCGTGTCCCTCTGCTTCTACCA AGGGGCCCAGCGTGTTCCTCCCTGGCCCCCTGCTCC AGAAGCACCAGCGAGAGCACAGCCGCCCTGGGCTG CCTGGTGAAGGACTACTTCCCCGAGCCCGTGACCG TGTCTGGAACAGCGGAGCCCTGACCAGCGGCGTG CACACCTTCCCCGCGGTGCTGCAGAGCAGCGCCCT GTACAGCCTGAGCAGCGTGGTGACCGTGCCAGCA GCAGCCTGGGCACCAAGACCTACACCTGTAACGTG GACCACAAGCCCAGCAACACCAAGGTGGACAAGAG GGTGGAGAGCAAGTACGGCCCACCTGCCCCCCT GCCAGCCCCCGAGTTCCTGGGCGGACCCAGCGTG TTCCTGTTCCTCCCAAGCCCAAGGACACCCCTGAT GATCAGCAGAACCCCGAGGTGACCTGTGTGGTGG TGGACGTGTCCAGGAGGACCCCGAGGTCCAGTTC AACTGGTACGTGGACGGCGTGGAGGTGCACAACGC CAAGACCAAGCCCAGAGAGGAGCAGTTTAAACAGCA CCTACCGGGTGGTGTCCGTGCTGACCGTGTGAC CAGGACTGGCTGAACGGCAAAGAGTACAAGTGTA GGTCTCCAACAAGGGCTTGCCAAGCAGCATCGAAA AGACCATCAGCAAGGCCAAGGGCCAGCCTAGAGAG CCCAGGTCTACACCCTGCCACCCAGCCAAGAGGA GATGACCAAGAACCAGGTGTCCCTGACCTGTCTGG TGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAG TGGGAGAGCAACGGCCAGCCCGAGAACAACCTACAA GACCACCCCCCAGTGTGGACAGCGACGGCAGCT TCTTCTGTACAGCAGGCTGACCGTGGACAAGTCC AGATGGCAGGAGGGCAACGTCTTTAGCTGCTCCGT GATGCACGAGGCCCTGCACAACCACTACCCAGCA AGAGCCTGAGCCTGTCCCTGGGC</p>

BAP050-Clone-G LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 36	VL	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGT FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 118	DNA VL	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTC TGCTTCCGTGGGCGACAGAGTGACCATCACCTGTT CCTCCAGCCAGGACATCTCCAACCTGAACTGG TATCAGCAGAAGCCCGGCAAGGCCCAAGCTGCT GATCTACTACACCTCCACCCTGCACCTGGGCATCC CCCCTAGATTCTCCGGCTCTGGCTACGGCACCGAC TTCACCCTGACCATCAACAACATCGAGTCCGAGGA CGCCGCTACTACTTCTGCCAGCAGTACTACAACC TGCCCTGGACCTTCGGCCAGGGCACCAAGGTGGAA ATCAAG
SEQ ID NO: 38	LC	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGT FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNRFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC
SEQ ID NO: 120	DNA LC	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTC TGCTTCCGTGGGCGACAGAGTGACCATCACCTGTT CCTCCAGCCAGGACATCTCCAACCTGAACTGG TATCAGCAGAAGCCCGGCAAGGCCCAAGCTGCT GATCTACTACACCTCCACCCTGCACCTGGGCATCC CCCCTAGATTCTCCGGCTCTGGCTACGGCACCGAC TTCACCCTGACCATCAACAACATCGAGTCCGAGGA CGCCGCTACTACTTCTGCCAGCAGTACTACAACC TGCCCTGGACCTTCGGCCAGGGCACCAAGGTGGAA ATCAAGCGTACGGTGGCCGCTCCCAGCGTGTTTCAT CTTCCCCCAAGCGACGAGCAGCTGAAGAGCGGCA CCGCCAGCGTGGTGTGTCTGCTGAACAACCTTCTAC CCCAGGGAGGCCAAGGTGCAGTGGAAAGGTGGACAA CGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCA CCGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCTGACCCTGAGCAAGGCCGACTACGA GAAGCACAAAGGTGTACGCTGTGAGGTGACCCACC AGGGCTGTCCAGCCCCGTGACCAAGAGCTTCAAC AGGGGCGAGTGCTGATGAATTC
BAP050-Clone-H HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFTLTNY

SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 104	VH	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMN WVRQARGQRLEWIGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 121	DNA VH	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCTGGCGCCTCCGTGAAGGTGTCCTGCAAGG CCTCTGGCTTCACCCTGACCAACTACGGCATGAAC TGGGTGCGACAGGCCAGGGCCAGCGGCTGGAATG GATCGGCTGGATCAACACCGACACCGGCGAGCCTA CCTACGCCGACGACTTCAAGGGCAGATTCTGTGTTT TCCCTGGACACCTCCGTGTCCACCGCTACCTGCA GATCTCCAGCCTGAAGGCCGAGGATACCGCCGTGT ACTACTGCGCCCGGAACCCCTTACTACTACGGC ACCAACAACGCCGAGGCCATGGACTATTGGGGCCA GGGCACCACCGTGACCGTGTCTCT
SEQ ID NO: 122	HC	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMN WVRQARGQRLEWIGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVDKRVESKYGPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDPEVQF NWIYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQIAVE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPPVLDSGDGSFFLYRSLTVDKS RWQEGNVFSCSVMHEALHNHYTQKLSLSLSLG
SEQ ID NO: 123	DNA HC	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCTGGCGCCTCCGTGAAGGTGTCCTGCAAGG CCTCTGGCTTCACCCTGACCAACTACGGCATGAAC TGGGTGCGACAGGCCAGGGCCAGCGGCTGGAATG GATCGGCTGGATCAACACCGACACCGGCGAGCCTA CCTACGCCGACGACTTCAAGGGCAGATTCTGTGTTT TCCCTGGACACCTCCGTGTCCACCGCTACCTGCA GATCTCCAGCCTGAAGGCCGAGGATACCGCCGTGT ACTACTGCGCCCGGAACCCCTTACTACTACGGC ACCAACAACGCCGAGGCCATGGACTATTGGGGCCA GGGCACCACCGTGACCGTGTCTCTGCTTCTACCA AGGGGCCCAGCGTGTTCCTTGGCCCCCTGCTCC AGAAGCACCAGCGAGAGCACAGCCGCCCTGGGCTG CCTGGTGAAGGACTACTTCCCCGAGCCCGTGACCG TGTCTGGAACAGCGGAGCCCTGACCAGCGGCGTG CACACCTTCCCCGCCGTGCTGCAGAGCAGCGGCCCT GTACAGCCTGAGCAGCGTGGTGACCGTGCCAGCA GCAGCCTGGGCACCAAGACCTACACCTGTAACGTG GACCACAAGCCCAGCAACACCAAGGTGGACAAGAG GGTGGAGAGCAAGTACGGCCCACCCTGCCCCCCT GCCCAGCCCCGAGTTCCTGGGCGGACCCAGCGTG TTCTGTTCCTTCCCCCAAGCCCAAGGACACCCTGAT GATCAGCAGAACCCCGAGGTGACCTGTGTGGTGG TGGACGTGTCCAGGAGGACCCCGAGGTCCAGTTC AACTGGTACGTGGACGGCGTGGAGGTGCACAACGC CAAGACCAAGCCCAGAGAGGAGCAGTTTAAACAGCA

		CCTACCGGGTGGTGTCCGTGCTGACCGTGCTGCAC CAGGACTGGCTGAACGGCAAAGAGTACAAGTGTA GGTCTCCAACAAGGGCCGCAAGCAGCATCGAAA AGACCATCAGCAAGGCCAAGGGCCAGCCTAGAGAG CCCCAGGTCTACACCCTGCCACCCAGCCAAGAGGA GATGACCAAGAACCAGGTGTCCCTGACCTGTCTGG TGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAG TGGGAGAGCAACGGCCAGCCCAGAAACAACACTAAA GACCACCCCCCAGTGTGGACAGCGACGGCAGCT TCTTCTGTACAGCAGGCTGACCGTGGACAAGTCC AGATGGCAGGAGGGCAACGTCTTTAGCTGCTCCGT GATGCACGAGGCCCTGCACAACCCTACACCCAGA AGAGCCTGAGCCTGTCCCTGGGC
BAP050-Clone-H LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 36	VL	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGT FTLTINNIESEDAAYYFCQYYNLPWTFGQGTKVE IK
SEQ ID NO: 118	DNA VL	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTC TGCTTCCGTGGGCGACAGAGTGACCATCACCTGTT CCTCCAGCCAGGACATCTCCAACCTGAACTGG TATCAGCAGAAGCCCGGCAAGGCCCAAGCTGCT GATCTACTACACCTCCACCTGCACCTGGGCATCC CCCCTAGATTCTCCGGCTCTGGCTACGGCACCGAC TTCACCCTGACCATCAACAACATCGAGTCCGAGGA CGCCGCTACTACTTCTGCCAGCAGTACTACAACC TGCCCTGGACCTTCGGCCAGGGCACCAAGGTGGAA ATCAAG
SEQ ID NO: 38	LC	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGT FTLTINNIESEDAAYYFCQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEN
Nucleotides 1-642 of SEQ ID NO: 120	DNA LC	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTC TGCTTCCGTGGGCGACAGAGTGACCATCACCTGTT CCTCCAGCCAGGACATCTCCAACCTGAACTGG TATCAGCAGAAGCCCGGCAAGGCCCAAGCTGCT GATCTACTACACCTCCACCTGCACCTGGGCATCC CCCCTAGATTCTCCGGCTCTGGCTACGGCACCGAC TTCACCCTGACCATCAACAACATCGAGTCCGAGGA CGCCGCTACTACTTCTGCCAGCAGTACTACAACC TGCCCTGGACCTTCGGCCAGGGCACCAAGGTGGAA ATCAAGCGTACGGTGGCCGCTCCAGCGTGTTCAT CTCCCCCAAGCGACGAGCAGCTGAAGAGCGGCA CCGCCAGCGTGGTGTGTCTGCTGAACAACCTTCTAC CCAGGGAGGCCAAGGTGCAGTGAAGGTGGACAA

		CGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCA CCGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCCCTGACCCTGAGCAAGGCCGACTACGA GAAGCACAAGGTGTACGCCTGTGAGGTGACCCACC AGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAAC AGGGGCGAGTGC
BAP050-Clone-I HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 104	VH	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 124	DNA VH	CAAGTGCAGCTGGTGCAGTCGGGAGCCGAAGTGAA GAAGCCTGGAGCCTCGGTGAAGGTGTCGTGCAAGG CATCCGGATTACCCCTACCAATTACGGGATGAAC TGGGTCAGACAGGCCCGGGGTCAACGGCTGGAGTG GATCGGATGGATTAAACACCGACACCGGGGAGCCTA CCTACGCGGACGATTTCAAGGGACGGTTCGTGTTC TCCCTCGACACCTCCGTGTCCACCGCCTACCTCCA AATCTCCTCACTGAAAGCGGAGGACACCGCGGTGT ACTATTGCGCGAGGAACCCGCCCTACTACTACGGA ACCAACAACGCCGAAGCCATGGACTACTGGGGCCA GGGCACCACCTGTGACTGTGTCCAGC
SEQ ID NO: 125	DNA VH	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCTGGCGCCTCCGTGAAGGTGTCCTGCAAGG CCTCTGGCTTCACCCCTGACCAACTACGGCATGAAC TGGGTGCGACAGGCCAGGGCCAGCGGCTGGAATG GATCGGCTGGATCAACACCGACACCGGCGAGCCTA CCTACGCCGACGACTTCAAGGGCAGATTTCGTGTTC TCCCTGGACACCTCCGTGTCCACCGCCTACCTGCA GATCTCCAGCCTGAAGGCCGAGGATACCGCCGTGT ACTACTGCGCCCGGAACCCCTTACTACTACGGC ACCAACAACGCCGAGGCCATGGACTATTGGGGCCA GGGCACCACCGTGACCGTGTCTCT
SEQ ID NO: 122	HC	QVQLVQSGAEVKKPGASVKVSKASGFLLTNYGMN WVRQARGQRLEWIGWINTDTGEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGTKTYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMEALHNHYTQKSLSLSLG
SEQ ID NO: 126	DNA HC	CAAGTGCAGCTGGTGCAGTCGGGAGCCGAAGTGAA GAAGCCTGGAGCCTCGGTGAAGGTGTCGTGCAAGG

		<p>CATCCGGATTACCCCTACCAATTACGGGATGAAC TGGGTGAGACAGGCCCGGGTCAACGGCTGGAGTG GATCGGATGGATTAACACCGACACCGGGGAGCCTA CCTACGCGGACGATTTCAAGGGACGGTTCGTGTTT TCCCTCGACACCTCCGTGTCCACCGCCTACCTCCA AATCTCCTCACTGAAAGCGGAGGACACCGCCGTGT ACTATTGCGCGAGGAACCCGCCCTACTACTACGGA ACCAACAACGCCGAAGCCATGGACTACTGGGGCCA GGGCACCACTGTGACTGTGTCCAGCGCGTCCACTA AGGGCCCGTCCGTGTTCCCCCTGGCACCTTGTAGC CGGAGCACTAGCGAATCCACCGCTGCCCTCGGCTG CCTGGTCAAGGATTACTTCCCGGAGCCCGTGACCG TGTCCTGGAACAGCGGAGCCCTGACCTCCGGAGTG CACACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCT GTACTCGCTGTCTCGGTGGTCCAGGTGCCTTCAT CTAGCCTGGGTACCAAGACCTACACTTGCAACGTG GACCACAAGCCTTCCAACACTAAGGTGGACAAGCG CGTCGAATCGAAGTACGGGCCACCGTGCCCGCCTT GTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTC TTTCTGTTCCACCGAAGCCCAAGGACACTTTGAT GATTTCCCGCACCCCTGAAGTGACATGCGTGGTTCG TGGACGTGTCACAGGAAGATCCGGAGGTGCAGTTC AATTGGTACGTGGATGGCGTGCAGGTGCACAACGC CAAAACCAAGCCGAGGGAGGAGCAGTTCAACTCCA CTTACCGCGTCCGTGTCCGTGCTGACGGTGTGCAT CAGGACTGGCTGAACGGGAAGGAGTACAAGTGCAA AGTGTCCAACAAGGGACTTCTTAGCTCAATCGAAA AGACCATCTCGAAAGCCAAGGGACAGCCCCGGGAA CCCCAAGTGTATAACCTGCCACCGAGCCAGGAAGA AATGACTAAGAACCAAGTCTCATTGACTTGCCTTG TGAAGGGCTTCTACCCATCGGATATCGCCGTGGAA TGGGAGTCCAACGGCCAGCCGAAAACAAC TACAA GACCACCCCTCCGGTGTGGACTCAGACGGATCCT TCTTCTCTACTCGCGGCTGACCGTGGATAAGAGC AGATGGCAGGAGGGAAATGTGTTTCTAGCTGTTCTGT GATGCATGAAGCCCTGCACAACCACTACACTCAGA AGTCCCTGTCCCTCTCCCTGGGA</p>
SEQ ID NO: 127	DNA HC	<p>CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCTGGCGCCTCCGTGAAGGTGTCTGCAAGG CCTCTGGCTTACCCCTGACCAACTACGGCATGAAC TGGGTGCGACAGGCCAGGGCCAGCGGCTGGAATG GATCGGCTGGATCAACACCGACACCGGCGAGCCTA CCTACGCGGACGACTTCAAGGGCAGATTTCGTGTTT TCCCTGGACACCTCCGTGTCCACCGCCTACCTGCA GATCTCCAGCCTGAAGGCCGAGGATAACCGCGTGT ACTACTGCGCCCCGAACCCCTTACTACTACGGC ACCAACAACGCCGAGGCCATGGACTATTGGGGCCA GGGCACCACCGTGACCGTGTCTCTGCTTCTACCA AGGGGCCAGCGTGTCCCCCTGGCCCCCTGTCTCC AGAAGCACCAGCGAGAGCACAGCCGCCCTGGGCTG CCTGGTGAAGGACTACTTCCCGAGCCCGTGACCG TGTCCTGGAACAGCGGAGCCCTGACCAGCGGCGTG CACACCTTCCCCGCGTGTGCAGAGCAGCGGCCT GTACAGCCTGAGCAGCGTGGTGACCGTGCCCAGCA GCAGCCTGGGCACCAAGACCTACACCTGTAACGTG GACCACAAGCCCAGCAACCAAGGTGGACAAGAG GGTGGAGAGCAAGTACGGCCACCCCTGCCCCCT</p>

		GCCCAGCCCCCGAGTTCCCTGGGCGGACCCAGCGTG TTCCTGTTCCCCCAAGCCCAAGGACACCCTGAT GATCAGCAGAACCCCGAGGTGACCTGTGTGGTGG TGGACGTGTCCCAGGAGGACCCCGAGGTCCAGTTC AACTGGTACGTGGACGGCGTGGAGGTGCACAACGC CAAGACCAAGCCCAGAGAGGAGCAGTTTAACAGCA CCTACCGGGTGGTGTCCGTGCTGACCGTGTGCAC CAGGACTGGCTGAACGGCAAAGAGTACAAGTGTA GGTCTCCAACAAGGGCCTGCCAAGCAGCATCGAAA AGACCATCAGCAAGGCCAAGGGCCAGCCTAGAGAG CCCCAGGTCTACACCCTGCCACCCAGCCAAGAGGA GATGACCAAGAACCAGGTGTCCCTGACCTGTCTGG TGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAG TGGGAGAGCAACGGCCAGCCCGAGAACAACCTACAA GACCACCCCCCAGTGTGGACAGCGACGGCAGCT TCTTCCGTGTACAGCAGGCTGACCGTGGACAAGTCC AGATGGCAGGAGGGCAACGTCTTTAGCTGCTCCGT GATGCACGAGGCCCTGCACAACCACTACCCAGA AGAGCCTGAGCCTGTCCCTGGGC
BAP050-Clone-I LC		
SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 56	VL	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 128	DNA VL	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAG CGCTAGTGTGGGCGATAGAGTACTATCACCTGTA GCTCTAGTCAGGATATCTCTAACTACCTGAACTGG TATCTGCAGAAGCCCGGTCAATCACCTCAGCTGCT GATCTACTACACTAGCACCCCTGCACCTGGGCGTGC CCTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGAG TTCACCCTGACTATCTCTAGCCTGCAGCCCGACGA CTTCGCTACCTACTACTGTCTAGCAGTACTATAACC TGCCCTGGACCTTCGGTCAAGGCACTAAGGTCGAG ATTAAG
SEQ ID NO: 129	DNA VL	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTC TGCTTCCGTGGGCGACAGAGTGACCATCACCTGTT CCTCCAGCCAGGACATCTCCAACACTGAACTGG TATCTGCAGAAGCCCGGCACTCCCTCAGCTGCT GATCTACTACACCTCCACCCTGCACCTGGGCGTGC CCTCCAGATTTTCCGGCTCTGGCTCTGGCACCGAG TTTACCCTGACCATCAGCTCCCTGCAGCCCGACGA CTTCGCCACCTACTACTGCCAGCAGTACTACAACC TGCCCTGGACCTTCGGCCAGGGCACCAAGGTGGAA ATCAAG
SEQ ID NO: 58	LC	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YLQKPGQSPQLLIYYTSTLHLGVPSRFSGSGSGTE FTLTISSLQPDDFATYYCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFFY

		PREAKVQWKVDNALQSGNSQESVTEQDSKDYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE
SEQ ID NO: 130	DNA LC	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAG CGCTAGTGTGGGCGATAGAGTGACTATCACCTGTA GCTCTAGTCAGGATATCTCTAACTACCTGAACTGG TATCTGCAGAAGCCCGGTCAATCACCTCAGCTGCT GATCTACTACACTAGCACCTGCACCTGGGCGTGC CCTCTAGGTTTAGCGGTAGCGGTAGTGGCACCAG TTCACCTGACTATCTCTAGCCTGCAGCCCGACGA CTTCGCTACCTACTACTGTCTCAGCAGTACTATAACC TGCCCTGGACCTTCGGTCAAGGCACTAAGGTCGAG ATTAAGCGTACGGTGGCCGCTCCCAGCGTGTTCAT CTTCCCCCAGCGACGAGCAGCTGAAGAGCGGCA CCGCCAGCGTGGTGTGCTGTGAACAACCTCTAC CCCCGGGAGGCCAAGGTGCAGTGGAAAGGTGGACAA CGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCA CCGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCTGACCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCCGTGCGAGGTGACCCACC AGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAAC AGGGGCGAGTGC
SEQ ID NO: 131	DNA LC	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTC TGCTTCCGTGGGCGACAGAGTGACCATCACCTGTT CCTCCAGCCAGGACATCTCCAACCTGAACTGG TATCTGCAGAAGCCCGGCCAGTCCCCCTCAGCTGCT GATCTACTACACCTCCACCCTGCACCTGGGCGTGC CCTCCAGATTTTCCGGCTCTGGCTCTGGCACCAG TTTACCCTGACCATCAGCTCCCTGCAGCCCGACGA CTTCGCCACCTACTACTGCCAGCAGTACTACAACC TGCCCTGGACCTTCGGCCAGGGCACCAAGGTGGAA ATCAAGCGTACGGTGGCCGCTCCCAGCGTGTTCAT CTTCCCCCAAGCGACGAGCAGCTGAAGAGCGGCA CCGCCAGCGTGGTGTGTCTGTGAACAACCTCTAC CCCAGGGAGGCCAAGGTGCAGTGGAAAGGTGGACAA CGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCA CCGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCTGACCTGAGCAAGGCCGACTACGA GAAGCACAAGGTGTACGCCGTGTGAGGTGACCCACC AGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAAC AGGGGCGAGTGC
BAP050-Clone-J HC		
SEQ ID NO: 1 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 2 (Kabat)	HCDR2	WINTDTGEPYADDFKG
SEQ ID NO: 3 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 4 (Chothia)	HCDR1	GFLLTNY
SEQ ID NO: 5 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 3 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 108	VH	QVQLVQSGAEVKKPGASVKVCSKASGFLLTNYGMN WVRQAPGGGLEWMGWINTDTGEPYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYYG TNNAEAMDYWGQGTITVSS
SEQ ID NO: 132	DNA VH	CAGGTGCAGCTGGTGCAGTCAGGCCCGCAAGTGAA GAAACCCGGCGCTAGTGTGAAAGTCAGCTGTAAG

		<p>CTAGTGGCTTCACCCCTGACTAACTACGGGATGAAC TGGGTCCGCCAGGCCCCAGGTCAAGGCCTCGAGTG GATGGGCTGGATTAAACACCGACACCGGCGAGCCTA CCTACGCCGACGACTTTAAGGGCAGATTTCGTGTTT AGCCTGGACACTAGTGTGTCTACCGCCTACCTGCA GATCTCTAGCCTGAAGGCCGAGGACACCGCCGTCT ACTACTGCGCTAGAAACCCCCCTACTACTACGGC ACTAACAACGCCGAGGCTATGGACTACTGGGGTCA AGGCACTACCGTGACCGTGTCTAGC</p>
<p>SEQ ID NO: 133</p>	<p>DNA VH</p>	<p>CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCTGGCGCCTCCGTGAAGGTGTCTGCAAGG CCTCTGGCTTCACCCCTGACCAACTACGGCATGAAC TGGGTGCGACAGGCCCTGGACAGGGCCTGGAATG GATGGGCTGGATCAACACCGACACCGGCGAGCCTA CCTACGCCGACGACTTCAAGGGCAGATTTCGTGTTT TCCCTGGACACCTCCGTGTCCACCGCCTACCTGCA GATCTCCAGCCTGAAGGCCGAGGATACCGCCGTGT ACTACTGCGCCCCGAACCCCCCTACTACTACGGC ACCAACAACGCCGAGGCCATGGACTATTGGGGCCA GGGCACCACCGTGACCGTGTCTCT</p>
<p>SEQ ID NO: 134</p>	<p>HC</p>	<p>QVQLVQSGAEVKKPGASVKVCSKASGFTLTNYGMN WVRQAPGQGLEWMGWINTDTEPTYADDFKGRFVF SLDTSVSTAYLQISSLKAEDTAVYYCARNPPYYG TNNAEAMDYWGQTTVTVSSASTKGPSVFLAPCS RSTSESTAALGCLVKDYFPEPVTVSWNSGALTSV HTFPAVLQSSGLYSLSSVTVPSSSLGTKTYTCNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSV FLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCVMHEALHNHYTQKLSLSLSLG</p>
<p>SEQ ID NO: 135</p>	<p>DNA HC</p>	<p>CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCCGGCGCTAGTGTGAAAGTCAGCTGTAAAG CTAGTGGCTTCACCCCTGACTAACTACGGGATGAAC TGGGTCCGCCAGGCCCCAGGTCAAGGCCTCGAGTG GATGGGCTGGATTAAACACCGACACCGGCGAGCCTA CCTACGCCGACGACTTTAAGGGCAGATTTCGTGTTT AGCCTGGACACTAGTGTGTCTACCGCCTACCTGCA GATCTCTAGCCTGAAGGCCGAGGACACCGCCGTCT ACTACTGCGCTAGAAACCCCCCTACTACTACGGC ACTAACAACGCCGAGGCTATGGACTACTGGGGTCA AGGCACTACCGTGACCGTGTCTAGCGCTAGCACTA AGGGCCCGTCCGTGTTCCCCCTGGCACCTTGTAGC CGGAGCACTAGCGAATCCACCGCTGCCCTCGGCTG CCTGGTCAAGGATTACTTCCCGGAGCCCGTGACCG TGTCTGGAAACAGCGGAGCCCTGACCTCCGGAGTG CACACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCT GTACTCGCTGTCGTCCGTGGTACCGGTGCCTTCAT CTAGCCTGGGTACCAAGACCTACACTTGCAACGTG GACCACAAGCCTTCCAACACTAAGGTGGACAAGCG CGTCGAATCGAAGTACGGCCACCGTGCCCGCCTT GTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTC TTTCTGTTCACCCGAAGCCCAAGGACACTTTGAT GATTTCCCGCACCCCTGAAGTGACATGCGTGGTCCG</p>

		<p>TGGACGTGTCACAGGAAGATCCGGAGGTGCAGTTC AATTGGTACGTGGATGGCGTTCGAGGTGCACAACGC CAAAACCAAGCCGAGGGAGGAGCAGTTCAACTCCA CTTACCGCGTCGTGTCCGTGCTGACGGTGTGCAT CAGGACTGGCTGAACGGGAAGGAGTACAAGTGCAA AGTGTCACAACAAGGGACTTCCTAGCTCAATCGAAA AGACCATCTCGAAAGCCAAGGGACAGCCCCGGGAA CCCCAAGTGATACCCCTGCCACCGAGCCAGGAAGA AATGACTAAGAACCAAGTCTCATTGACTTGCCTTG TGAAGGGCTTCTACCCATCGGATATCGCCGTGGAA TGGGAGTCCAACGGCCAGCCGGAAAACAAC TACAA GACCACCCCTCCGGTGTGGACTCAGACGGATCCT TCTTCCTCTACTCGCGGCTGACCGTGGATAAGAGC AGATGGCAGGAGGGAAATGTGTT CAGCTGTTCTGT GATGCATGAAGCCCTGCACAACCACTACACTCAGA AGTCCCTGTCCCTCTCCCTGGGA</p>
<p>SEQ ID NO: 136</p>	<p>DNA HC</p>	<p>CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCTGGCGCCTCCGTGAAGGTGTCTGCAAGG CCTCTGGCTTCACCCCTGACCAACTACGGCATGAAC TGGGTGCGACAGGCCCTGGACAGGGCCTGGAATG GATGGGCTGGATCAACACCGACACCGGCGAGCCTA CCTACGCCGACGACTTCAAGGGCAGATTCTGTGTT TCCCTGGACACCTCCGTGTCCACCGCCTACCTGCA GATCTCCAGCCTGAAGGCCGAGGATACCGCCGTGT ACTACTGCGCCCGGAACCCCTTACTACTACGGC ACCAACAACGCCGAGGCCATGGACTATTGGGGCCA GGGCACCACCGTGACCGTGTCTCTGCTTCTACCA AGGGGCCAGCGTGTTCCTCCCTGGCCCCCTGCTCC AGAAGCACCAGCGAGAGCACAGCCGCCCTGGGCTG CCTGGTGAAGGACTACTTCCCCGAGCCCGTGACCG TGTCTGGAACAGCGGAGCCCTGACCAGCGGCGTG CACACCTTCCCCGCGTGTGTCAGAGCAGCGGCCCT GTACAGCCTGAGCAGCGTGGTGACCGTGCCAGCA GCAGCCTGGGCACCAAGACCTACACCTGTAACGTG GACCACAAGCCCAGCAACACCAAGGTGGACAAGAG GGTGGAGAGCAAGTACGGCCCACCTGCCCCCCCT GCCAGCCCCCGAGTTCCTGGGCGGACCCAGCGTG TTCCTGTTCCTCCCAAGCCCAAGGACACCCGTGAT GATCAGCAGAACCCCGAGGTGACCTGTGTGGTGG TGGACGTGTCCCAGGAGGACCCCGAGGTCCAGTTC AACTGGTACGTGGACGGCGTGGAGGTGCACAACGC CAAGACCAAGCCCAGAGAGGAGCAGTTTAACAGCA CCTACCGGGTGGTGTCCGTGCTGACCGTGTGCAC CAGGACTGGCTGAACGGCAAAGAGTACAAGTGTA GGTCTCCAACAAGGGCCTGCCAAGCAGCATCGAAA AGACCATCAGCAAGGCCAAGGGCCAGCCTAGAGAG CCCCAGGTCTACACCCCTGCCACCCAGCCAAGAGGA GATGACCAAGAACCAGGTGTCCCTGACCTGTCTGG TGAAGGGCTTCTACCCAAGCGACATCGCCGTGGAG TGGGAGAGCAACGGCCAGCCCGAGAACAAC TACAA GACCACCCCCAGTGTGCTGGACAGCGACGGCAGCT TCTTCCTGTACAGCAGGCTGACCGTGGACAAGTCC AGATGGCAGGAGGGCAACGTCTTTAGCTGCTCCGT GATGCACGAGGCCCTGCACAACCACTACACCCAGA AGAGCCTGAGCCTGTCCCTGGGC</p>
<p>BAP050-Clone-J LC</p>		

SEQ ID NO: 10 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 11 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 12 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 13 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 14 (Chothia)	LCDR2	YTS
SEQ ID NO: 15 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 36	VL	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGT FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IK
SEQ ID NO: 137	DNA VL	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAG CGCTAGTGTGGGCGATAGAGTGACTATCACCTGTA GCTCTAGTCAGGATATCTCTAACTACCTGAACTGG TATCAGCAGAAGCCCGGTAAAGCCCCCTAAGCTGCT GATCTACTACACTAGCACCTGCACCTGGGAATCC CCCCTAGGTTTAGCGGTAGCGGCTACGGCACCGAC TTCACCCTGACTATTAACAATATCGAGTCAGAGGA CGCCGCTACTACTTCTGTCAGCAGTACTATAACC TGCCCTGGACCTTCGGTCAAGGCACTAAGGTCGAG ATTAAG
SEQ ID NO: 118	DNA VL	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTC TGCTTCCGTGGGCGACAGAGTGACCATCACCTGTT CCTCCAGCCAGGACATCTCCAACCTGAACTGG TATCAGCAGAAGCCCGGCAAGGCCCAAGCTGCT GATCTACTACACCTCCACCTGCACCTGGGCATCC CCCCTAGATTCTCCGGCTCTGGCTACGGCACCGAC TTCACCCTGACCATCAACAACATCGAGTCCGAGGA CGCCGCTACTACTTCTGCCAGCAGTACTACAACC TGCCCTGGACCTTCGGCCAGGGCACCAAGGTGGAA ATCAAG
SEQ ID NO: 38	LC	DIQMTQSPSSLSASVGDRTITCSSSQDISNYLNW YQQKPGKAPKLLIYYTSTLHLGIPPRFSGSGYGT FTLTINNIESEDAAYYFCQQYYNLPWTFGQGTKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFFY PREAKVQWKVDNALQSGNSQESVTEQDSKSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGE
SEQ ID NO: 138	DNA LC	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAG CGCTAGTGTGGGCGATAGAGTGACTATCACCTGTA GCTCTAGTCAGGATATCTCTAACTACCTGAACTGG TATCAGCAGAAGCCCGGTAAAGCCCCCTAAGCTGCT GATCTACTACACTAGCACCTGCACCTGGGAATCC CCCCTAGGTTTAGCGGTAGCGGCTACGGCACCGAC TTCACCCTGACTATTAACAATATCGAGTCAGAGGA CGCCGCTACTACTTCTGTCAGCAGTACTATAACC TGCCCTGGACCTTCGGTCAAGGCACTAAGGTCGAG ATTAAGCGTACGGTGGCCGCTCCCAGCGTGTTCAT CTCCCCCCCAGCGACGAGCAGCTGAAGAGCGGCA CCGCCAGCGTGGTGTGCCTGCTGAACAACCTTCTAC CCCCGGGAGGCCAAGGTGCAGTGGAAAGGTGGACAA CGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCA CCGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCTGACCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCTGCGAGGTGACCCACC

		AGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAAC AGGGGCGAGTGC
SEQ ID NO: 139	DNA LC	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTC TGCTTCCGTGGGGCAGAGTGACCATCACCTGTT CCTCCAGCCAGGACATCTCCAACCTACCTGAACTGG TATCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCT GATCTACTACACCTCCACCCTGCACCTGGGCATCC CCCCTAGATTCTCCGGCTCTGGCTACGGCACCAGAC TTCACCCTGACCATCAACAACATCGAGTCCGAGGA CGCCGCCTACTACTTCTGCCAGCAGTACTACAACC TGCCCTGGACCTTCGGCCAGGGCACCAAGGTGGAA ATCAAGCGTACGGTGGCCGCTCCCAGCGTGTTCAT CTTCCCCCAAGCGACGAGCAGCTGAAGAGCGGCA CCGCCAGCGTGGTGTGTCTGTGAACAACCTTCTAC CCCAGGGAGGCCAAGGTGCAGTGGAAAGGTGGACAA CGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCA CCGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCCCTGACCCCTGAGCAAGGCCGACTACGA GAAGCACAAAGGTGTACGCCCTGTGAGGTGACCCACC AGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAAC AGGGGCGAGTGC
BAP050 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 142 (Kabat)	HCDR3	AACCCCCCTTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 142 (Chothia)	HCDR3	AACCCCCCTTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-chi HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 142 (Kabat)	HCDR3	AACCCCCCTTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 142 (Chothia)	HCDR3	AACCCCCCTTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-chi LC		

SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum01 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCATTACTACGGTACTAATAACGCGGA
SEQ ID NO: 151 (Chothia)	HCDR3	GGCTATGGACTAC
BAP050-hum01 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum02 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA
SEQ ID NO: 151 (Chothia)	HCDR3	GGCTATGGACTAC
BAP050-hum02 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum03 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC
SEQ ID NO: 141 (Kabat)	HCDR2	TGATGACTTCAAGGGA

SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum03 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum04 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum04 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum05 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum05 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT

SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum06 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACATATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum06 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTC AAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum07 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACATATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum07 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTC AAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum08 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACATATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA

		GGCTATGGACTAC
BAP050-hum08 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum09 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum09 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum10 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum10 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum11 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC

SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum11 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum12 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum12 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum13 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum13 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA

SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum14 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum14 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACTACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum15 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum15 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACTACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum16 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCCTCACAAACTAT

SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum16 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum17 HC		
SEQ ID NO: 152 (Kabat)	HCDR1	AACTATGGCATGAAT
SEQ ID NO: 153 (Kabat)	HCDR2	TGGATCAACACCGACACTGGGGAGCCAACGTATGC CGATGACTTCAAGGGA
SEQ ID NO: 142 (Kabat)	HCDR3	AACCCCCCTTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 154 (Chothia)	HCDR1	GGATTCACCCTGACTAACTAT
SEQ ID NO: 155 (Chothia)	HCDR2	AACACCGACACTGGGGAG
SEQ ID NO: 142 (Chothia)	HCDR3	AACCCCCCTTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum17 LC		
SEQ ID NO: 156 (Kabat)	LCDR1	TCCTCTAGTCAGGACATTAGCAACTATTTAAAT
SEQ ID NO: 157 (Kabat)	LCDR2	TATACATCCACTTTGCACCTG
SEQ ID NO: 158 (Kabat)	LCDR3	CAACAGTATTATAATCTCCCTTGGACG
SEQ ID NO: 159 (Chothia)	LCDR1	AGTCAGGACATTAGCAACTAT
SEQ ID NO: 160 (Chothia)	LCDR2	TATACATCC
SEQ ID NO: 161 (Chothia)	LCDR3	TATTATAATCTCCCTTGG
BAP050-hum18 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum18 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG

BAP050-hum19 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum19 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum20 HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum20 LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum01-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum01-Ser LC		

SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum02-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum02-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum03-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum03-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum04-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA

SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum04-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum05-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum05-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum06-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum06-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT

SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum07-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum07-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum08-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum08-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum09-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCTCCCTATTACTACGGTACTAATAACGCGGA

		GGCTATGGACTAC
BAP050-hum09-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum10-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum10-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum11-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum11-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum12-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC

SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum12-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum13-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum13-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum14-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum14-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA

SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum15-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum15-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum18-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum18-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum19-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAACTAT

SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum19-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-hum20-Ser HC		
SEQ ID NO: 140 (Kabat)	HCDR1	AACTATGGAATGAAC
SEQ ID NO: 141 (Kabat)	HCDR2	TGGATAAACACCGACACTGGAGAGCCAACATATGC TGATGACTTCAAGGGA
SEQ ID NO: 151 (Kabat)	HCDR3	AACCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
SEQ ID NO: 143 (Chothia)	HCDR1	GGATTTACCCTCACAACTAT
SEQ ID NO: 144 (Chothia)	HCDR2	AACACCGACACTGGAGAG
SEQ ID NO: 151 (Chothia)	HCDR3	AACCCTCCCTATTACTACGGTACTAATAACGCGGA GGCTATGGACTAC
BAP050-hum20-Ser LC		
SEQ ID NO: 145 (Kabat)	LCDR1	AGTTCAAGTCAGGACATCAGCAATTATTTAAAC
SEQ ID NO: 146 (Kabat)	LCDR2	TACACATCAACCTTACACTTA
SEQ ID NO: 147 (Kabat)	LCDR3	CAGCAGTATTATAACCTTCCGTGGACG
SEQ ID NO: 148 (Chothia)	LCDR1	AGTCAGGACATCAGCAATTAT
SEQ ID NO: 149 (Chothia)	LCDR2	TACACATCA
SEQ ID NO: 150 (Chothia)	LCDR3	TATTATAACCTTCCGTGG
BAP050-Clone-F HC		
SEQ ID NO: 162 (Kabat)	HCDR1	AACTACGGCATGAAC
SEQ ID NO: 163 (Kabat)	HCDR2	TGGATCAACACCGACACCGGCGAGCCTACCTACGC CGACGACTTCAAGGGA
SEQ ID NO: 164 (Kabat)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGA GGCCATGGACTAT
SEQ ID NO: 165 (Chothia)	HCDR1	GGCTTCACCCTGACCAACTAC
SEQ ID NO: 166 (Chothia)	HCDR2	AACACCGACACCGGCGAG
SEQ ID NO: 164 (Chothia)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGA GGCCATGGACTAT
BAP050-Clone-F LC		
SEQ ID NO: 167 (Kabat)	LCDR1	TCCTCCAGCCAGGACATCTCCAACCTACCTGAAC
SEQ ID NO: 168 (Kabat)	LCDR2	TACACCTCCACCCTGCACCTG
SEQ ID NO: 169 (Kabat)	LCDR3	CAGCAGTACTACAACCTGCCCTGGACC
SEQ ID NO: 170 (Chothia)	LCDR1	AGCCAGGACATCTCCAACCTAC
SEQ ID NO: 171 (Chothia)	LCDR2	TACACCTCC
SEQ ID NO: 172 (Chothia)	LCDR3	TACTACAACCTGCCCTGG

BAP050-Clone-G HC		
SEQ ID NO: 162 (Kabat)	HCDR1	AACTACGGCATGAAC
SEQ ID NO: 163 (Kabat)	HCDR2	TGGATCAACACCGACACCGGGGAGCCTACCTACGC CGACGACTTCAAGGGC
SEQ ID NO: 164 (Kabat)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGA GGCCATGGACTAT
SEQ ID NO: 165 (Chothia)	HCDR1	GGCTTCACCCTGACCAACTAC
SEQ ID NO: 166 (Chothia)	HCDR2	AACACCGACACCGGGCGAG
SEQ ID NO: 164 (Chothia)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGA GGCCATGGACTAT
BAP050-Clone-G LC		
SEQ ID NO: 167 (Kabat)	LCDR1	TCCTCCAGCCAGGACATCTCCAACCTACCTGAAC
SEQ ID NO: 168 (Kabat)	LCDR2	TACACCTCCACCCTGCACCTG
SEQ ID NO: 169 (Kabat)	LCDR3	CAGCAGTACTACAACCTGCCCTGGACC
SEQ ID NO: 170 (Chothia)	LCDR1	AGCCAGGACATCTCCAACCTAC
SEQ ID NO: 171 (Chothia)	LCDR2	TACACCTCC
SEQ ID NO: 172 (Chothia)	LCDR3	TACTACAACCTGCCCTGG
BAP050-Clone-H HC		
SEQ ID NO: 162 (Kabat)	HCDR1	AACTACGGCATGAAC
SEQ ID NO: 163 (Kabat)	HCDR2	TGGATCAACACCGACACCGGGGAGCCTACCTACGC CGACGACTTCAAGGGC
SEQ ID NO: 164 (Kabat)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGA GGCCATGGACTAT
SEQ ID NO: 165 (Chothia)	HCDR1	GGCTTCACCCTGACCAACTAC
SEQ ID NO: 166 (Chothia)	HCDR2	AACACCGACACCGGGCGAG
SEQ ID NO: 164 (Chothia)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGA GGCCATGGACTAT
BAP050-Clone-H LC		
SEQ ID NO: 167 (Kabat)	LCDR1	TCCTCCAGCCAGGACATCTCCAACCTACCTGAAC
SEQ ID NO: 168 (Kabat)	LCDR2	TACACCTCCACCCTGCACCTG
SEQ ID NO: 169 (Kabat)	LCDR3	CAGCAGTACTACAACCTGCCCTGGACC
SEQ ID NO: 170 (Chothia)	LCDR1	AGCCAGGACATCTCCAACCTAC
SEQ ID NO: 171 (Chothia)	LCDR2	TACACCTCC
SEQ ID NO: 172 (Chothia)	LCDR3	TACTACAACCTGCCCTGG
BAP050-Clone-I HC		
SEQ ID NO: 173 (Kabat)	HCDR1	AATTACGGGATGAAC
SEQ ID NO: 162 (Kabat)	HCDR1	AACTACGGCATGAAC
SEQ ID NO: 174 (Kabat)	HCDR2	TGGATTAACACCGACACCGGGGAGCCTACCTACGC GGACGATTTCAAGGGA
SEQ ID NO: 163 (Kabat)	HCDR2	TGGATCAACACCGACACCGGGGAGCCTACCTACGC CGACGACTTCAAGGGC
SEQ ID NO: 175 (Kabat)	HCDR3	AACCCGCCCTTACTACTACGGAACCAACAACGCCGA AGCCATGGACTAC
SEQ ID NO: 164 (Kabat)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGA GGCCATGGACTAT
SEQ ID NO: 176 (Chothia)	HCDR1	GGATTCACCCTCACCAATTAC

SEQ ID NO: 165 (Chothia)	HCDR1	GGCTTCACCCTGACCAACTAC
SEQ ID NO: 177 (Chothia)	HCDR2	AACACCGACACCGGGGAG
SEQ ID NO: 166 (Chothia)	HCDR2	AACACCGACACCGGGGAG
SEQ ID NO: 175 (Chothia)	HCDR3	AACCCGCCCTACTACTACGGGAACCAACAACGCCGA AGCCATGGACTAC
SEQ ID NO: 164 (Chothia)	HCDR3	AACCCCCCTTACTACTACGGCACCACCAACAACGCCGA GGCCATGGACTAT
BAP050-Clone-I LC		
SEQ ID NO: 178 (Kabat)	LCDR1	AGCTCTAGTCAGGATATCTCTAACTACCTGAAC
SEQ ID NO: 167 (Kabat)	LCDR1	TCTCCAGCCAGGACATCTCCAACTACCTGAAC
SEQ ID NO: 179 (Kabat)	LCDR2	TACTACTAGCACCCCTGCACCTG
SEQ ID NO: 168 (Kabat)	LCDR2	TACACCTCCACCCTGCACCTG
SEQ ID NO: 180 (Kabat)	LCDR3	CAGCAGTACTATAACCTGCCCTGGACC
SEQ ID NO: 169 (Kabat)	LCDR3	CAGCAGTACTACAACCTGCCCTGGACC
SEQ ID NO: 181 (Chothia)	LCDR1	AGTCAGGATATCTCTAACTAC
SEQ ID NO: 170 (Chothia)	LCDR1	AGCCAGGACATCTCCAACTAC
SEQ ID NO: 182 (Chothia)	LCDR2	TACTACTAGC
SEQ ID NO: 171 (Chothia)	LCDR2	TACACCTCC
SEQ ID NO: 183 (Chothia)	LCDR3	TACTATAACCTGCCCTGG
SEQ ID NO: 172 (Chothia)	LCDR3	TACTACAACCTGCCCTGG
BAP050-Clone-J HC		
SEQ ID NO: 184 (Kabat)	HCDR1	AACTACGGGATGAAC
SEQ ID NO: 162 (Kabat)	HCDR1	AACTACGGCATGAAC
SEQ ID NO: 185 (Kabat)	HCDR2	TGGATTAACACCGACACCGGCGAGCCTACCTACGC CGACGACTTTAAGGGC
SEQ ID NO: 163 (Kabat)	HCDR2	TGGATCAACACCGACACCGGCGAGCCTACCTACGC CGACGACTTCAAGGGC
SEQ ID NO: 186 (Kabat)	HCDR3	AACCCCCCTTACTACTACGGCACTAACAACGCCGA GGCTATGGACTAC
SEQ ID NO: 164 (Kabat)	HCDR3	AACCCCCCTTACTACTACGGCACCACCAACAACGCCGA GGCCATGGACTAT
SEQ ID NO: 287 (Chothia)	HCDR1	GGCTTCACCCTGACTAACTAC
SEQ ID NO: 165 (Chothia)	HCDR1	GGCTTCACCCTGACCAACTAC
SEQ ID NO: 177 (Chothia)	HCDR2	AACACCGACACCGGGGAG
SEQ ID NO: 166 (Chothia)	HCDR2	AACACCGACACCGGGGAG
SEQ ID NO: 186 (Chothia)	HCDR3	AACCCCCCTTACTACTACGGCACTAACAACGCCGA GGCTATGGACTAC
SEQ ID NO: 164 (Chothia)	HCDR3	AACCCCCCTTACTACTACGGCACCACCAACAACGCCGA GGCCATGGACTAT
BAP050-Clone-J LC		
SEQ ID NO: 178 (Kabat)	LCDR1	AGCTCTAGTCAGGATATCTCTAACTACCTGAAC
SEQ ID NO: 167 (Kabat)	LCDR1	TCTCCAGCCAGGACATCTCCAACTACCTGAAC
SEQ ID NO: 179 (Kabat)	LCDR2	TACTACTAGCACCCCTGCACCTG
SEQ ID NO: 168 (Kabat)	LCDR2	TACACCTCCACCCTGCACCTG
SEQ ID NO: 180 (Kabat)	LCDR3	CAGCAGTACTATAACCTGCCCTGGACC

SEQ ID NO: 169 (Kabat)	LCDR3	CAGCAGTACTACAACCTGCCCTGGACC
SEQ ID NO: 181 (Chothia)	LCDR1	AGTCAGGATATCTCTAACTAC
SEQ ID NO: 170 (Chothia)	LCDR1	AGCCAGGACATCTCCAACACTAC
SEQ ID NO: 182 (Chothia)	LCDR2	TACACTAGC
SEQ ID NO: 171 (Chothia)	LCDR2	TACACCTCC
SEQ ID NO: 183 (Chothia)	LCDR3	TACTATAACCTGCCCTGG
SEQ ID NO: 172 (Chothia)	LCDR3	TACTACAACCTGCCCTGG

Table 2. Amino acid and nucleotide sequences of the heavy and light chain framework regions for humanized mAbs BAP050-hum01 to BAP050-hum20, BAP050-hum01-Ser to BAP050-hum15-Ser, BAP050-hum18-Ser to BAP050-hum20-Ser, and BAP050-Clone-F to BAP050-Clone-J

	Amino Acid Sequence	Nucleotide Sequence
VHFW1 (type a)	EVQLVQSGAEVKKPGATVKISCKVS (SEQ ID NO: 187)	GAAGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCCGGCGCTACCGTGAAGATCTCCTGCAAGG TGTC (SEQ ID NO: 188) GAGGTCCAGCTGGTACAGTCTGGGGCTGAGGTGAA GAAGCCTGGGGCTACAGTGAATAATCTCCTGCAAGG TTTCT (SEQ ID NO: 189)
VHFW1 (type b)	QVQLVQSGAEVKKPGASVKVSCAS (SEQ ID NO: 190)	CAAGTGCAGCTGGTGCAGTCGGGAGCCGAAGTGAA GAAGCCTGGAGCCTCGGTGAAGGTGTCTGCAAGG CATCC (SEQ ID NO: 191) CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAA GAAACCTGGCGCCTCCGTGAAGGTGTCTGCAAGG CCTCT (SEQ ID NO: 192) CAGGTTTCAGCTGGTGCAGTCCGGAGCTGAGGTGAA GAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGG CTTCT (SEQ ID NO: 193)
VHFW1 (type c)	EVQLVQSGAEVKKPGESLRISCKGS (SEQ ID NO: 194)	GAAGTGCAGCTGGTGCAGTCTGGAGCAGAGGTGAA AAAGCCCGGGGAGTCTCTGAGGATCTCCTGTAAGG GTTCT (SEQ ID NO: 195)
VHFW1 (type d)	QVQLVQSGSELKKPGASVKVSCAS (SEQ ID NO: 196)	CAGGTGCAGCTGGTGAATCTGGGTCTGAGTTGAA GAAGCCTGGGGCCTCAGTGAAGGTTTCTGCAAGG CTTCT (SEQ ID NO: 197)
VHFW2 (type a)	WVRQAPGQGLEWMG (SEQ ID NO: 198)	TGGTCCGCCAGGCCCCAGGTCAAGGCCTCGAGTG GATGGGC (SEQ ID NO: 199) TGGGTGCGACAGGCCCTGGACAGGGCCTGGAATG GATGGGC (SEQ ID NO: 200) TGGGTGCGACAGGCCCTGGACAAGGGCTTGAGTG GATGGGT (SEQ ID NO: 201)
VHFW2 (type b)	WVRQARGQRLEWIG (SEQ ID NO: 202)	TGGTCCAGACAGGCCCCGGGTCAACGGCTGGAGTG GATCGGA (SEQ ID NO: 203) TGGGTGCGACAGGCCAGGGCCAGCGGCTGGAATG GATCGGC (SEQ ID NO: 204) TGGGTGCGACAGGCTCGTGGACAACGCCTTGAGTG GATAGGT (SEQ ID NO: 205)

VHFW2 (type c)	WIRQSPSRGLEWLG (SEQ ID NO: 206)	TGGATCAGGCAGTCCCCATCGAGAGGCCTTGAGTG GCTGGGT (SEQ ID NO: 207)
VHFW2 (type d)	WVRQATGQGLEWMG (SEQ ID NO: 208)	TGGGTGCGACAGGCCACTGGACAAGGGCTTGAGTG GATGGGT (SEQ ID NO: 209)
VHFW3 (type a)	RFVFSLDTSVSTAYLQICSLKAEDT AVYYCAR (SEQ ID NO: 210)	AGATTTGTCTTCTCCTTGGACACCTCTGTCAGCAC GGCATACTGTCAGATCTGCAGCCTAAAGGCTGAGG ACACTGCCGTGTATTACTGTGCAAGA (SEQ ID NO: 211)
VHFW3 (type a - Ser)	RFVFSLDTSVSTAYLQISSLKAEDT AVYYCAR (SEQ ID NO: 212)	CGGTTCGTGTTCTCCCTCGACACCTCCGTGTCCAC CGCCTACCTCCAAATCTCCTCACTGAAAGCGGAGG ACACCGCCGTGTACTATTGCGCGAGG SEQ ID NO: 213) AGATTCGTGTTTAGCCTGGACACTAGTGTGTCTAC CGCCTACCTGCAGATCTCTAGCCTGAAGGCCGAGG ACACCGCCGTCTACTACTGCGCTAGA SEQ ID NO: 214) AGATTCGTGTTCTCCCTGGACACCTCCGTGTCCAC CGCCTACCTGCAGATCTCCAGCCTGAAGGCCGAGG ATACCGCCGTGTACTACTGCGCCCGG (SEQ ID NO: 215) AGATTTGTCTTCTCCTTGGACACCTCTGTCAGCAC GGCATACTGTCAGATCAGCAGCCTAAAGGCTGAGG ACACTGCCGTGTATTACTGTGCAAGA (SEQ ID NO: 216)
VHFW3 (type b)	RVTISADKSISTAYLQWSSLKASDT AMYYCAR (SEQ ID NO: 217)	AGAGTCACCATCTCAGCCGACAAGTCCATCAGCAC CGCCTACCTGCAGTGGAGCAGCCTGAAGGCCCTCGG ACACCGCCATGTATTACTGTGCAAGA (SEQ ID NO: 218)
VHFW3 (type c)	RFVFSLDTSVSTAYLQISTLKAEDT ATYFCAR (SEQ ID NO: 219)	CGGTTTGTCTTCTCCTTGGACACCTCTGTCAGCAC GGCATACTGTCAGATCAGCAGCCTAAAGGCTGAGG ACACTGCTACATATTTCTGTGCAAGA (SEQ ID NO: 220)
VHFW4	WGQGTTVTVSS (SEQ ID NO: 221)	TGGGGCCAGGGCACCCTGTGACTGTGTCCAGC (SEQ ID NO: 222) TGGGGTCAAGGCACTACCGTGACCGTGTCTAGC (SEQ ID NO: 223) TGGGGCCAGGGCACCACCGTGACCGTGTCTCT (SEQ ID NO: 224)

		TGGGGCCAGGGCACCACCGTGACCGTGTCTCC (SEQ ID NO: 225)
VLFW1 (type a)	DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 226)	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAG CGCTAGTGTGGGCGATAGAGTGACTATCACCTGT (SEQ ID NO: 227) GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTC TGCTTCCGTGGGCGACAGAGTGACCATCACCTGT (SEQ ID NO: 228) GACATCCAGATGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTACCATCACTTGC (SEQ ID NO: 229)
VLFW1 (type b)	EIVLTQSPATLPVTLGQPASISC (SEQ ID NO: 230)	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGCC CGTCACCCTTGGACAGCCGGCCTCCATCTCCTGC (SEQ ID NO: 231)
VLFW1 (type c)	EIVLTQSPATLSLSPGERATLSC (SEQ ID NO: 232)	GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTC TTTGTCTCCAGGGAAAGAGCCACCCTCTCCTGC (SEQ ID NO: 233)
VLFW1 (type d)	DIVMTQTPLSLPVTPGEPASISC (SEQ ID NO: 234)	GATATTGTGATGACCCAGACTCCACTCTCCCTGCC CGTCACCCCTGGAGAGCCGGCCTCCATCTCCTGC (SEQ ID NO: 235)
VLFW1 (type e)	EIVLTQSPDFQSVTPKEKVTITC (SEQ ID NO: 236)	GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTC TGTGACTCCAAAGGAGAAAGTCACCATCACCTGC (SEQ ID NO: 237)
VLFW1 (type f)	AIQLTQSPSSLSASVGDRVTITC (SEQ ID NO: 238)	GCCATCCAGTTGACCCAGTCTCCATCCTCCCTGTC TGCATCTGTAGGAGACAGAGTACCATCACTTGC (SEQ ID NO: 239)
VLFW2 (type a)	WYQQKPGKAPKLLIY (SEQ ID NO: 240)	TGGTATCAGCAGAAGCCCGGTAAAGCCCCTAAGCT GCTGATCTAC (SEQ ID NO: 241) TGGTATCAGCAGAAGCCCGGCAAGGCCCCCAAGCT GCTGATCTAC (SEQ ID NO: 242) TGGTATCAGCAGAAACCAGGGAAAGCTCCTAAGCT CCTGATCTAT (SEQ ID NO: 243)
VLFW2 (type b)	WYQQKPGQAPRLLIY (SEQ ID NO: 244)	TGGTACCAGCAGAAACCTGGCCAGGCTCCAGGCT CCTCATCTAT (SEQ ID NO: 245)
VLFW2 (type c)	WYLQKPGQSPQLLIY (SEQ ID NO: 246)	TGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCT CCTGATCTAT (SEQ ID NO: 247)
VLFW2 (type d)	WYLQKPGQSPQLLIY (SEQ ID NO: 248)	TGGTATCTGCAGAAGCCCGGTCAATCACCTCAGCT GCTGATCTAC (SEQ ID NO: 249)

		<p>TGGTATCTGCAGAAGCCCCGGCCAGTCCCCTCAGCT GCTGATCTAC (SEQ ID NO: 250)</p> <p>TGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCT CCTGATCTAT (SEQ ID NO: 251)</p>
VLFW3 (type a)	GVPSRFSGSGSGTDFTFITISSLEAE DAATYYC (SEQ ID NO: 252)	<p>GGCGTGCCCTCCAGATTTTCCGGCTCTGGCTCTGG CACCGACTTTACCTTCACCATCAGCTCCCTGGAAG CCGAGGACGCCGCCACCTACTACTGC (SEQ ID NO: 253)</p> <p>GGGGTCCCCTCGAGGTTTTCAGTGGCAGTGGATCTGG GACAGATTTACCTTTACCATCAGTAGCCTGGAAG CTGAAGATGCTGCAACATATTACTGT (SEQ ID NO: 254)</p>
VLFW3 (type b)	GIPPRFSGSGYGTDFTLTINNIESE DAAYYFC (SEQ ID NO: 255)	<p>GGAATCCCCCTAGGTTTAGCGGTAGCGGCTACGG CACCGACTTCACCCTGACTATTAACAATATCGAGT CAGAGGACGCCGCCTACTACTTCTGT (SEQ ID NO: 256)</p> <p>GGCATCCCCCTAGATTCTCCGGCTCTGGCTACGG CACCGACTTCACCCTGACCATCAACAACATCGAGT CCGAGGACGCCGCCTACTACTTCTGC (SEQ ID NO: 257)</p> <p>GGGATCCCACCTCGATTTCAGTGGCAGCGGGTATGG AACAGATTTTACCCTCACAATTAATAACATAGAAT CTGAGGATGCTGCATATTACTTCTGT (SEQ ID NO: 258)</p>
VLFW3 (type c)	GIPDRFSGSGSGTDFTLTISRLEPE DFAVYYC (SEQ ID NO: 259)	<p>GGGATCCCAGACAGGTTTTCAGTGGCAGTGGGTCTGG GACAGACTTCACTCTCACCATCAGCAGACTGGAGC CTGAAGATTTTGCAGTGTATTACTGT (SEQ ID NO: 260)</p>
VLFW3 (type d)	GVPSRFSGSGSGTEFTLTISSLQPD DFATYYC (SEQ ID NO: 261)	<p>GGCGTGCCCTCTAGGTTTAGCGGTAGCGGTAGTGG CACCGAGTTTACCCTGACTATCTTAGCCTGCAGC CCGACGACTTCGCTACCTACTACTGT (SEQ ID NO: 262)</p> <p>GGCGTGCCCTCCAGATTTTCCGGCTCTGGCTCTGG CACCGAGTTTACCCTGACCATCAGCTCCCTGCAGC CCGACGACTTCGCCACCTACTACTGC (SEQ ID NO: 263)</p> <p>GGGGTCCCATCAAGGTTTTCAGCGGCAGTGGATCTGG GACAGAATTCCTCTCACCATCAGCAGCCTGCAGC CTGATGATTTTGCACCTTATTACTGT (SEQ ID NO: 264)</p>

VLFW3 (type e)	GVPSRFSGSGSGTDFTLTISSLQPE DFATYYC (SEQ ID NO: 265)	GGGTCCCATCAAGGTTTCAGCGGCAGTGGATCTGG GACAGATTTTACTTCTACCATCAGCAGCCTGCAGC CTGAAGATTTTGCACACTTATTACTGT (SEQ ID NO: 266)
VLFW3 (type f)	GVPSRFSGSGSGTDFTFTISSLQPE DIATYYC (SEQ ID NO: 267)	GGGTCCCATCAAGGTTTCAGTGGAAGTGGATCTGG GACAGATTTTACTTTTACCATCAGCAGCCTGCAGC CTGAAGATATTGCAACATATTACTGT (SEQ ID NO: 268)
VLFW3 (type g)	GIPDRFSGSGSGTDFTLTISRLEPE DFAVYYC (SEQ ID NO: 269)	GGGATCCCAGACAGGTTTCAGTGGCAGTGGGTCTGG GACAGACTTACTTCTACCATCAGCAGACTGGAGC CTGAAGATTTTGCAGTGTATTACTGT (SEQ ID NO: 270)
VLFW4	FGQGTKVEIK (SEQ ID NO: 271)	TTCGGTCAAGGCACTAAGGTCGAGATTAAG (SEQ ID NO: 272) TTCGGCCAGGGCACCAAGGTGGAATCAAG (SEQ ID NO: 273) TTCGGCCAAGGGACCAAGGTGGAATCAAA (SEQ ID NO: 274)

Table 3. Constant region amino acid sequences of human IgG heavy chains and human kappa light chain

HC	IgG4 (S228P) mutant constant region amino acid sequence (EU Numbering) ASTKGPSVFP LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSKV HTFPAVLQSS GLYSLSSVVT VPSSSLGTKT YTCNVDHKPS NTKVDKRVES KYGPPCPPCP APEFLGGPSV FLFPPKPKDT LMISRTPEVT CVVVDVSQED PEVQFNWYVD GVEVHNAKTK PREEQFNSTY RVVSVLTVLH QDWLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYTLPPSQQEEMTK NQVSLTCLVK GFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSRL TVDKSRWQEG NWFSCSVMHE ALHNHYTQKS LLSLGLK (SEQ ID NO: 275)
LC	Human kappa constant region amino acid sequence RTVAAPSVFIFPPSDEQLKSLTISLDVNAQWKVDNALQSGNSQESVTEQDD SKDSTYLSLSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 276)
HC	IgG4 (S228P) mutant constant region amino acid sequence lacking the C-terminal Lysine (K) (EU Numbering) ASTKGPSVFP LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSKV HTFPAVLQSS GLYSLSSVVT VPSSSLGTKT YTCNVDHKPS NTKVDKRVES KYGPPCPPCP APEFLGGPSV FLFPPKPKDT LMISRTPEVT CVVVDVSQED PEVQFNWYVD GVEVHNAKTK PREEQFNSTY RVVSVLTVLH QDWLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYTLPPSQQEEMTK

	NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSRL TVDKSRWQEG NVFSCSVMHE ALHNHYTQKS LSLSLG (SEQ ID NO: 277)
HC	IgG1 wild type ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSKV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT YICNVNHNKPS NTKVDKRVK KSCDKTHTCP PCPAPELLGG PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTTPV LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK (SEQ ID NO: 278)
HC	IgG1 (N297A) mutant constant region amino acid sequence (EU Numbering) ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSKV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT YICNVNHNKPS NTKVDKRVK KSCDKTHTCP PCPAPELLGG PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYA STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTTPV LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK (SEQ ID NO: 279)
HC	IgG1 (D265A, P329A) mutant constant region amino acid sequence (EU Numbering) ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSKV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT YICNVNHNKPS NTKVDKRVK KSCDKTHTCP PCPAPELLGG PSVFLFPPKP KDTLMISRTP EVTCVVVAVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LAAPIEKTIS KAKGQPREPQ VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTTPV LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK (SEQ ID NO: 280)
HC	IgG1 (L234A, L235A) mutant constant region amino acid sequence (EU Numbering) ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSKV HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT YICNVNHNKPS NTKVDKRVK KSCDKTHTCP PCPAPEAAGG PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VYTLPPSREE MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTTPV LDSDGSFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK (SEQ ID NO: 281)

Table 4. Amino acid sequences of the heavy and light chain leader sequences for humanized mAbs BAP050-Clone-F to BAP050-Clone-J

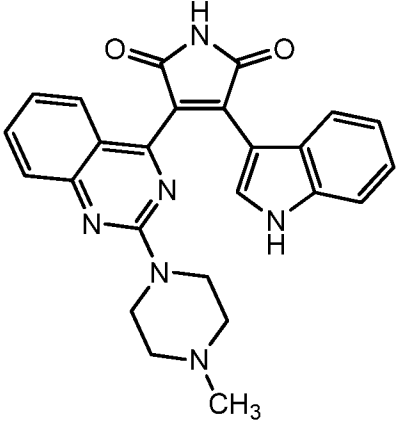
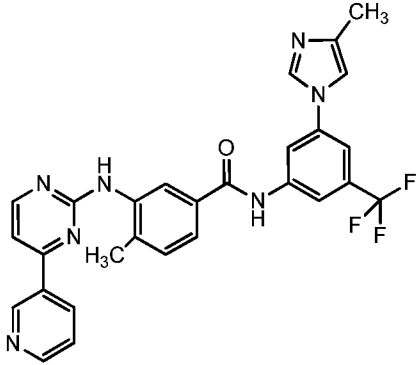
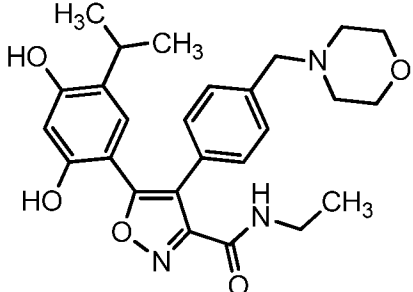
BAP050-Clone-F	HC	MEWSWVFLFFLSVTTGVHS (SEQ ID NO: 282)
BAP050-Clone-F	LC	MSVPTQVLGLLLLLWLT DARC (SEQ ID NO: 283)
BAP050-Clone-G	HC	MEWSWVFLFFLSVTTGVHS (SEQ ID NO: 282)
BAP050-Clone-G	LC	MSVPTQVLGLLLLLWLT DARC (SEQ ID NO: 283)
BAP050-Clone-H	HC	MEWSWVFLFFLSVTTGVHS (SEQ ID NO: 282)

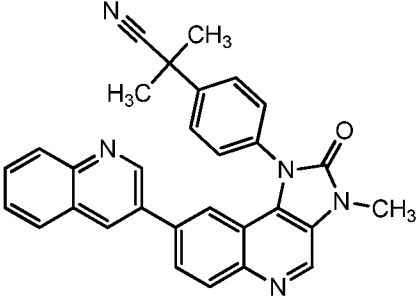
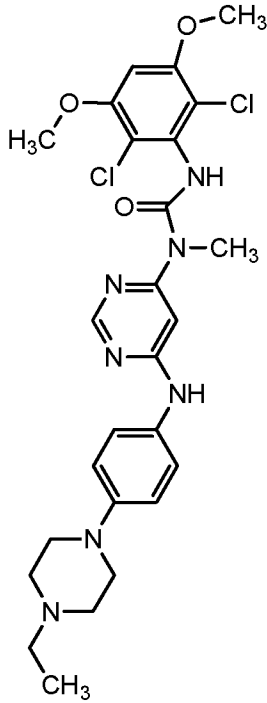
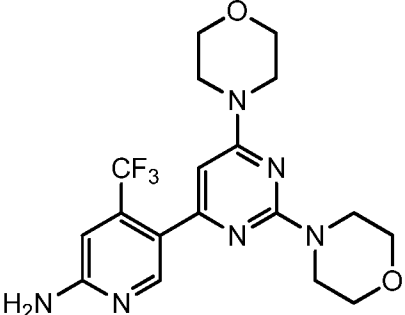
BAP050-Clone-H	LC	MSVPTQVLGLLLLLWLT DARC (SEQ ID NO: 283)
BAP050-Clone-I	HC	MAVWVWTL PFLMAAAQSVQA (SEQ ID NO: 284) MEWSWVFLF FLSVTTGVHS (SEQ ID NO: 282)
BAP050-Clone-I	LC	MSVLTQVLALLLLWLTGTRC (SEQ ID NO: 285) MSVPTQVLGLLLLLWLT DARC (SEQ ID NO: 283)
BAP050-Clone-J	HC	MAVWVWTL PFLMAAAQSVQA (SEQ ID NO: 284) MEWSWVFLF FLSVTTGVHS (SEQ ID NO: 282)
BAP050-Clone-J	LC	MSVLTQVLALLLLWLTGTRC (SEQ ID NO: 285) MSVPTQVLGLLLLLWLT DARC (SEQ ID NO: 283)

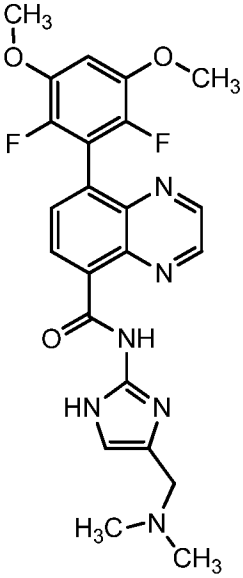
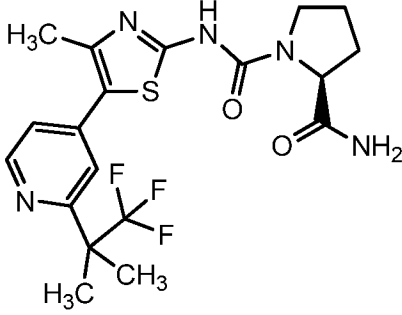
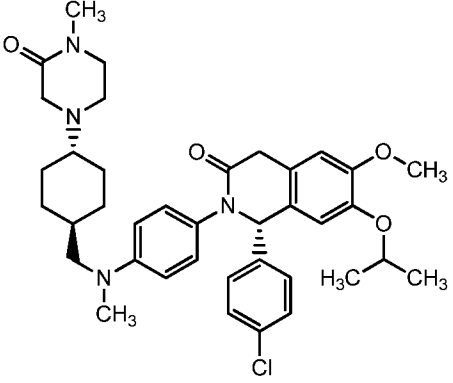
Table 5. See Examples.

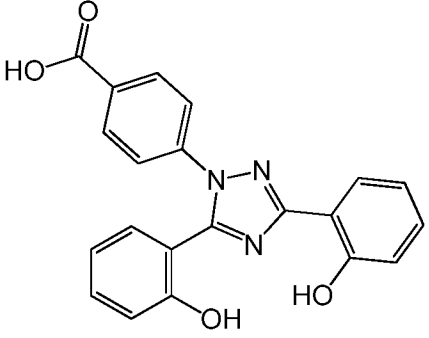
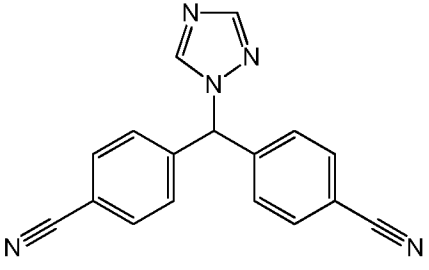
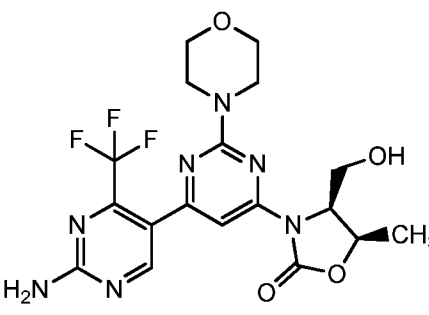
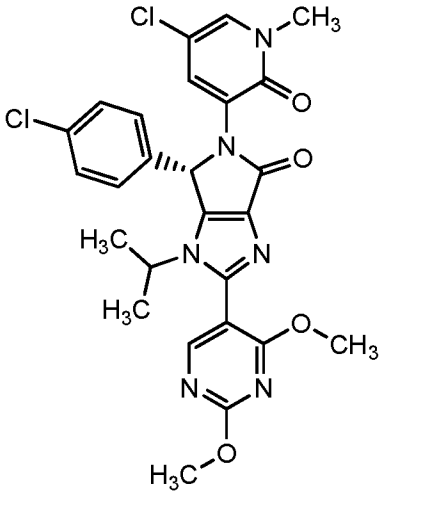
Table 6. See Examples.

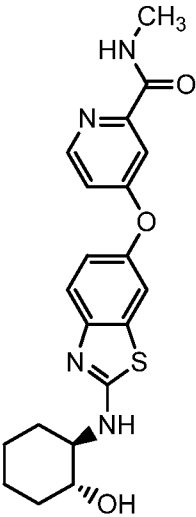
Table 7. Selected therapeutic agents that can be administered in combination with the anti-LAG-3 antibody molecules, *e.g.*, as a single agent or in combination with other immunomodulators described herein. Each publication listed in this Table is herein incorporated by reference in its entirety, including all structural formulae therein.

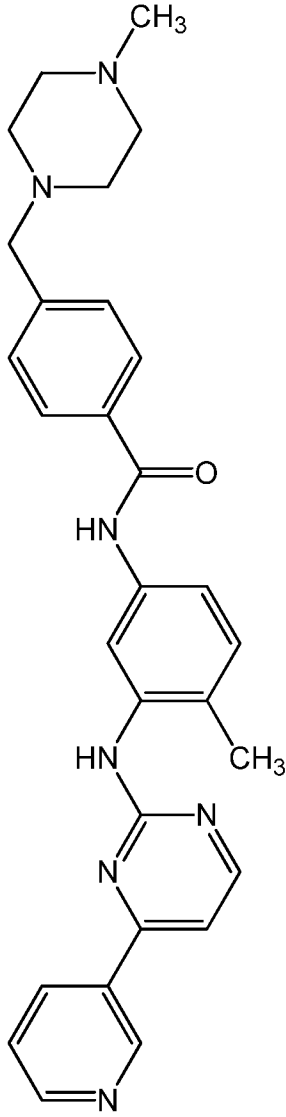
Compound No.	Generic Name Tradename	Compound Structure	Patents / Patent Application Publications
A1	Sotrastaurin		EP 1682103 US 2007/142401 WO 2005/039549
A2	Nilotinib HCl monohydrate TASIGNA®	 <p>HCl • H₂O</p>	WO 2004/005281 US 7,169,791
A3			WO 2010/060937 WO 2004/072051 EP 1611112 US 8,450,310

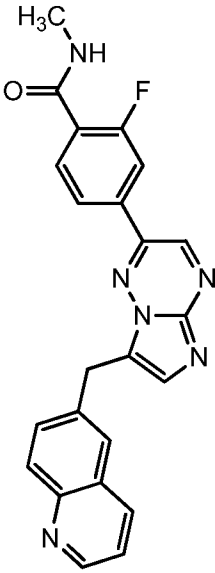
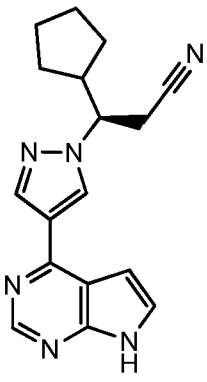
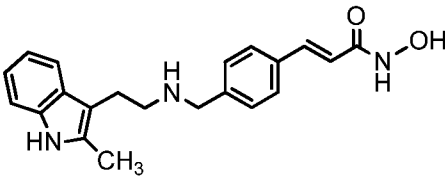
A4	Dactolisib	 <p>The chemical structure of Dactolisib consists of a quinoline ring system. At the 2-position of the quinoline, there is a 2-cyano-2-methylphenyl group. At the 4-position, there is a methylamino group (-NH-CH₃). At the 6-position, there is a 2-methoxy-3,4-dichlorophenyl group.</p>	WO 2006/122806
A5		 <p>The chemical structure of Buparlisib features a central benzimidazole ring system. The 2-position of the benzimidazole is substituted with a methylamino group (-NH-CH₃). The 4-position is substituted with a 2-ethylpiperazine ring. The 5-position is substituted with a 2-amino-5-(2-(2-ethylpiperidin-1-yl)phenyl)pyrimidin-4-yl group. The 6-position of the benzimidazole is substituted with a 2,4-dichloro-5-methoxyphenyl group.</p>	US 8,552,002
A6	Buparlisib	 <p>The chemical structure of Buparlisib features a central pyrimidine ring system. The 2-position of the pyrimidine is substituted with a morpholine ring. The 4-position is substituted with a 2-amino-5-(2-(2-ethylpiperidin-1-yl)phenyl)pyrimidin-4-yl group. The 6-position of the pyrimidine is substituted with a 2-(2-(2-ethylpiperidin-1-yl)phenyl)pyrimidin-4-yl group. The 5-position of the pyrimidine is substituted with a trifluoromethyl group (-CF₃).</p>	WO 2007/084786

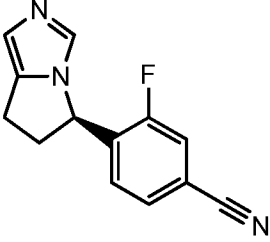
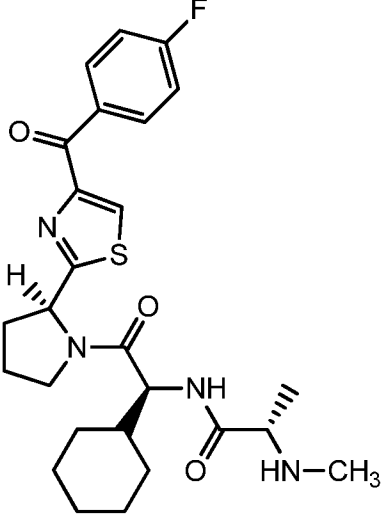
<p>A7</p>			<p>WO 2009/141386 US 2010/0105667</p>
<p>A8</p>			<p>WO 2010/029082</p>
<p>A9</p>		<p>CYP17 inhibitor</p>	<p>WO 2010/149755 US 8,263,635 B2 EP 2445903 B1</p>
<p>A10</p>			<p>WO 2011/076786</p>

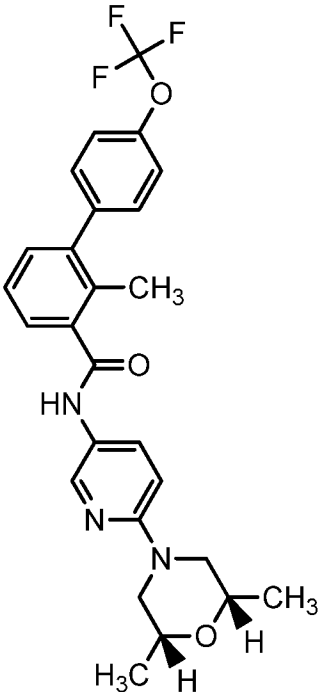
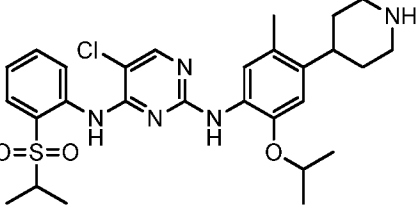
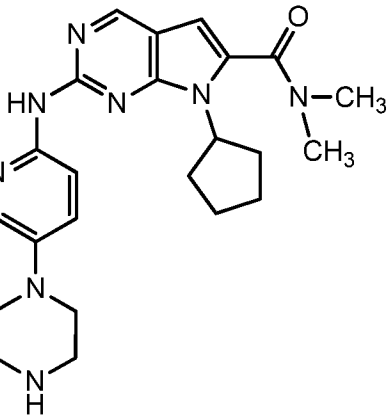
A11	Deferasirox EXJADE®	 <p>The chemical structure of Deferasirox consists of a central 1,2,4-triazole ring. One nitrogen of the triazole is bonded to a 4-(4-carboxyphenyl)phenyl group. The other two nitrogens of the triazole are bonded to a 2-hydroxyphenyl group and a 3-hydroxyphenyl group, respectively.</p>	WO 1997/049395
A12	Letrozole FEMARA®	 <p>The chemical structure of Letrozole features a central 1,2,4-triazole ring. The 1-position of the triazole is bonded to a 1,1'-bis(4-cyanophenyl)ethane group, where the two 4-cyanophenyl rings are attached to the same carbon atom.</p>	US 4,978,672
A13		 <p>The chemical structure is a complex molecule. It features a central pyrimidine ring system. One nitrogen of the pyrimidine is bonded to a morpholine ring. Another nitrogen is bonded to a 2-amino-5-(difluoromethyl)pyrimidin-4-yl group. The third nitrogen is bonded to a 2-methyl-3-hydroxyoxazolidinone ring.</p>	WO 2013/124826 US 2013/0225574
A14		 <p>The chemical structure is a complex molecule. It features a central imidazole ring system. One nitrogen of the imidazole is bonded to a 4-chlorophenyl group. The other nitrogen is bonded to a 2-methyl-5-(4-chlorophenyl)pyrimidin-4-yl group. The imidazole ring is also bonded to a 2-methoxy-5-(4-chlorophenyl)pyrimidin-4-yl group.</p>	WO 2013/111105

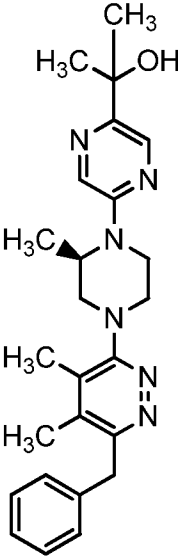
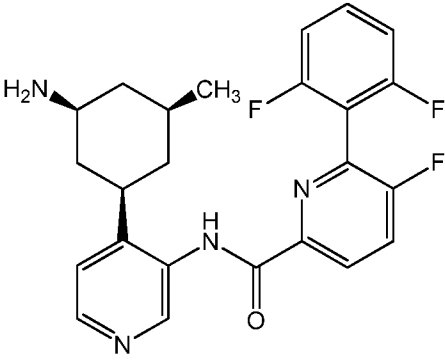
A15		 <chem>CN(C(=O)c1ccncc1Oc2ccc3nc(s3)NC[C@H]4CCCC[C@@H]4O)c5cccnc5</chem>	WO 2005/073224
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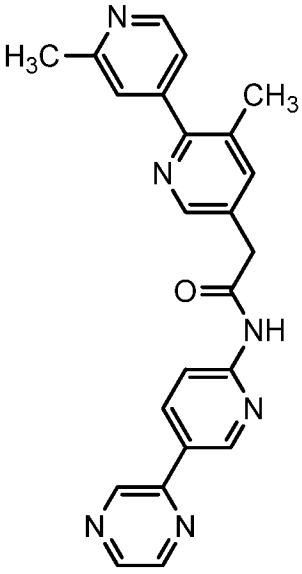
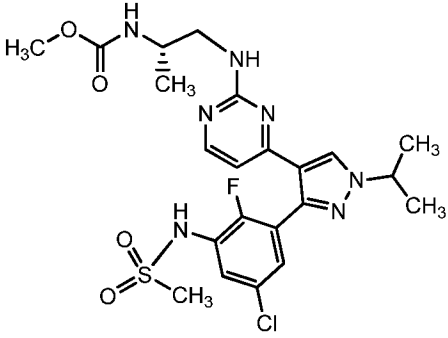
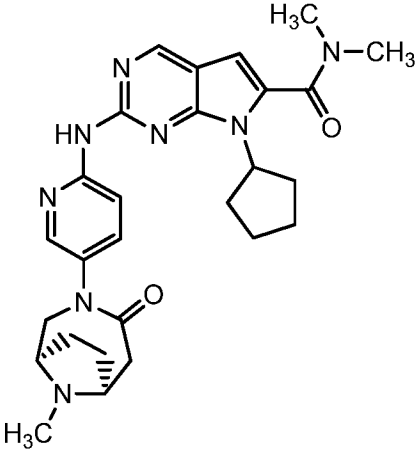
<p>A16</p>	<p>Imatinib mesylate GLEEVEC®</p>	 <p>Mesylate</p>	<p>WO 1999/003854</p>
<p>A17</p>			<p>EP 2099447 US 7,767,675 US 8,420,645</p>

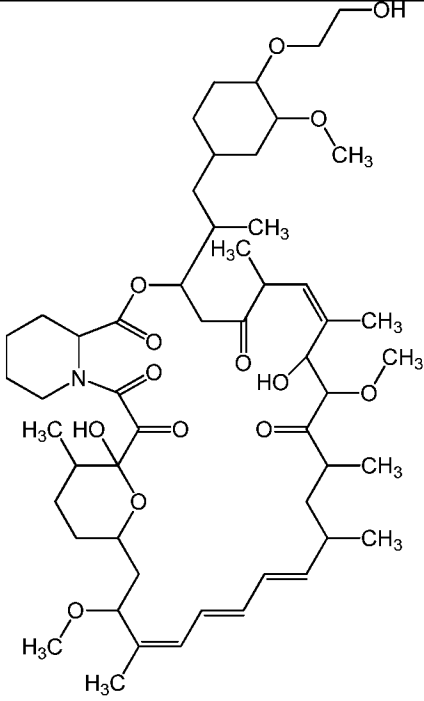
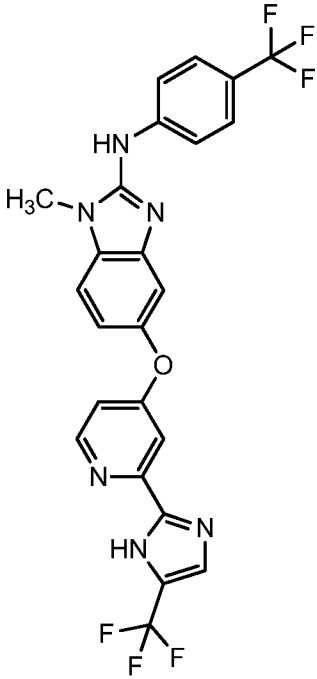
		 <p>Dihydrochloric salt</p>	
A18	Ruxolitinib Phosphate JAKAFI®	 <p>H₃PO₄</p>	WO 2007/070514 EP 2474545 US 7,598,257 WO 2014/018632
A19	Panobinostat		WO 2014/072493 WO 2002/022577 EP 1870399

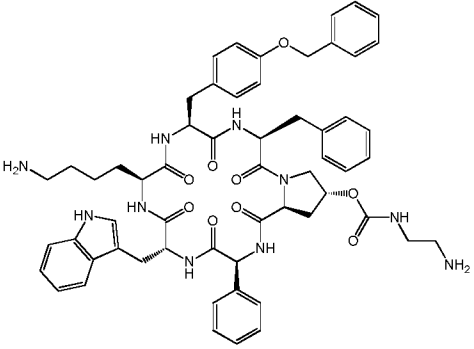
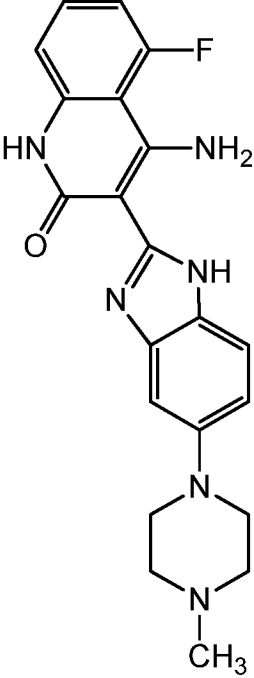
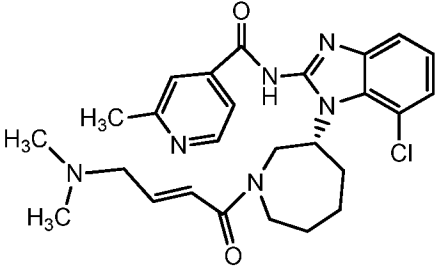
A20	Osilodrostat	 <p>The structure shows a pyrrolidine ring with a nitrogen atom at the top. Attached to the 2-position of the pyrrolidine is a phenyl ring. The phenyl ring has a fluorine atom at the 2-position and a cyano group (-C≡N) at the 5-position.</p>	WO 2007/024945
A21		 <p>The structure is a complex molecule. It features a thiazole ring with a sulfur atom at the bottom and a nitrogen atom at the top. A hydrogen atom is attached to the 4-position of the thiazole ring. The thiazole ring is connected to a cyclopentane ring. The cyclopentane ring is further connected to a cyclohexane ring. A carbonyl group is attached to the cyclohexane ring, and another carbonyl group is attached to the cyclopentane ring. A methylamino group (-NH-CH₃) is attached to the cyclohexane ring. A 4-fluorophenyl group is attached to the carbonyl group on the cyclopentane ring.</p>	WO 2008/016893 EP 2051990 US 8,546,336

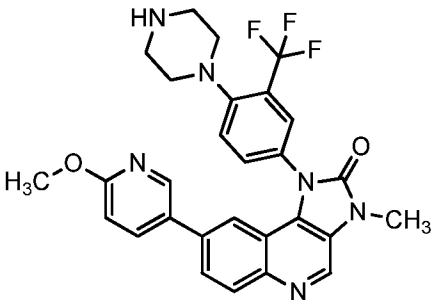
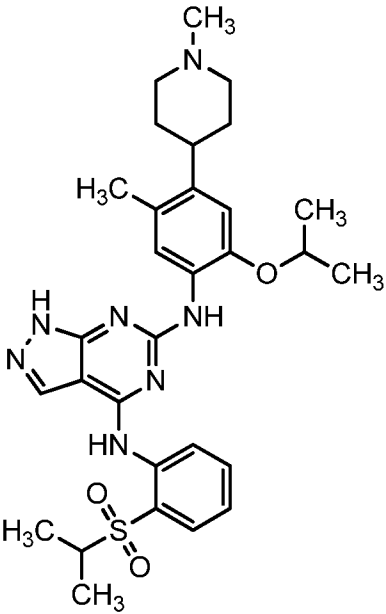
A22	Sonidegib phosphate	 <p>The structure shows Sonidegib phosphate. It features a central pyridine ring substituted at the 2-position with a piperazine ring. The piperazine ring has two methyl groups on one of its nitrogens, shown with wedged bonds. The 4-position of the pyridine ring is substituted with an amide group (-NH-C(=O)-). This amide group is further substituted with a 2-methylphenyl ring, which is in turn substituted at the para position with a 4-(trifluoromethoxy)phenyl ring.</p>	WO 2007/131201 EP 2021328 US 8,178,563
A23	ceritinib ZYKADIA™	 <p>The structure shows ceritinib. It consists of a central pyrimidopyrimidine bicyclic core. One nitrogen of the core is substituted with a chlorine atom and a sulfonamide group (-NH-SO₂-CH₂-CH(CH₃)₂). The other nitrogen is substituted with a piperidine ring and a methoxy group (-O-CH₂-CH(CH₃)₂).</p>	WO 2008/073687 US 8,039,479
A24		 <p>The structure shows a pyridopyrimidine derivative. The pyridine ring is substituted at the 4-position with a piperazine ring. The pyrimidine ring is substituted at the 2-position with a methylamino group (-NH-CH₃) and at the 4-position with a dimethylamino group (-N(CH₃)₂).</p>	US 8,415,355 US 8,685,980

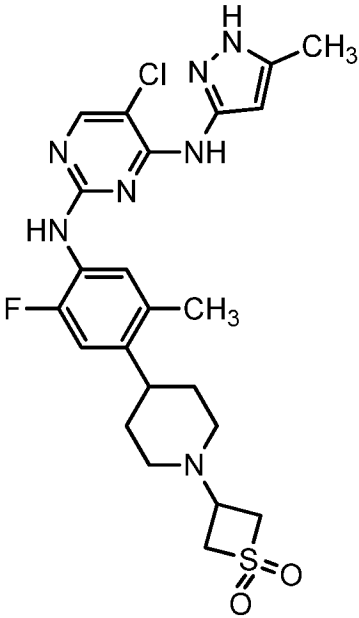
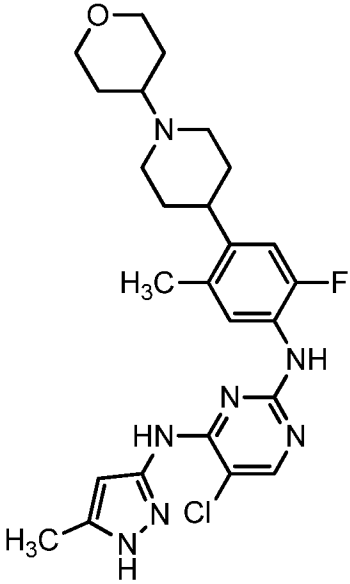
A25		 <p>Chemical structure of a complex molecule featuring a pyridine ring substituted with a 2-hydroxypropan-2-yl group, a piperazine ring with a methyl group, and a diazole ring substituted with two methyl groups and a benzyl group.</p>	WO 2010/007120
A26		Human monoclonal antibody to PRLR	US 7,867,493
A27		 <p>Chemical structure of a complex molecule featuring a piperidine ring substituted with an amino group and a methyl group, and a pyridine ring substituted with a methyl group and an amide group linked to a fluorinated benzene ring.</p>	WO 2010/026124 EP 2344474 US 2010/0056576 WO2008/106692

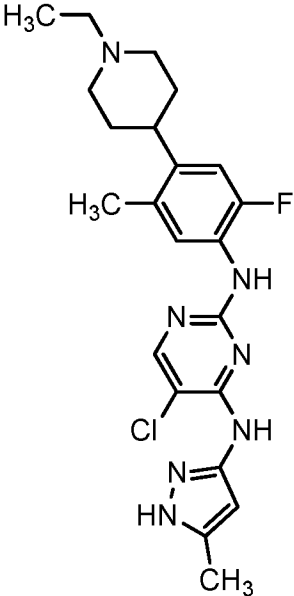
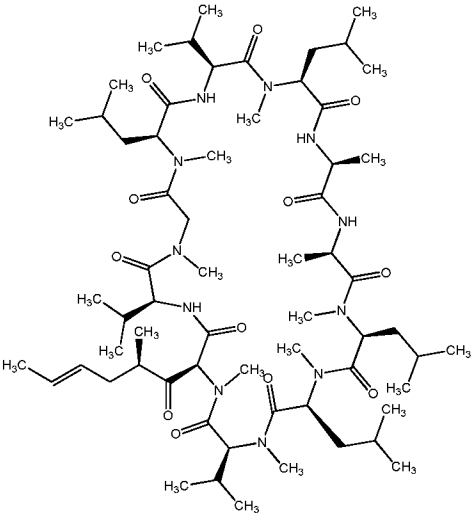
A28		 <p>The structure shows a 4-methylpyridine ring connected at its 2-position to the 4-position of another pyridine ring. This second pyridine ring has a methyl group at the 3-position and a propyl chain at the 5-position. The propyl chain is terminated by a primary amide group (-NH-).</p>	WO 2010/101849
A29	Encorafenib	 <p>The structure is a complex heterocyclic molecule. It features a central benzimidazole core. One of the imidazole nitrogens is substituted with a methyl group. The benzimidazole is fused to a benzene ring. This benzene ring has a chlorine atom at the 6-position and a methylsulfonamide group (-NH-SO₂-CH₃) at the 7-position. The benzimidazole core is also substituted with a methyl group on the other imidazole nitrogen and a propyl chain on the benzimidazole ring. The propyl chain is terminated by a methyl ester group (-NH-CO-O-CH₃).</p>	WO 2011/025927
A30		 <p>The structure is a complex heterocyclic molecule. It features a central benzimidazole core. One of the imidazole nitrogens is substituted with a methyl group. The benzimidazole is fused to a benzene ring. This benzene ring has a chlorine atom at the 6-position and a methylsulfonamide group (-NH-SO₂-CH₃) at the 7-position. The benzimidazole core is also substituted with a methyl group on the other imidazole nitrogen and a propyl chain on the benzimidazole ring. The propyl chain is terminated by a methyl ester group (-NH-CO-O-CH₃).</p>	WO 2011/101409

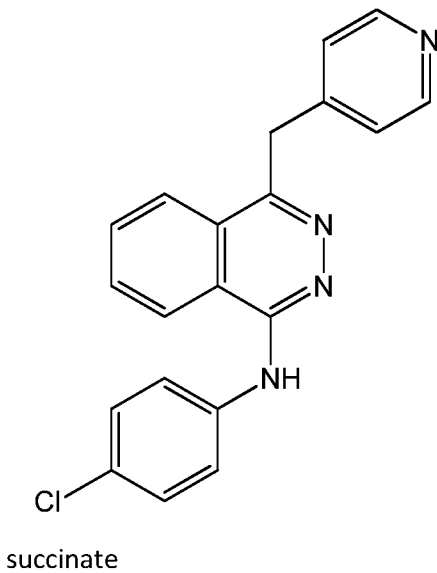
<p>A36</p>	<p>Everolimus AFINITOR®</p>		<p>WO 2014/085318</p>
<p>A37</p>			<p>WO 2007/030377 US 7,482,367</p>

A38	Pasireotide diaspartate SIGNIFOR®	 <p>The chemical structure of Pasireotide diaspartate is a complex peptide derivative. It features a central peptide backbone with several side chains. Notable features include a long-chain primary amine (H₂N-CH₂-CH₂-CH₂-CH₂-CH₂-), a benzimidazole ring system, a benzyl group, a piperazine ring, and a diethylamine group (-NH-CH₂-CH₂-NH₂). The structure is highly branched and contains multiple amide and ester linkages.</p>	WO2002/010192 US 7,473,761
A39	Dovitinib	 <p>The chemical structure of Dovitinib is a pyridone derivative. It consists of a pyridone ring substituted with a fluorine atom (F) at the 6-position and an amino group (-NH₂) at the 3-position. The 4-position of the pyridone ring is substituted with a 1H-imidazole ring. The 5-position of the imidazole ring is substituted with a 4-(N-methylpiperazine-1-yl)phenyl group.</p>	WO 2009/115562 US 8,563,556
A40		 <p>The chemical structure is a complex heterocyclic molecule. It features a central pyridine ring substituted with two methyl groups (-CH₃) at the 2 and 6 positions. The 4-position of the pyridine ring is substituted with a carbonyl group (-C(=O)-). This carbonyl group is part of a larger structure that includes a 1,2,4-triazole ring substituted with a chlorine atom (-Cl) at the 5-position. The structure also contains a piperazine ring and a dimethylamino group (-N(CH₃)₂-) attached to a chain that includes a double bond.</p>	WO 2013/184757

A41		 <p>Chemical structure of a complex molecule. It features a piperazine ring attached to a benzene ring. The benzene ring also has a difluoromethyl group (-CF₂H) and is connected to a pyridine ring with a methoxy group (-OCH₃). This pyridine ring is further connected to a fused pyridine system, which has a methyl group (-CH₃) attached to one of its nitrogen atoms.</p>	WO 2006/122806
A42		 <p>Chemical structure of a complex molecule. It features a piperazine ring attached to a benzene ring. The benzene ring also has a methyl group (-CH₃) and a methoxy group (-OCH₂CH₃). The benzene ring is connected to a pyrazole ring, which is further connected to a sulfonamide group (-NH-SO₂-CH₂-CH₃).</p>	WO 2008/073687 US 8,372,858

A43		 <chem>Cc1cc[nH]1Nc2nc(Cl)cnc2Nc3cc(F)c(C)cc3C4CCN(C4)C5CC(=O)S(=O)C5</chem>	WO 2010/002655 US 8,519,129
A44		 <chem>Cc1cc[nH]1Nc2nc(Cl)cnc2Nc3cc(F)c(C)cc3C4CCN(C4)C5CCOCC5</chem>	WO 2010/002655 US 8,519,129

<p>A45</p>			<p>WO 2010/002655</p>
<p>A46</p>	<p>Valspodar AMDRAY™</p>		<p>EP 296122</p>

A47	Vatalanib succinate	 <p>succinate</p>	WO 98/35958
A48		IDH inhibitor	WO2014/141104
A49		BCR-ABL inhibitor	WO2013/171639 WO2013/171640 WO2013/171641 WO2013/171642
A50		cRAF inhibitor	WO2014/151616
A51		ERK1/2 ATP competitive inhibitor	WO2015/066188

EXAMPLES

The Examples below are set forth to aid in the understanding of the inventions but are not intended to, and should not be construed to, limit its scope in any way.

Example 1: Humanization of Anti-LAG-3 Antibody, BAP050

A murine anti-LAG-3 monoclonal antibody, BAP050, was humanized. The sequences and test samples of twenty humanized BAP050 clones with unique variable region sequences were obtained. These clones were further analyzed for their biological functions (*e.g.*, antigen binding and ligand blocking), structural features, and transient expression in CHO cells.

Example 1.1: Humanization Technology and Process

Humanization of BAP050 was performed using a combinatorial library of human germ line variable region frameworks (FWs). The technology entails transferring the murine CDRs in frame to a library of human variable regions (VRs) that had been constructed by randomly combining human germ line FW1, FW2 and FW3 sequences. Only one FW4 sequence is used, which is WGQGTTVTVSS (SEQ ID NO: 221) for the heavy chain (HC) (Kabat human HC subgroup I, No. 21) and FGQGTKVEIK (SEQ ID NO: 271) for the light chain (LC) (Kabat human κ subgroup I, No. 5). The library of VR sequences is fused to human constant region (CR) sequences, human IgG4(S228P) of HC and human κ CR of LC, and the resulting library of whole IgG is expressed in CHO cells for screening. Screening was performed with tissue culture supernatants measuring binding avidity on antigen-expressing cells in a whole cell ELISA format or on FACS.

The humanization process was performed in a stepwise manner starting with the construction and expression of the appropriate chimeric mAb (murine VR, IgG4(S228P), human κ), which can serve as a comparator for the screening of the humanized clones. The constant region amino acid sequences for human IgG4(S228P) heavy chain and human kappa light chain are shown in Table 6.

Humanization of the VR of LC and HC were performed in two independent steps. The library of humanized LC (huLC) was paired with the chimeric HC (murine VR, IgG4(S228P)) and the resulting “half-humanized” mAbs were screened for binding activity by ELISA. The huLC of clones with adequate binding activity (\geq binding of chimeric mAb) were selected.

Analogously, the library of humanized HC (huHC) was paired with the chimeric LC (murine VR, human κ) and screened for binding activity by ELISA. The huHC of clones with appropriate binding activity (\geq binding of chimeric mAb) were selected.

The variable regions of the selected huLC and huHC were then sequenced to identify the huLC and huHC with unique sequences (some clones from the initial selection process may share the same LC or HC). The unique huLC and huHC were then randomly combined to form a small library of humAbs, which was expressed in CHO cells and screened on antigen-expressing cells in an ELISA and FACS format. Clones with binding activities that were equal or better than the binding of the chimeric comparator mAb are the final product of the humanization process.

Example 1.2: Sequence of Murine mAb BAP050

The LC and HC variable region sequences of the murine anti-LAG-3 mAb were determined. The sequences obtained from two independent analyses were identical and are shown in Figure 1.

Germline analysis was performed and part of the result is shown in Figure 2 as an amino acid sequence alignment. For the light chain, the V-gene is 96.88% identical to mIGkV10-94*01F (279/288 nts) and the J-gene is 97.30% identical to mIGkJ1*01F (36/37 nts). For the heavy chain, the V-gene is 96.88% identical to mIGHV9-3-1*01F (279/288 nts), the J-gene is 86.79% identical to mIGHJ4*01F, and the D-gene is mIGHD1-1*01F.

Example 1.3: Humanized Antibody Clones

As shown in Figure 3, the process of humanization yielded twenty humanized clones with binding affinities comparable to that of the chimeric antibody. In addition to binding data, for each clone, the VR sequences were provided along with a sample of the mAb. The samples had been prepared by transient transfections of CHO cells and were concentrated tissue culture supernatants. The mAb concentrations in the solutions had been determined by an IgG4-specific ELISA.

As shown in Figure 4, the twenty unique clones are combinations of six unique HC and twelve unique LC. The amino acid and nucleotide sequences of the heavy and light chain variable domains for the humanized BAP050 clones are shown in Table 1. The amino acid and

nucleotide sequences of the heavy and light chain CDRs of the humanized BAP050 clones are shown in Table 1.

Limited diversity was obtained for the HC FW3 region with eighteen clones having the same FWH3, which is from the human germ line IGHV7-4 and has an exposed Cys residue at position 84 of the humanized clones. Closely related VHF3 sequences typically have a Ser or Ala residue in this position. Therefore, Cys84 was replaced by Ser in selected humanized clones.

Figure 4 indicates that the samples varied in the concentration of the mAb, ranging from 3.2 µg/mL to 35.8 µg/mL. These numbers were representative of several transient expression experiments.

Example 1.4: Analysis of the Humanized Clones

Example 1.4.1: Analysis of binding activity and binding specificity of humanized clones

The binding activity and specificity was measured in a competition binding assay using a constant concentration of FITC-labeled murine mAb, serial dilutions of the test mAbs, and LAG-3-expressing CHO cells. Incubations with the mAb mixtures having different concentration ratios of test mAb to labeled mAb was at 4 °C for 30 min. Bound labeled murine mAb was then quantified using a FACS machine. The experiment was performed twice. The results are shown in Figures 5A-5B.

Within the accuracy of the experiment, all humanized clones show similar activity for competing with binding of labeled murine mAb. The activity is also comparable to the activity of the parent murine mAb and chimeric mAb. MAbs were ranked relative to each other. For example, it can be a weaker competitor if in both experiments the curve of a certain clone is to the right of the chimeric mAb curve or it can be a better competitor if the curve of a certain clone is to the left of the chimeric mAb curve. Such a ranking system was used in Figure 6.

Example 1.4.2: Sequence analysis of humanized clones

Based on structural features, the twenty humanized mAbs were divided into six groups and ranked them from A to F. The results are shown in Figure 6.

Example 1.4.3: Selection of humanized clones and generation of new versions with the C84S mutation

Figure 6 summarizes the data which was considered for the selection of humanized clones. Expression data (2nd column), the diversity in the composition of the variable regions (3rd column), relative rankings in binding studies (4th and 5th columns), and structural analysis (6th column), were considered. Certain characteristics that lead to the selection of individual clones are marked with grey fields.

Certain clones were mutated at position 84 of VHF3 from Cys to Ser (*see* Example 1.3 above). The new versions are called clones Nos. 1S, 2S, 5S, 9S, 11S, 12S, and 13S, and together huBAP050(Ser) clones.

Example 1.4.4: Analysis of binding activity and binding specificity of huBAP050(Ser) clones

The new versions of the selected clones with the C84S mutation in VHF3 were subject to an analogous competition binding assay as described under Example 1.4.1. The experiment included the original humanized clones with the Cys84 residue, the new humanized clones with the Ser84 residue, chimeric mAb and the parent murine mAb. The results are shown in Figure 7.

All tested variants were comparable to the murine parent mAb in blocking the binding of labeled murine mAb to LAG-3-expressing CHO cells. It follows that the behavior of the new humanized clones with the Ser84 residue was not different from the behavior of the original humanized clones with the Cys84 residue.

Example 1.4.5: Blocking of binding of LAG-3-Ig to MHC Class II on Daudi cells

LAG-3 binds to MHC class II, therefore the selected huBAP050(Ser) clones were tested for their ability to block the binding of soluble LAG-3-Ig to Daudi cells (a Burkitt's lymphoma cell line) that express MHC class II. The blocking capacity of the mAbs was evaluated in a competition binding assay using a constant concentration of LAG-3-huIgG1 Fc fusion protein (2 µg/mL), serial dilutions of the mAbs to be tested, and Daudi cells. Incubation was at 4 °C for 30 min. Bound ligand fusion protein was detected with PE-conjugated F(ab')₂ fragment of goat anti-human IgG which doesn't recognize IgG4 mAbs (Southern Biotech 2043-09), and flow cytometry. The results are shown in Figure 8.

Within the accuracy of the experiments, the seven huBAP050(Ser) clones, chimeric mAb and murine parent mAb demonstrated comparable blocking activity for LAG-3-Ig.

Example 1.4.6: T cell epitope analysis

Humanized mAbs were analyzed for T cell epitopes using Epibase™. The algorithm analyzes each possible peptide (each 10-mer along the protein advancing by one amino acid) for binding to HLA class II. It estimates free energy of binding (ΔG_{bind}) for each peptide and calculates a putative KD ($\Delta G_{\text{bind}} = RT \ln K_D$). Then peptides are labeled S, M, or N for strong, medium, and non-binders. Threshold values used for this classification are different for each allotype.

The data was normalized to a risk score. The overall “risk score” is the sum of all potential epitopes to all tested alleles, weighted by the affinities of the respective peptides but leaving out all potential epitopes in germ line sequences (lower value therefor is “better”)

There are roughly three categories of mAbs, derived from a large set of mAbs of different composition as described below.

Risk score of around 500: fully human mAbs generated from humans, “humanized” mice, and phage libraries (“values below 500 are really good even for fully human antibodies”). Humanized mAbs specifically engineered (even the CDRs) to have a low score are typically in the 500-700 risk category.

Risk score around 900: typical CDR-grafted antibodies, which have fully murine CDRs with or without changes in the FW region (“Gary Queen technology”); approved CDR-grafted mAbs are basically all in this category.

Risk score around 1500: chimeric mAbs.

The results for selected humanized BAP050 mAbs are:

Clone No.	Risk score
01	999
02	1006
05	967
09	998
11	1042
12	1042
13	950

The risk scores of the seven selected humanized clones are in the typical CDR-grafted mAb category. For example, the human mAb, adalimumab (Humira®), has a score of 654, which is relatively high for human mAbs (at the upper end of the Gaussian curve) but low in comparison to a typical CDR-grafted mAb.

The scores come from the murine CDRs, specifically the Y residues. These are acceptable scores for antibodies for cancer treatment. Changing the score would mean engineering the murine CDRs, specifically removing Y residues.

Summary and Conclusions

Murine anti-LAG-3 monoclonal antibody, BAP050, was humanized. The technology entails the cloning of the murine CDRs in-frame into an ordered library of human germ line variable region frameworks, expressing the library of cloned variable regions as intact IgG4(S228P) humanized mAbs in CHO cells, and selecting clones that bind with comparable or higher affinity to the target as the parent mAb. Therefore, the murine CDRs were asked to select the best human germ line framework sequences that preserve their conformations and thus the binding affinity and specificity of the parent murine mAb. The sequences and test samples of twenty humanized versions with unique variable region sequences were obtained, which had also passed a binding test with LAG-3-transfected CHO cells. Eighteen clones contained the same HC FW3 germ line sequence, which has a rare Cys at position 84. In seven selected clones, Cys was replaced by Ser creating new mAbs labeled huBAP050(Ser) clones. These clones were further analyzed for their biological functions (*e.g.*, antigen binding and ligand blocking), structural features, and transient expression in CHO cells.

Example 2: Expression of Humanized Anti-LAG-3 Antibody, BAP050

Five humanized clones described in Example 1 were selected for evaluation of expression in Chinese Hamster Ovary (CHO) cells.

Single gene vectors (SGVs) were constructed using Lonza's GS Xceed vectors (IgG4proΔk for heavy chain and Kappa for light chain). The SGVs were amplified and transiently co-transfected into CHOK1SV GS-KO cells for expression at a volume of 2.8 L.

Expression cultures were harvested Day 6 post-transfection and clarified by centrifugation and sterile filtration. The clarified cell culture supernatant was purified using one-

step Protein A chromatography. Product quality analysis in the form of SE-HPLC, SDS-PAGE, IEF, and LAL was carried out using purified material at a concentration of 1 mg/ml including an antibody as a control sample.

Example 2.1: Vector Construction

The sequences of the light and heavy chain variable domain encoding regions were synthesised by GeneArt AG. Light chain variable domain encoding regions were sub-cloned into pXC-Kappa and heavy chain variable domain encoding regions into pXC-IgG4pro Δ K vectors respectively using the N-terminal restriction site Hind III and the C-terminal restriction sites BsiWI (light chain) and ApaI (heavy chain). Positive clones were screened by PCR amplification (primers 1053: GCTGACAGACTAACAGACTGTTCC (SEQ ID NO: 288) and 1072: CAAATGTGGTATGGCTGA (SEQ ID NO: 289)) and verified by restriction digest (using a double digest of EcoRI-HF and HindIII-HF) and nucleotide sequencing of the gene of interest.

Example 2.2: DNA Amplification

A single bacterial colony was picked into 15 ml Luria Bertani (LB) medium (LB Broth, Sigma-Aldrich, L7275) containing 50 μ g/ml ampicillin and incubated at 37 °C overnight with shaking at 220 rpm. The resulting starter culture was used to inoculate 1 L Luria Bertani (LB) medium containing 50 μ g/ml ampicillin and incubated at 37 °C overnight with shaking at 220 rpm. Vector DNA was isolated using the QIAGEN Plasmid Plus Gigaprep system (QIAGEN, 12991). In all instances, DNA concentration was measured using a Nanodrop 1000 spectrophotometer (Thermo-Scientific) and adjusted to 1 mg/ml with EB buffer (10 mM Tris-Cl, pH 8.5). DNA quality for the single gene vectors was assessed by measuring the absorbance ratio A260/A280. This was found to be between 1.88 and 1.90.

Example 2.3: Culture of CHOK1SV GS-KO Cells

CHOK1SV GS-KO cells were cultured in CD-CHO media (Invitrogen, 10743-029) supplemented with 6 mM glutamine (Invitrogen, 25030-123). Cells were incubated in a shaking incubator at 36.5 °C, 5% CO₂, 85% humidity, 140 rpm. Cells were routinely sub-cultured every

3-4 days, seeding at 2×10^5 cells/ml and were propagated in order to have sufficient cells available for transfection. Cells were discarded by passage 20.

Example 2.4: Transient Transfections of CHOK1SV GS-KO Cells

Transient transfections were performed using CHOK1SV GS-KO cells which had been in culture a minimum two weeks. Cells were sub-cultured 24 h prior to transfection and cell viability was >99% at the time of transfection.

All transfections were carried out via electroporation using a Gene Pulse MXCell (Bio-Rad), a plate based system for electroporation. For each transfection, viable cells were resuspended in pre-warmed media to 2.86×10^7 cells/ml. 80 μ g DNA (1:1 ratio of heavy and light chain SGVs) and 700 μ l cell suspension were aliquotted into each cuvette/well. Cells were electroporated at 300 V, 1300 μ F. Transfected cells were transferred to pre-warmed media in Erlenmeyer flasks and the cuvette/wells rinsed twice with pre-warmed media which was also transferred to the flasks. Transfected cell cultures were incubated in a shaking incubator at 36.5 °C, 5% CO₂, 85% humidity, 140 rpm for 6 days. Cell viability and viable cell concentrations were measured at the time of harvest using a Cedex HiRes automated cell counter (Roche).

Example 2.5: Protein A Affinity Chromatography

Cell culture supernatant was harvested and clarified by centrifugation at 2000 rpm for 10 min, then filtered through a 0.22 μ m PES membrane filter. Clarified supernatant was purified using a pre-packed 5 ml HiTrap MabSelect SuRE column (GE Healthcare, 11-0034-94) on an AKTA purifier (10 ml/min). The column was equilibrated with 50 mM sodium phosphate, 125 mM sodium chloride, pH 7.0 (equilibration buffer) for 5 column volumes (CVs). After sample loading, the column was washed with 2 CVs of equilibration buffer followed by 3 CVs of 50 mM sodium phosphate, 1 M sodium chloride pH 7.0 and a repeat wash of 2 CVs of equilibration buffer. The Product was then eluted with 10 mM sodium formate, pH 3.5 over 5 CVs. Protein containing, eluted fractions were immediately pH adjusted to pH 7.2 and filtered through a 0.2 μ m filter.

A single protein-containing peak was observed during the elution phase. This peak was shown to contain the mAb, when analyzed by SE-HPLC and SDS-PAGE. Recovered protein yield is shown in Table 5. The clones expressed transiently in a range from 21.9 to 29.4 mg/L.

Table 5. Summary of yield, titre, monomer content and endotoxin levels

Product	Yield* (mg)	Titre* (mg/L)	Monomer Content (%)	Endotoxin levels (EU/mg)
Clone F	79.1	28.25	95.63	0.22
Clone G	61.3	21.88	95.31	0.15
Clone H	76.0	27.13	97.07	0.20
Clone I	82.3	29.38	97.82	0.05
Clone J	64.0	24.63‡	96.97	0.27
*Post Protein A purification; ‡from a 2.6 L expression culture				

Example 2.6: SE-HPLC Analysis

Samples of Protein A purified antibodies were analyzed in duplicate by SE-HPLC on an Agilent 1200 series HPLC system, using a Zorbax GF-250 4 µm 9.4 mm ID x 250 mm column (Agilent). Aliquots of sample at a concentration of 1 mg/ml were filtered through a 0.2 µm filter prior to injection. 80 µl aliquots were injected respectively and run at 1 ml/min for 15 minutes. Soluble aggregate levels were analysed using Chemstation (Agilent) software.

Chromatography profiles with retention time showing the percentage of the overall detected peak areas were obtained for the tested antibodies and a control IgG4 antibody. The products show a single protein peak at approximately 8.59 to 8.61 min comparable to the human IgG4 antibody control (about 8.64 min) and consistent with a monomeric antibody. Small amounts (up to about 3-4%) of higher molecular weight impurities, consistent with soluble aggregates, were detected at retention times around 7.90 min.

Example 2.7: SDS-PAGE Analysis

Reduced samples were prepared for analysis by mixing with NuPage 4x LDS sample buffer (Invitrogen, NP0007) and NuPage 10x sample reducing agent (Invitrogen, NP0009), and incubated at 70 °C, 10 min. For non-reduced samples, the reducing agent and heat incubation were omitted. Samples were electrophoresed on 1.5 mm NuPage 4-12% Bis-Tris Novex pre-cast gels (Invitrogen, NP0335PK2) with NuPage MES SDS running buffer under denaturing conditions. 10 µl aliquots of SeeBlue Plus 2 pre-stained molecular weight standard (Invitrogen,

LC5925) and a control IgG4 antibody at 1 mg/ml were included on the gel. 1 µl of each sample at 1 mg/ml were loaded onto the gel. Once electrophoresed, gels were stained with InstantBlue (TripleRed, ISB01L) for 30 min at room temperature. Images of the stained gels were analysed on a BioSpectrum Imaging System (UVP).

The analysis confirmed the presence of the antibody products and good levels of purity. Under non-reducing conditions, a predominant protein band close to 98 kDa was observed comparable with the control IgG4 antibody. The control IgG4 antibody and one tested clone display an additional fainter band corresponding to a heavy plus light chain half-antibody at approximately 70 kDa under non-reducing conditions. This is expected for the control antibody. Two bands were observed under reducing conditions consistent with the size of heavy (close to the position of the 49 kDa marker) and light chains (close to the position of the 28 kDa marker) and comparable with the bands found for the control IgG4 antibody.

Example 2.8: Iso-electric Focussing (IEF) Analysis

Non-reduced samples of Protein A purified antibody were electrophoresed as described below.

5 µg of Protein A purified samples were electrophoresed on a 1.0 mm Novex pH 3-10 gradient gel (Invitrogen, EC66552BOX) using manufacturers recommended running conditions. A 10 µl aliquot of IEF pH 3 – 10 markers (Invitrogen, 39212-01) was included on the gel. Once electrophoresed, gels were fixed with 10% TCA solution for 30 min and then stained with InstantBlue (TripleRed, ISB01L) over night at room temperature. Images of the stained gels were analysed on a BioSpectrum Imaging System (UVP).

As shown in Table 6, the tested clones display charge isoforms between pH 6.0 and 7.45. The detected charge isoforms are comparable to the theoretically calculated pIs for these antibodies which were predicted to be between 6.35 and 6.82. Clones F and G both have a predicted pI of 6.35 and show comparable charge isoforms, which is also consistent with the theoretically calculated pI being the same for both (6.35). The control IgG4 antibody behaved as expected.

Table 6. Charge isoforms as detected by Novex IEF analysis

Product	pI of predominant charge isoform*	Acidic charge isoforms*	Basic charge isoforms*
Clone F	6.2	2x; 6.0 to 6.1	6.3
Clone G	6.2	2x; 6.0 to 6.1	6.3
Clone H	7.4	2x; 6.9 to 7.3	7.45
Clone I	7.0	2x; 6.7 to 6.9	7.3
Clone J	6.5	2x; 6.0 to 6.4	6.8

*pI readings are estimated from the staining positions correlated against the IEF 3-10 marker.

Example 2.9: Endotoxin Analysis

Endotoxin levels of purified proteins were measured at final concentrations (up to 3.44 mg/ml) using an Endosafe-PTS instrument, a cartridge based method based on the LAL assay (Charles River).

As shown in Table 8, the endotoxin content was found to range from 0.05 to 0.27 EU/mg.

Conclusion

GS single gene expression vectors for selected humanized anti-LAG-3 mAbs were constructed and used to transiently transfect CHOK1SV GS-KO cells. 2.6 to 2.8 litres of expression culture were incubated under standard conditions for 6 days and the resulting cell culture supernatant purified using Protein A chromatography. Post-purification titres are indicated in Table 8 and were found to be ranging from 21.88 to 29.38 mg/L. The recovered yields range from 61.3 to 82.3 mg.

SDS-PAGE and SE-HPLC analysis indicated the presence of a small amount (up to 4.69%) of soluble aggregates present in the products being predominantly consistent with dimeric antibody for the mAb. The mAbs also showed higher molecular weight impurities at retention times consistent with that of trimeric antibodies.

Iso-electric focusing detected a number of charge isoforms for all mAbs. The mAbs showed isoforms generally more basic when based on theoretically calculated pI for these molecules indicating some level of post translation modification. The mAbs were found to be comparable to their theoretically calculated pI values.

The endotoxin levels for all samples were measured prior to provision of samples and found to be below 0.63 EU/mg.

Example 3: Characterization of Murine and Humanized Anti-LAG-3 Antibodies

Example 3.1: Characterization of Murine Anti-LAG-3 Antibody

The binding affinity of murine anti-LAG-3 antibody BAP050 to LAG-3 was investigated. As shown by FACS analyses, the murine anti-LAG-3 antibody binds to human LAG-3 transfected CHO cells with a K_D of 0.2 nM, to human T cells with a K_D of 0.26 nM, and to human LAG-3 transfected 300.19 cells with a K_D of 13.6 nM.

The blocking activity of murine anti-LAG-3 antibody BAP050 was examined by competition binding assays. The murine anti-LAG-3 antibody blocked LAG-3-Ig binding to MHC class II molecules on Raji cells with an IC_{50} of 2.3 nM.

The effect of murine anti-LAG-3 antibody BAP050 on interferon gamma ($IFN-\gamma$) expression was tested. The murine anti-LAG-3 antibody resulted in 3.0 ± 2.1 fold increase in $IFN-\gamma$ expression on cells stimulated with anti-CD3 (0.1 $\mu\text{g/mL}$), 1.6 ± 0.4 fold increase on cells stimulated with Staphylococcal enterotoxin B (SEB) (3 $\mu\text{g/mL}$), and 1.4 ± 0.3 fold increase on cells stimulated with CMV peptides.

The regions in LAG-3 that may bind murine anti-LAG-3 antibody BAP050 were examined. As shown by ELISA, the murine anti-LAG-3 antibody binds a LAG-3 Ig fusion protein (sLAG-3 D1-D4Ig) that contains all four extracellular Ig-like domains (D1-D4), as well as a LAG-3 Ig fusion protein (sLAG-3 D1-D2Ig) that only contains Domain 1 (D1) to Domain 2 (D2). Further analysis shows that the anti-LAG-3 antibody binds CHO cells that express full length LAG-3, LAG-3 with D2 deletion (CHO-LAG-3 Δ D2), and LAG-3 with partial deletion of D1 extra loop (CHO-LAG-3 Δ P48A60). Thus, the anti-LAG-3 antibody binds D1 of LAG-3.

The murine anti-LAG-3 antibody BAP050 was also found to increase $IFN-\gamma$ secretion in CD3-stimulated PBMCs compared to mouse IgG1 control and no antibody control. The fold of increase ranges from 1.4 to 2.9-fold among four donors.

Example 3.2: Characterization of Humanized Anti-LAG-3 Antibody

Binding affinity and specificity

The binding of an exemplary humanized anti-LAG-3 antibody on human LAG-3 protein

was measured using Biacore method. The results are: $K_a = 6.41 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$; $K_d = 7.00 \times 10^{-5} \text{ s}^{-1}$; $K_D = 0.109 \pm 0.008 \text{ nM}$. The anti-LAG-3 antibody also binds cynomolgus LAG-3 as measured by Biacore method.

The binding of the same humanized anti-LAG-3 antibody on human LAG-3-expressing CHO cells and cynomologous monkey LAG-3 expressing HEK 209 cells. was measured using FACS analysis. The result shows that the anti-LAG-3 antibody (human IgG4) binds with high affinity to human LAG-3 compared to a human IgG4 isotype control. The anti-LAG-3 antibody binds human LAG-3-expressing cells with a K_D of 1.92 nM and binds cynomologous monkey LAG-3-expressing cells with a K_D of 2.3 nM.

The binding of the anti-LAG-3 antibody on rhesus LAG-3-expressing 300.19 cells was also measured. The results show that the anti-LAG-3 antibody binds rhesus LAG-3 with a K_D of 8.03 nM.

Additional binding analyses show that the exemplary humanized anti-LAG-3 antibody is not cross-reactive with mouse LAG-3 or cross-reactive with parental cell line.

Blocking of interactions between LAG-3 and its ligands

The ability of the exemplary humanized anti-LAG-3 antibody to block the interactions between LAG-3 and both of its known ligand, MHC class II molecules, was examined. The results show that the anti-LAG-3 antibody blocked the interaction between LAG-3 and MHC class II molecules on Daudi cells with an IC_{50} of 5.5 nM, compared to a human IgG4 isotype control.

LAG-3 stimulation of cytokine release in vitro in the absence of T cell receptor engagement

Anti-LAG-3 antibody is not expected to stimulate detectable cytokine responses without specific stimulation by the T cell receptor. Anti-LAG-3 antibody was immobilized and highly crosslinked by air-drying on a tissue culture plate and tested for its ability to stimulate cytokine production using a method derived from Stebbings R., *et al.* (J Immunol. 2007 179(5):3325-3331). No IL-2 or IFN- γ production was induced by anti-LAG-3 antibody or control IgG in the absence of staphylococcal enterotoxin B (SEB) stimulation of whole blood.

Example 4: Patient Selection Based on PD-L1/CD8/IFN- γ status

For each of several types of cancer, samples from multiple patients were tested for PD-L1/CD8/IFN- γ status. Each sample was classified as: triple-negative for PD-L1/CD8/IFN- γ , single or double positive for these markers, or triple-positive for these markers. Figure 11 shows that in this experiment, within a population of patients, the following types of cancer are frequently triple-positive for PD-L1/CD8/IFN- γ : Lung cancer (squamous), lung cancer (adenocarcinoma), head and neck cancer, cervical cancer (squamous), stomach cancer, thyroid cancer, melanoma, and nasopharyngeal cancer. Patients having these types of cancer are good candidates for therapy with anti PD-1 antibodies in combination therapies as described herein, *e.g.*, anti-LAG-3 antibodies. The likelihood of successful treatment can be further boosted by determining which patients are triple-positive for PD-L1/CD8/IFN- γ , and treating the triple-positive patients with anti-PD-1 or anti-PD-L1 antibodies and combination therapies as described herein, *e.g.*, anti-LAG-3 antibodies.

Figure 12 shows that within a population of patients, the following types of cancer are rarely triple positive for PD-L1/CD8/IFN- γ : ER+ breast cancer and pancreatic cancer. Notably, even in cancers that are generally not positive for for PD-L1/CD8/IFN- γ , one can increase the likelihood of successful treatment by determining which patients are triple-positive for PD-L1/CD8/IFN- γ , and treating the triple-positive patients with anti-PD-1 or anti-PD-L1 antibodies and combination therapies as described herein, *e.g.*, anti-LAG-3 antibodies.

Figure 13 shows the proportion of breast cancer patients that are triple positive for PDL1/CD8/IFN- γ . Considering breast cancer in general, the proportion of triple-positives is somewhat low. However, when one focuses only on IM-TN breast cancer, it can be seen that a much larger percentage of patients is triple positive for PD-L1/CD8/IFN- γ . IM-TN breast cancer is particularly difficult to treat with conventional therapies. The discovery that IM-TN breast cancer is often triple-positive for PD-L1/CD8/IFN- γ opens up new avenues of therapy for this cancer with anti-PD-1 or anti-PD-L1 antibodies and combination therapies as described herein, *e.g.*, anti-LAG-3 antibodies.

Figure 14 shows the proportion of colon cancer patients that are triple positive for PD-L1/CD8/IFN- γ . Considering colon cancer in general, the proportion of triple-positive is somewhat low. However, when one focuses only on MSI-high (high microsatellite instability) breast cancer, it can be seen that a much larger percentage of patients is triple positive for PD-

L1/CD8/IFN- γ . MSI levels can be assayed using, *e.g.*, commercially available PCR-based methods.

Gastric cancer samples were tested for levels of PD-L1/CD8/IFN- γ (data not shown). It was found that in MSI-high or EBV+ gastric cancers, about 49% were positive for PD-L1, and a high proportion of the PD-L1-positive cells were triple positive for PD-L1/CD8/IFN- γ . It was also found that a proportion of PD-L1-positive cells and PD-L1/CD8/IFN- γ positive cells were also positive for PIK3CA. This finding suggests that these cancers may be treated with a PD-1 or an anti-PD-L1 antibody, *e.g.*, in combination with an anti-LAG-3 antibody, optionally in combination with a PIK3 therapeutic.

MSI-high CRC samples were tested for a combination of markers (data not shown). It was found that in MSI-high CRC samples, a high proportion of the PD-L1/CD8/IFN- γ samples are also positive for LAG-3, PD-1 (also called PDCD1), RNF43, and BRAF. This finding suggests that these cancers may be treated with a LAG-3 antibody, optionally in combination with a therapeutic that targets one or more of PD-1, PD-L1, PDCD1, RNF43, and BRAF.

Squamous cell lung cancers were tested for a combination of markers (data not shown). It was found that in squamous cell lung cancer samples, a high proportion of the PD-L1/CD8/IFN- γ samples are also positive for LAG-3. This finding suggests that these cancers may be treated with a LAG-3 antibody, optionally in combination with a therapeutic that targets PD-1 or PD-L1, *e.g.*, an anti-PD-1 antibody or an anti-PD-L1 antibody.

Papillary thyroid cancers were tested for a combination of markers including the BRAF V600E mutation (data not shown). It was found that a high proportion of thyroid cancer samples that are positive for PD-L1 are also positive for BRAF V600E. This finding suggests that these cancers may be treated with an anti-PD-1 antibody or an anti-PD-L1 antibody, *e.g.*, in combination with an anti-LAG-3 antibody, optionally in combination with a therapeutic that targets BRAF.

Example 5: Patient Selection Based on PD-L1 Status

To enable broad examination of cancer indications for immunomodulator (*e.g.*, LAG-3 alone or in combination with PD1/PD-L1) based therapies, PD-L1 expression was evaluated at both the protein and mRNA levels in human cancers including both lung and hepatic tumors.

PD-L1 protein expression was evaluated in a set of formalin-fixed paraffin-embedded

non-small cell lung (NSCLC) adenocarcinoma (ACA), NSCLC squamous cell carcinoma (SCC), and hepatocellular carcinoma (HCC) tumors by immunohistochemistry (IHC). PD-L1 expression was scored semi-quantitatively by a manual histo-score (H-score) methodology based on staining intensity and percentage of positive tumor cells. In our IHC analysis, PD-L1 positivity (PD-L1+) was defined as an H-score ≥ 20 . In parallel, PD-L1 mRNA expression data was examined from The Cancer Genome Atlas (TCGA) in these same indications (503 NSCLC ACA, 489 NSCLC SCC, and 191 HCC) and analyzed by comparing the expression in matched normal tissues from TCGA.

With RNAseq analysis, data was calculated as $\log_2(\text{RPKM}+0.1)$ after RSEM normalization, utilizing OmicSoft RNASeq pipelines across TCGA tumor indications. The expression of PD-L1 is elevated in NSCLC ACA and SCC, relative to that in HCC. By overlaying the distributions and comparing the expression levels across all indications in TCGA, we ranked overexpression profiles for PD-L1 and found the TCGA HCC cohort to have much reduced PD-L1 mRNA levels, with a median level of -0.8 compared to 1.3 for ACA and 1.5 for SCC, which amounts to more than a 2-fold change of median level expression. With RNAseq, our analysis defines 50% of NSCLC adenocarcinoma, 54% of NSCLC squamous cell carcinoma, and 6% of HCC as high expressers for PD-L1.

Tumor cell PD-L1 protein expression was measured in 45 lung adenocarcinoma (ACA) samples, 47 lung squamous cell carcinoma (SCC) samples, and 36 hepatocellular carcinoma (HCC) samples. 16/45 (35.6%) lung ACA, 21/47 (44.7%) lung SCC were PD-L1 positive. In contrast, PD-L1 positivity was seen in only 2/36 (5.6%) HCC samples.

In summary, with IHC and RNAseq analysis in large and independent human NSCLC and HCC sample sets, PD-L1 expression was found to be more enriched in NSCLC than in HCC. Within NSCLC, there are comparable findings between adenocarcinoma and squamous cell carcinomas. Importantly, amongst the large number of samples (128 for IHC and 1183 for RNAseq) in the 3 indications, very good concordance is observed between protein- and mRNA-based analyses. This finding thus establishes the basis for large scale mRNA-based data mining in TCGA for indications and patient segments that may be enriched for responses to immunomodulator (*e.g.*, PD-1/PD-L1, *e.g.*, in combination with LAG-3) based immune therapies.

INCORPORATION BY REFERENCE

All publications, patents, and Accession numbers mentioned herein are hereby incorporated by reference in their entirety as if each individual publication or patent was specifically and individually indicated to be incorporated by reference.

EQUIVALENTS

While specific embodiments of the subject invention have been discussed, the above specification is illustrative and not restrictive. Many variations of the invention will become apparent to those skilled in the art upon review of this specification and the claims below. The full scope of the invention should be determined by reference to the claims, along with their full scope of equivalents, and the specification, along with such variations.

What is claimed is:

1. A combination comprising an anti-LAG-3 antibody molecule and an agent that enhances tumor antigen presentation for use in treating a cancer in a subject,

wherein the anti-LAG-3 antibody molecule comprises:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15;

(b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15; or

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12, and

wherein the agent that enhances tumor antigen presentation is chosen from a STING agonist, a TLR agonist, an A2AR antagonist, or an oncolytic virus, or a combination thereof.

2. A method of treating a cancer in a subject, comprising administering to the subject a combination of an anti-LAG-3 antibody molecule and an agent that enhances tumor antigen presentation

thereby treating the cancer,

wherein the anti-LAG-3 antibody molecule, comprises:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15;

(b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15; or

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12, and

wherein the agent that enhances tumor antigen presentation is chosen from a STING agonist, a TLR agonist, an A2AR antagonist, or an oncolytic virus, or a combination thereof.

3. The combination for use of claim 1, or the method of claim 1, wherein the anti-LAG-3 antibody molecule comprises:

(a) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 32;

(b) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 36;

(c) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 40;

(d) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 44;

(e) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 48;

(f) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 52;

(g) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 56;

(h) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60;

(i) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 36;

(j) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 40;

(k) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 56;

(l) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60.

(m) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 68 or SEQ ID NO: 108; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 36;

(n) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 72 or SEQ ID NO: 8; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 40;

(o) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 72 or SEQ ID NO: 8; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60.

(p) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 76; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60;

(q) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 80; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 84;

(r) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 88;

(s) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 100; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 92; or

(t) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 64 or SEQ ID NO: 104; and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 96.

4. The combination for use of claim 1 or 3, or the method of claim 2 or 3, wherein the cancer is chosen from a lung cancer, a melanoma, a renal cancer, a liver cancer, a prostate cancer, a breast cancer, a colorectal cancer, a gastric cancer, a pancreatic cancer, a thyroid cancer, a head and neck cancer, an endometrial cancer, a brain cancer, a nasopharyngeal cancer, a hematological cancer, or a metastatic lesion of the cancer.

5. The combination for use of claim 4, or the method of claim 4, wherein the lung cancer is chosen from a non-small cell lung cancer (NSCLC), a lung adenocarcinoma, a

squamous cell lung carcinoma, or a small cell lung cancer, optionally, wherein the NSCLC comprises a KRAS mutation.

6. The combination for use of claim 4, or the method of claim 4, wherein the melanoma is chosen from an advanced melanoma, an unresectable melanoma, a metastatic melanoma, a melanoma with a BRAF mutation, a melanoma with an NRAS mutation, a cutaneous melanoma, or an intraocular melanoma.

7. The combination for use of claim 4, or the method of claim 4, wherein the renal cancer is chosen from a renal cell carcinoma (RCC), a metastatic renal cell carcinoma, or a clear cell renal cell carcinoma (CCRCC).

8. The combination for use of claim 4, or the method of claim 4, wherein the hematologic cancer is chosen from a lymphoma, a myeloma, or a leukemia, optionally, wherein the lymphoma is a non-Hodgkin lymphoma.

9. The combination for use of claim 4, or the method of claim 4, wherein the brain cancer is a glioblastoma.

10. The combination for use of claim 4, or the method of claim 4, wherein the breast cancer chosen from a triple negative breast cancer or an ER+ breast cancer.

11. The combination for use of claim 4, or the method of claim 4, wherein the liver cancer is a hepatocellular carcinoma.

12. The combination for use of any of claims 1 or 3-11, or the method of any of claims 2-11, wherein the cancer is a MSI-high (high microsatellite instability) cancer.

13. The combination for use of any of claims 1 or 3-12, or the method of any of claims 2-12, wherein the combination comprises an anti-LAG-3 antibody molecule and a STING agonist.

14. The combination for use of claim 13, or the method of claim 13, wherein the STING agonist comprises a cyclic dinucleotide, optionally, wherein the cyclic dinucleotide is a modified cyclic dinucleotide, *e.g.*, comprising a modified nucleobase, a modified ribose, or a modified phosphate linkage.

15. The combination for use of claim 13 or 14, or the method of claim 13 or 14, wherein the STING agonist is chosen from Rp,Rp dithio 2',3' c-di-AMP or a cyclic dinucleotide analog thereof; c-[G(2',5')pG(3',5')p] or a dithio ribose O-substituted derivative thereof; c-[A(2',5')pA(3',5')p] or a dithio ribose O-substituted derivative thereof; c-[G(2',5')pA(3',5')p] or a dithio ribose O-substituted derivative thereof; or 2'-O-propargyl-cyclic-[A(2',5')pA(3',5')p] (2'-O-propargyl- ML-CDA).

16. The combination for use of any of claims 13-15, or the method of any of claims 13-15, wherein the combination is used to treat a cancer chosen from a melanoma, a head and neck cancer, or a lung cancer, optionally, wherein the lung cancer is a non-small cell lung cancer (NSCLC).

17. The combination for use of any of claims 1 or 3-12, or the method of any of claims 2-12, wherein the combination comprises an anti-LAG-3 antibody molecule and a TLR agonist.

18. The combination for use of claim 17, or the method of claim 17, wherein the TLR agonist is chosen from one or more of a TLR-1 agonist, a TLR-2 agonist, a TLR-3 agonist, a TLR-4 agonist, a TLR-5 agonist, a TLR-6 agonist, a TLR-7 agonist, a TLR-8 agonist, a TLR-9 agonist, a TLR-10 agonist, a TLR-1/2 agonist, a TLR-2/6 agonist, or a TLR-7/8 agonist, optionally, wherein the TLR agonist is a TLR7 agonist.

19. The combination for use of claim 17 or 18, or the method of claim 17 or 18, wherein the TLR agonist is chosen from imiquimod or 3-(2-Methylpropyl)-3,5,8-triazatricyclo[7.4.0.0^{2,6}]trideca-1(9),2(6),4,7,10,12-hexaen-7-amine, 852A, Bacille Calmette-

Guérin (BCG), EMD 120108, IMO-2055, Pam3Cys, CFA, MALP2, Pam2Cys, FSL-1, Hib-OMPC), polyribosinic:polyribocytidic acid (Poly I:C), polyadenosine-polyuridylic acid (poly AU), polyinosinic-polycytidylic acid stabilized with poly-L-lysine and carboxymethylcellulose, monophosphoryl lipid A (MPL), LPS, sialyl-Tn (STn), bacterial flagellin, resiquimod, loxoribine, or unmethylated CpG dinucleotide (CpG-ODN).

20. The combination for use of any of claims 17-19, or the method of any of claims 17-19, wherein the combination is used to treat a cancer chosen from a melanoma, a lymphoma, or a colon cancer.

21. The combination for use of any of claims 1 or 3-12, or the method of any of claims 2-12, wherein the combination comprises an anti-LAG-3 antibody molecule and an A2aR antagonist.

22. The combination for use of claim 21, or the method of claim 21, wherein the A2aR antagonist is an inhibitor of A2aR or an A2aR pathway antagonist, optionally, wherein the A2aR pathway antagonist is a CD73 inhibitor, e.g., an anti-CD73 antibody.

23. The combination for use of claim 21 or 22, or the method of claim 21 or 22, wherein the A2aR antagonist is chosen from istradefylline, tozadenant, preladenant, vipadenan, PBF-509, ATL-444, MSX-3, SCH-58261, SCH-412,348, SCH-442,416, VER-6623, VER-6947, VER-7835, CGS-15943, ZM-241,385, or MEDI9447.

24. The combination for use of any of claims 21-23, or the method of any of claims 21-23, wherein the combination is used to treat a lung cancer, optionally, wherein the lung cancer is a non-small cell lung cancer (NSCLC).

25. The combination for use of any of claims 1 or 3-12, or the method of any of claims 2-12, wherein the combination comprises an anti-LAG-3 antibody molecule and an oncolytic virus.

26. The combination for use of claim 25, or the method of claim 25, wherein the oncolytic viruses is chosen from an oncolytic adenovirus, an oncolytic herpes simplex virus, an oncolytic retrovirus, an oncolytic parvovirus, an oncolytic vaccinia virus, an oncolytic Sindbis virus, an oncolytic influenza virus, or an oncolytic RNA virus, optionally, wherein the oncolytic RNA virus is an oncolytic reovirus, an oncolytic Newcastle disease virus (NDV), an oncolytic measles virus, or an oncolytic vesicular stomatitis virus (VSV), optionally, wherein the oncolytic adenovirus is a conditionally replicative adenovirus (CRAd).

27. The combination for use of claim 25 or 26, or the method of claim 25 or 26, wherein the oncolytic virus comprises a nucleic acid sequence encoding an inhibitor of an immune or inflammatory response, a pro-apoptotic protein, a cytokine, an immunoglobulin, a tumor associated antigen, or a bispecific adapter protein.

28. The combination for use of any of claims 25-27, or the method of any of claims 25-27, wherein the oncolytic virus is chosen from ColoAd1, ONCOS-102, VCN-01, ICOVIR-5, Celyvir, CG0070, or DNX-2401.

29. The combination for use of any of claims 25-28, or the method of any of claims 25-28, wherein the combination is used to treat a brain cancer, optionally, wherein the brain cancer is a glioblastoma.

30. The combination for use of any of claims 1 or 3-29, or the method of any of claims 2-29, wherein the combination further comprises an agent that enhances tumor antigen presentation chosen from one or more of: a TIM-3 modulator, a vascular endothelial growth factor receptor (VEGFR) inhibitor, a c-Met inhibitor, a TGFb inhibitor, an IDO/TDO inhibitor, a vaccine, or a bi- or tri-specific cell engager.

31. The combination for use of claim 30, or the method of claim 30, wherein the combination comprises a TIM-3 modulator, e.g., to treat a cancer chosen from a lung cancer, a melanoma, or a renal cancer, optionally, wherein the lung cancer is a non-small cell lung cancer, or wherein the renal cancer is a renal cell carcinoma.

32. The combination for use of claim 30, or the method of claim 30, wherein the combination comprises a c-MET inhibitor, e.g., to treat a liver cancer, optionally, wherein the liver cancer is a hepatocellular carcinoma.

33. The combination for use of any of claims 1 or 3-32, or the method of any of claims 2-32, wherein the combination further comprises an agent that decreases tumor immunosuppression chosen from one or more of: a GITR agonist, an inhibitor of an immune checkpoint molecule chosen from one or more of PD-L1, LAG-3, TIM-3 or CTLA-4, a CSF-1/1R inhibitor, an IL-17 inhibitor, an IL-1 β inhibitor, a CXCR2 inhibitor, an inhibitor of PI3K γ or PI3K δ , a BAFF-R inhibitor, a MALT-1/BTK inhibitor, a JAK inhibitor, a CRTH2 inhibitor, a VEGFR inhibitor, an IL-15 or a variant thereof, an IDO/TDO inhibitor, an A2aR antagonist, a TGF β inhibitor, or a PFKFB3 inhibitor, wherein the inhibitor of LAG-3 is other than the anti-LAG-3 antibody molecule of Table 1.

34. The combination for use of claim 33, or the method of claim 33, wherein the combination comprises a GITR agonist, e.g., to treat a cancer chosen from a lung cancer, a head and neck cancer, or a FoxP3-expressing cancer, optionally, wherein the lung cancer is a non-small cell lung cancer.

35. The combination for use of claim 33, or the method of claim 33, wherein the combination comprises an inhibitor of PD-L1, e.g., to treat a cancer chosen from a thyroid cancer, a lung cancer, a breast cancer, an endometrial cancer, or a lymphoma.

36. The combination for use of claim 33, or the method of claim 33, wherein the combination comprises an inhibitor of PD-1, e.g., to treat a cancer chosen from a lung cancer, a melanoma, a renal cancer, or a hematologic cancer, optionally, wherein the lung cancer is a non-small cell lung cancer, or the renal cancer is a renal cell carcinoma.

37. The combination for use of claim 33, or the method of claim 33, wherein the combination comprises a CSF-1/1R inhibitor, e.g., to treat a cancer chosen from a brain cancer, a

pancreatic cancer, a breast cancer, an endometrial cancer, or a melanoma, optionally, wherein the brain cancer is a glioblastoma, or the breast cancer is a triple-negative breast cancer.

38. The combination for use of claim 33, or the method of claim 33, wherein the combination comprises an IL-17 inhibitor, e.g., to treat a cancer chosen from a breast cancer, a lung cancer, or colon cancer, optionally, wherein the breast cancer is a triple-negative breast cancer or the lung cancer is a non-small cell lung cancer.

39. The combination for use of claim 33, or the method of claim 33, wherein the combination comprises an IL-1 β inhibitor, e.g., to treat a cancer chosen from a breast cancer, a lung cancer, or colon cancer, optionally, wherein the breast cancer is a triple-negative breast cancer or the lung cancer is a non-small cell lung cancer.

40. The combination for use of claim 33, or the method of claim 33, wherein the combination comprises an IL-15 or a variant thereof, e.g., to treat a solid tumor.

41. The combination for use of claim 33, or the method of claim 33, wherein the combination comprises a TGF β inhibitor.

42. The combination for use of any of claims 1 or 3-41, or the method of any of claims 2-41, wherein the combination further comprises an agent that enhances an effector cell response chosen from one or more of: a GITR agonist, a PD-1 inhibitor, a PD-L1 inhibitor, an inhibitor of IAP (Inhibitor of Apoptosis Protein), an inhibitor of EGFR (Epidermal Growth Factor Receptor), an inhibitor of target of rapamycin (mTOR), IL-15 or a variant thereof, a CTLA-4 inhibitor, a bispecific antibody molecule that binds to CD3 and a tumor antigen, a CD40 agonist, an OX40 agonist, or a CD27 agonist.

43. The combination for use of claim 42, or the method of claim 42, wherein the combination comprises an inhibitor of IAP, e.g., to treat a cancer chosen from a breast cancer, a lung cancer, or colon cancer, optionally, wherein the breast cancer is a triple-negative breast cancer or the lung cancer is a non-small cell lung cancer.

44. The combination for use of claim 42, or the method of claim 42, wherein the combination comprises an inhibitor of mTOR, e.g., to treat a cancer chosen from a breast cancer, a lung cancer, or colon cancer, optionally, wherein the breast cancer is a triple-negative breast cancer or the lung cancer is a non-small cell lung cancer.

45. The combination for use of claim 42, or the method of claim 42, wherein the combination comprises an inhibitor of EGFR, e.g., to treat a cancer chosen from a breast cancer, a lung cancer, or colon cancer, optionally, wherein the breast cancer is a triple-negative breast cancer or the lung cancer is a non-small cell lung cancer.

46. A composition (e.g., one or more compositions or dosage forms), comprising an anti-LAG-3 antibody molecule and an agent that enhances tumor antigen presentation, wherein the anti-LAG-3 antibody molecule, comprises:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15;

(b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286, a VHCDR2 amino acid sequence of SEQ ID NO: 5, and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 13, a VLCDR2 amino acid sequence of SEQ ID NO: 14, and a VLCDR3 amino acid sequence of SEQ ID NO: 15; or

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 286; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 10, a VLCDR2 amino acid sequence of SEQ ID NO: 11, and a VLCDR3 amino acid sequence of SEQ ID NO: 12, and

wherein the agent that enhances tumor antigen presentation is chosen from a STING agonist, a TLR agonist, an A2AR antagonist, or an oncolytic virus, or a combination thereof,

28 JUL 2016

Light chain (murine κ)

FWL1	CDRL1	FWL2	CDRL2	FWL3
DIQMTQTSS LSASLGDRVT ISCSSQDIS <u>NVLNWIYQQK</u> DGTVKVLIYY <u>TSILHLGVPS</u> RFSGSGSGTD				
YSLTISNLEL EDIATYYCQQ <u>YNLPWTFGG</u> GTKLEIK	CDRL3	FWL4		

Heavy Chain (murine IgG1)

FWH1	CDRH1	FWH2	CDRH2
QIQLVQSGPE LKKPGETVKI SCKASGFTLT <u>NYGMNWRQ</u> T PKGGLKWMGW <u>INTDTGEPTY</u> ADDFKGRFAF			
FWH3	CDRH3	FWH4	
SLETSASTAS LQINNLKNAD TATYFCARNP <u>PYYGTTNAE</u> <u>AMDYWGQ</u> GTA VIVSS			

FIGURE 1

Light chain

GL DIQMTQTSS LSASLGDRVT ISCSASOGIS NYLNWYQQKP DGTVKLLIYY TSSLHSGVPS
 Mu mAb -----S--D-----V-----T--L-----

GL RFSGSGGTD YSLTISNLEP EDIATYYCQQ YSKLP
 Mu mAb -----L-----YN--MIFGG GTKLEIK

Heavy chain

GL QIQLVQSGPE LKKPGETVKI SCKASGYTFT NYGMNWVKQA PGKGLKWMGW INFYTGEPTY
 Mu mAb -----F-L-----R-T-----D-----

GL ADDFKGRFAF SLETSASTAY LQINNPKNED TATYFCAR
 Mu mAb -----S-----A-----NP PYYGTTNNAE AMDYWCQGTA

GL
 Mu mAb VTVSS

FIGURE 2

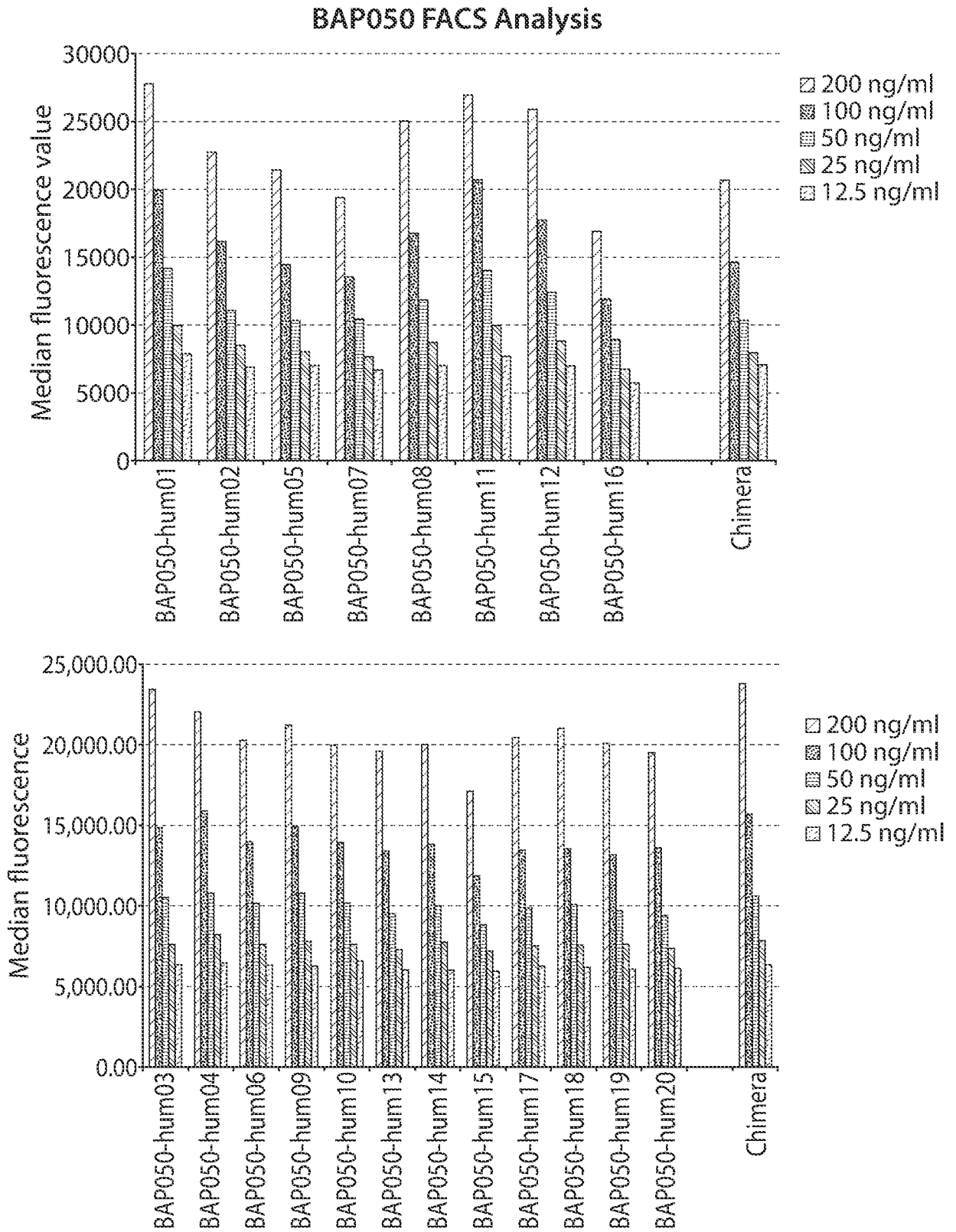


FIGURE 3

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Clone No.	$\mu\text{g/mL}$	Sequence					
		HC			LC		
		FW1	FW2	FW3	FW1	FW2	FW3
chimera	31.7	6 unique HC			12 unique LC		
1	35.4	a	a	a	a	a	a
2	25.2	a	a	a	a	a	b
3	3.2	a	a	a	b	b	a
4	26	a	a	a	a	c	c
5	16.9	a	a	a	c	a	a
6	9.1	a	a	a	d	b	d
7	35.8	a	a	a	a	d	d
8	24.7	a	a	a	e	b	e
9	19.9	b	b	a	a	a	b
10	7.7	b	b	a	b	b	a
11	34.9	b	b	a	a	d	d
12	17.9	b	b	a	e	b	e
13	24.9	b	a	a	a	a	b
14	7.5	a	c	a	b	b	a
15	21.9	a	c	a	e	b	e
16	17.7	c	d	b	e	b	e
17	21.2	d	a	c	a	a	f
18	8.1	a	a	a	f	b	e
19	7.5	a	a	a	e	b	a
20	3.2	b	b	a	d	b	g

FIGURE 4

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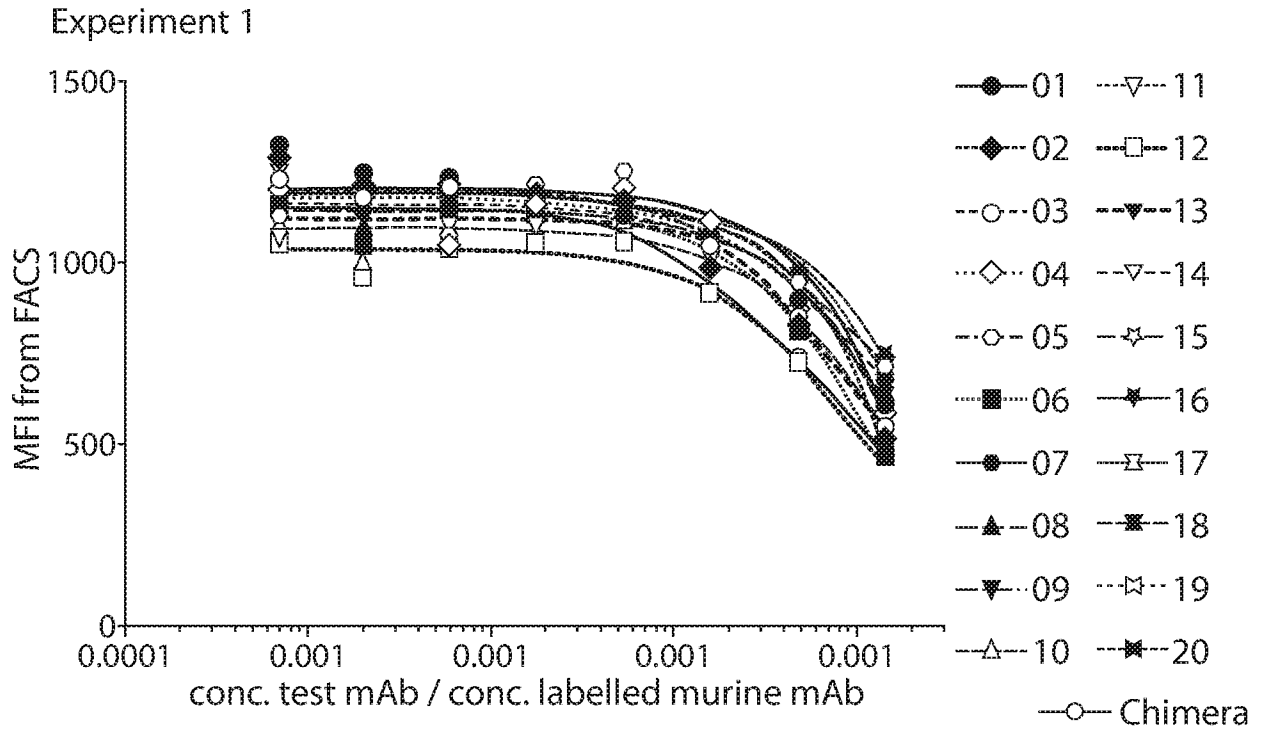


FIGURE 5A

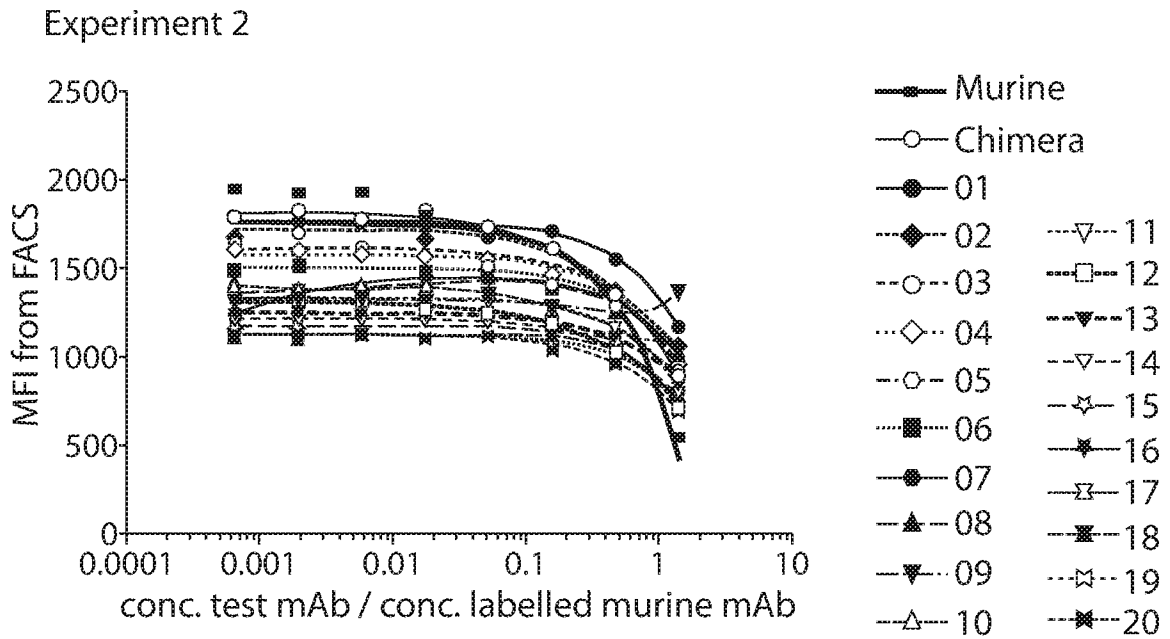


FIGURE 5B

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Clone No.	Conc. $\mu\text{g/mL}$	Sequence						Ranking		Structure
		HC			LC			Binding data	Compet. data	
		FW1	FW2	FW3	FW1	FW2	FW3			
		6 unique HC			12 unique LC				*	
1	35.4	a	a	a	a	a	a	1	2	D
2	25.2	a	a	a	a	a	b	5	1	B
3	3.2	a	a	a	b	b	a	7	1	E
4	26	a	a	a	a	c	c	8	2	E
5	16.9	a	a	a	c	a	a	6		E
6	9.1	a	a	a	d	b	d	9	1	E
7	35.8	a	a	a	a	d	d	8		C
8	24.7	a	a	a	e	b	e	4		E
9	19.9	b	b	a	a	a	b	8	2	B
10	7.7	b	b	a	b	b	a	9	2	E
11	34.9	b	b	a	a	d	d	2	2	C
12	17.9	b	b	a	e	b	e	3	2	E
13	24.9	b	a	a	a	a	b	9	3	A
14	7.5	a	c	a	b	b	a	9		F
15	21.9	a	c	a	e	b	e	20	20	F
16	17.7	c	d	b	e	b	e	20	20	D
17	21.2	d	a	c	a	a	f	9		E
18	8.1	a	a	a	f	b	e	8		C
19	7.5	a	a	a	e	b	a	9		D
20	3.2	b	b	a	d	b	g	9	3	C

*empty boxes means worse than 3.

FIGURE 6

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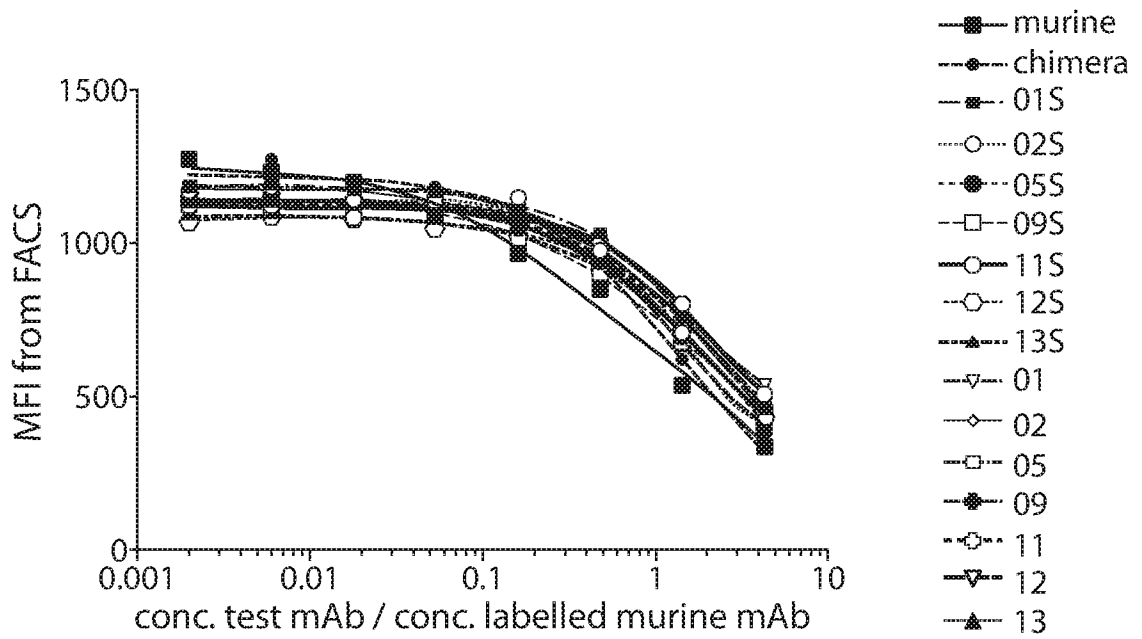


FIGURE 7

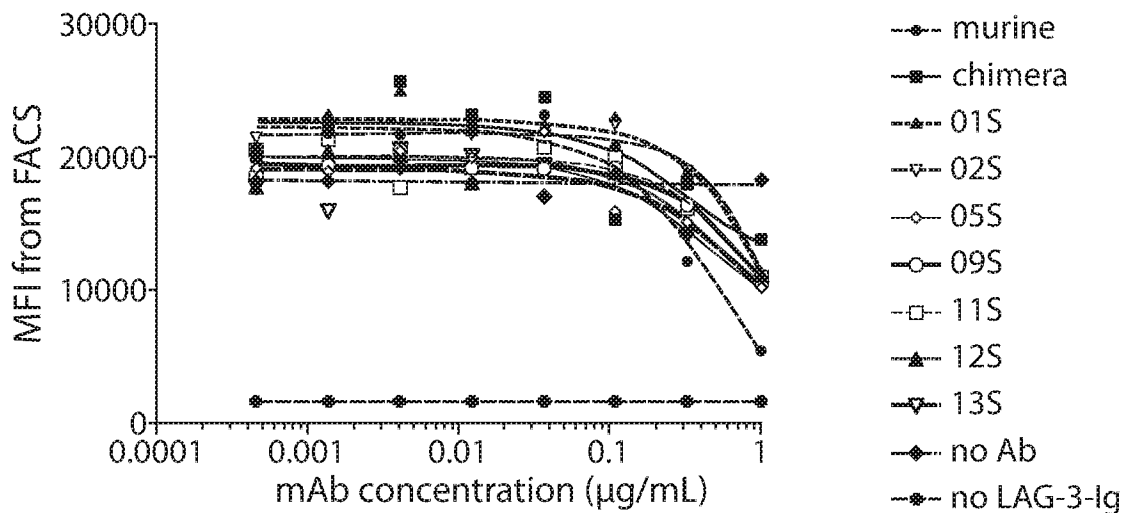


FIGURE 8

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		10	20	30	40	50	60
						
BAP050-chi-HC	QIQLVQSGPELKKPGETVKISCKASGFTLTNYGMNWVRQTPGKGLKWMGWINTDTGEPTY						
BAP050-hum01-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
BAP050-hum02-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
BAP050-hum03-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
BAP050-hum04-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
BAP050-hum05-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
BAP050-hum06-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
BAP050-hum07-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
BAP050-hum08-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
BAP050-hum18-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
BAP050-hum19-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
BAP050-hum09-HC	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMNWVRQARGQRLEWIGWINTDTGEPTY						
BAP050-hum10-HC	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMNWVRQARGQRLEWIGWINTDTGEPTY						
BAP050-hum11-HC	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMNWVRQARGQRLEWIGWINTDTGEPTY						
BAP050-hum12-HC	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMNWVRQARGQRLEWIGWINTDTGEPTY						
BAP050-hum20-HC	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMNWVRQARGQRLEWIGWINTDTGEPTY						
BAP050-hum13-HC	QVQLVQSGAEVKKPGASVKVSKASGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
BAP050-hum14-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWIRQSPSRGLEWLGWINTDTGEPTY						
BAP050-hum15-HC	EVQLVQSGAEVKKPGATVKISCKVSGFTLTNYGMNWIRQSPSRGLEWLGWINTDTGEPTY						
BAP050-hum16-HC	EVQLVQSGAEVKKPGEISLRISCKGSGFTLTNYGMNWVRQATGQGLEWWMGWINTDTGEPTY						
BAP050-hum17-HC	QVQLVQSGSELKKPGASVKVSKASGFTLTNYGMNWVRQAPGQGLEWWMGWINTDTGEPTY						
		70	80	90	100	110	120
						
BAP050-chi-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum01-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum02-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum03-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum04-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum05-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum06-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum07-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum08-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum18-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum19-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum09-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum10-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum11-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum12-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum20-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum13-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum14-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum15-HC	ADDFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum16-HC	ADDFKGRVTISADKSI STAYLQWSSSLKASDTAMYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						
BAP050-hum17-HC	ADDFKGRFVFSLDTSVSTAYLQISTLKAEDTAVYYCARNPPYYYGTNNAEAMDYWGQGTIVTVSS						

FIGURE 9A

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		10	20	30	40	50	60
	
BAP050-chi-HC	QIQLVQSGPELKKPGETVKISCKASGFTLTNYGMNWVRQTPGKGLKWMGWINTDTGPTY						
BAP050-hum01-HC	EV.....A.V....A.....V.....A.Q..E.....						
BAP050-hum02-HC	EV.....A.V....A.....V.....A.Q..E.....						
BAP050-hum03-HC	EV.....A.V....A.....V.....A.Q..E.....						
BAP050-hum04-HC	EV.....A.V....A.....V.....A.Q..E.....						
BAP050-hum05-HC	EV.....A.V....A.....V.....A.Q..E.....						
BAP050-hum06-HC	EV.....A.V....A.....V.....A.Q..E.....						
BAP050-hum07-HC	EV.....A.V....A.....V.....A.Q..E.....						
BAP050-hum08-HC	EV.....A.V....A.....V.....A.Q..E.....						
BAP050-hum18-HC	EV.....A.V....A.....V.....A.Q..E.....						
BAP050-hum19-HC	EV.....A.V....A.....V.....A.Q..E.....						
BAP050-hum09-HC	.V.....A.V....AS.V.....AR.QR.E.I.....						
BAP050-hum10-HC	.V.....A.V....AS.V.....AR.QR.E.I.....						
BAP050-hum11-HC	.V.....A.V....AS.V.....AR.QR.E.I.....						
BAP050-hum12-HC	.V.....A.V....AS.V.....AR.QR.E.I.....						
BAP050-hum20-HC	.V.....A.V....AS.V.....AR.QR.E.I.....						
BAP050-hum13-HC	.V.....A.V....AS.V.....A.Q..E.....						
BAP050-hum14-HC	EV.....A.V....A.....V.....I..S.SR..E.L.....						
BAP050-hum15-HC	EV.....A.V....A.....V.....I..S.SR..E.L.....						
BAP050-hum16-HC	EV.....A.V....SLR...G.....AT.Q..E.....						
BAP050-hum17-HC	.V.....S.....AS.V.....A.Q..E.....						

		70	80	90	100	110	120
	
BAP050-chi-HC	ADDFKGRFAFSLETSASTASLQINNLLKNADTATYFCARNPPYYGTNNAEAMDYWGQGTTVTVSS						
BAP050-hum01-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum02-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum03-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum04-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum05-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum06-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum07-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum08-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum18-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum19-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum09-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum10-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum11-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum12-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum20-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum13-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum14-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum15-HCV..D..V..Y...CS..AE...V.Y.....						
BAP050-hum16-HCVTI.ADK.I..Y..WSS..AS..M.Y.....						
BAP050-hum17-HCV..D..V..Y...ST..AE.....						

FIGURE 9B

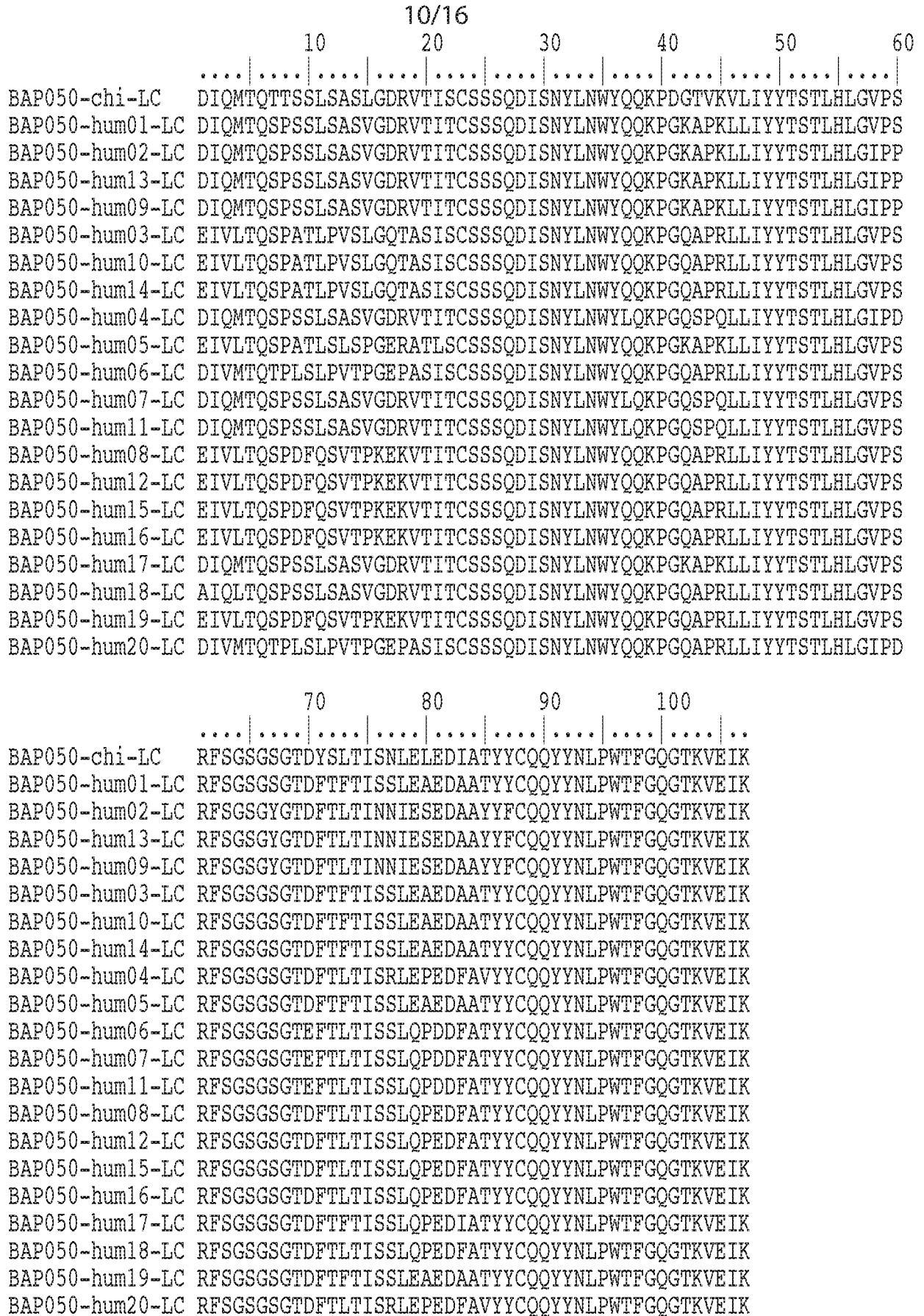


FIGURE 10A

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	10	20	30	40	50	60
BAP050-chi-LC	DIQMTQTTSSLSASLGDRVTISCS	SSSQDISNYLNWYQOKPDGTVK	VLIYYTSTLHLGVPS			
BAP050-hum01-LCSP.....V.....T.....			GKAP.L.....		
BAP050-hum02-LCSP.....V.....T.....			GKAP.L.....I.P		
BAP050-hum13-LCSP.....V.....T.....			GKAP.L.....I.P		
BAP050-hum09-LCSP.....V.....T.....			GKAP.L.....I.P		
BAP050-hum03-LC	E.VL..SPAT.PV...QTAS.....			GQAPRL.....		
BAP050-hum10-LC	E.VL..SPAT.PV...QTAS.....			GQAPRL.....		
BAP050-hum14-LC	E.VL..SPAT.PV...QTAS.....			GQAPRL.....		
BAP050-hum04-LCSP.....V.....T.....		L..GQSPQL.....			I.D
BAP050-hum05-LC	E.VL..SPAT..L.P.E.A.L.....			GKAP.L.....		
BAP050-hum06-LC	..V...PL..PVTP.EPAS.....			GQAPRL.....		
BAP050-hum07-LCSP.....V.....T.....		L..GQSPQL.....			
BAP050-hum11-LCSP.....V.....T.....		L..GQSPQL.....			
BAP050-hum08-LC	E.VL..SPDFQ.VTPKEK...T.....			GQAPRL.....		
BAP050-hum12-LC	E.VL..SPDFQ.VTPKEK...T.....			GQAPRL.....		
BAP050-hum15-LC	E.VL..SPDFQ.VTPKEK...T.....			GQAPRL.....		
BAP050-hum16-LC	E.VL..SPDFQ.VTPKEK...T.....			GQAPRL.....		
BAP050-hum17-LCSP.....V.....T.....			GKAP.L.....		
BAP050-hum18-LC	A..L..SP.....V.....T.....			GQAPRL.....		
BAP050-hum19-LC	E.VL..SPDFQ.VTPKEK...T.....			GQAPRL.....		
BAP050-hum20-LC	..V...PL..PVTP.EPAS.....			GQAPRL.....I.D		

	70	80	90	100
BAP050-chi-LC	RFSGSGSGTDYSLTISNLELEDIATYYCQOYYNLPWTFGQGTKEIK			
BAP050-hum01-LCFTF...S..A..A.....			
BAP050-hum02-LCY...FT...N.I.S..A.Y.F.....			
BAP050-hum13-LCY...FT...N.I.S..A.Y.F.....			
BAP050-hum09-LCY...FT...N.I.S..A.Y.F.....			
BAP050-hum03-LCFTF...S..A..A.....			
BAP050-hum10-LCFTF...S..A..A.....			
BAP050-hum14-LCFTF...S..A..A.....			
BAP050-hum04-LCFT...R..P..F.V.....			
BAP050-hum05-LCFTF...S..A..A.....			
BAP050-hum06-LCEFT...S.QPD.F.....			
BAP050-hum07-LCEFT...S.QPD.F.....			
BAP050-hum11-LCEFT...S.QPD.F.....			
BAP050-hum08-LCFT...S.QP..F.....			
BAP050-hum12-LCFT...S.QP..F.....			
BAP050-hum15-LCFT...S.QP..F.....			
BAP050-hum16-LCFT...S.QP..F.....			
BAP050-hum17-LCFTF...S.QP.....			
BAP050-hum18-LCFT...S.QP..F.....			
BAP050-hum19-LCFTF...S..A..A.....			
BAP050-hum20-LCFT...R..P..F.V.....			

FIGURE 10B

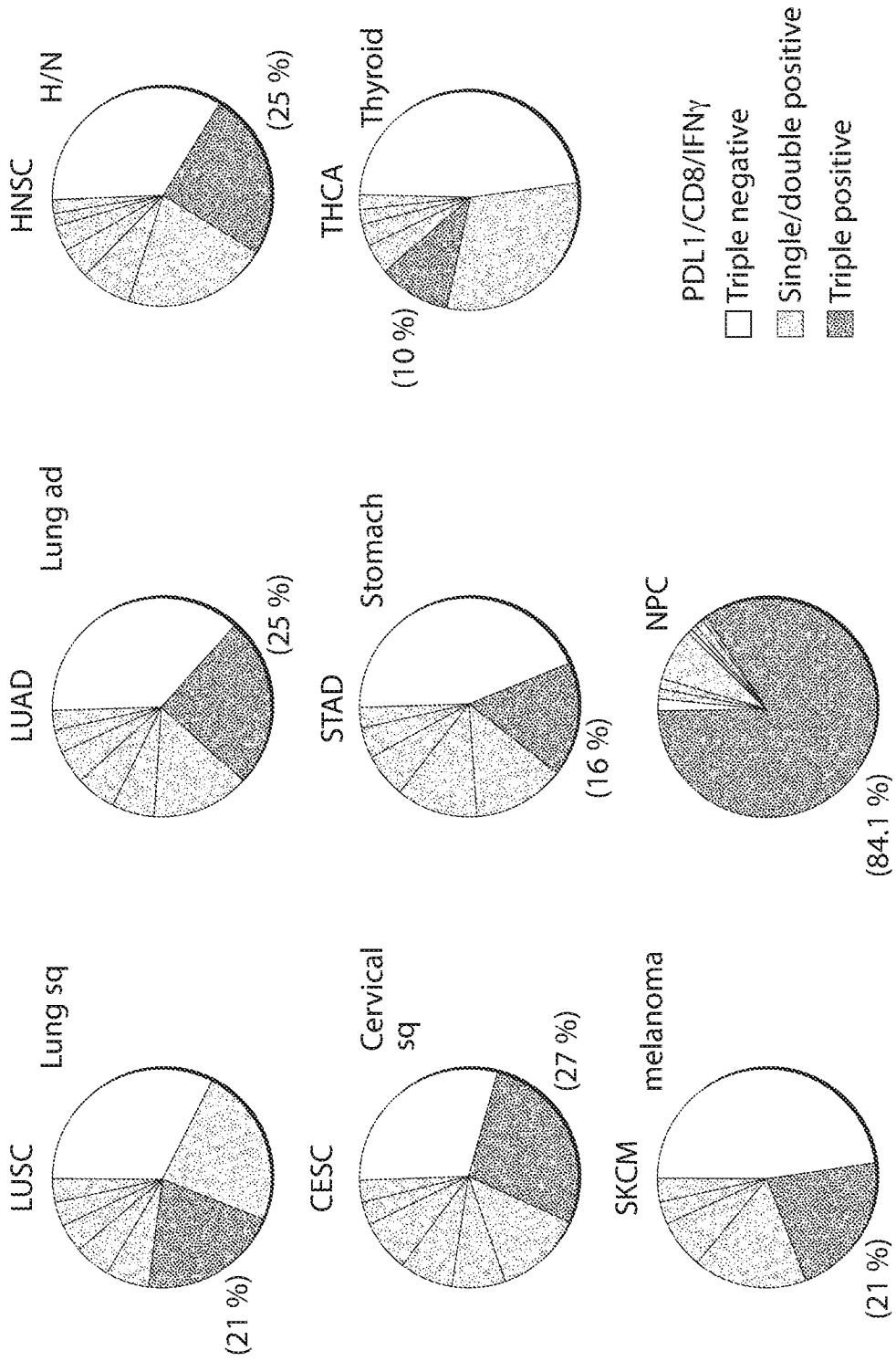


FIGURE 11

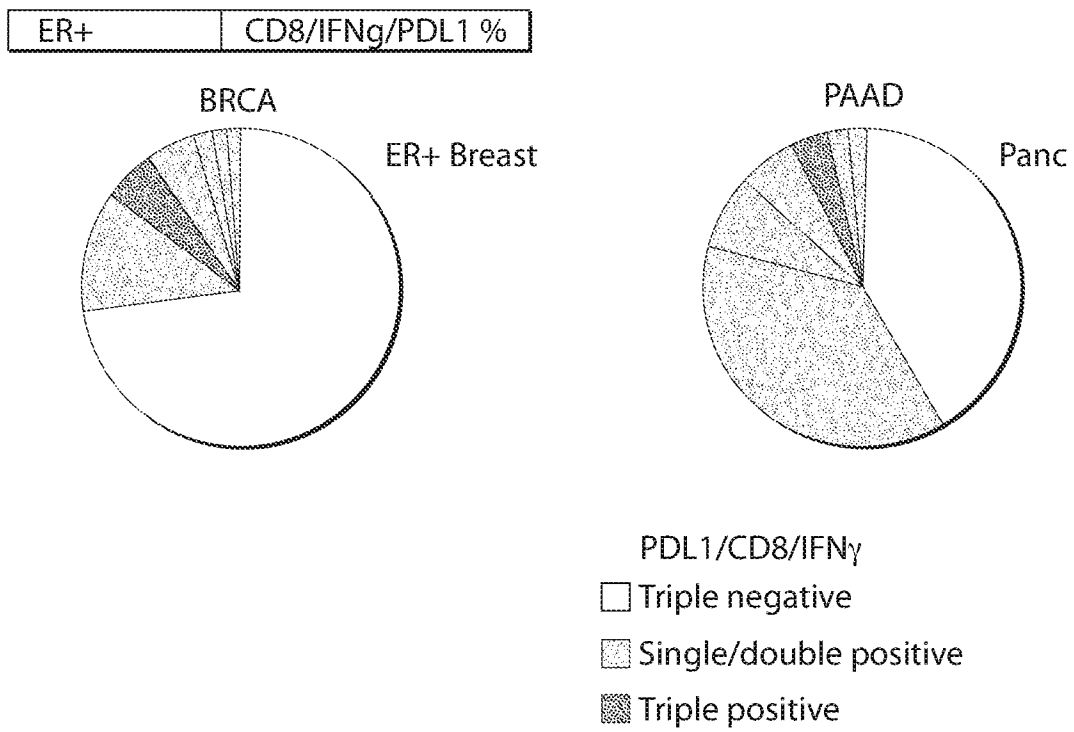


FIGURE 12

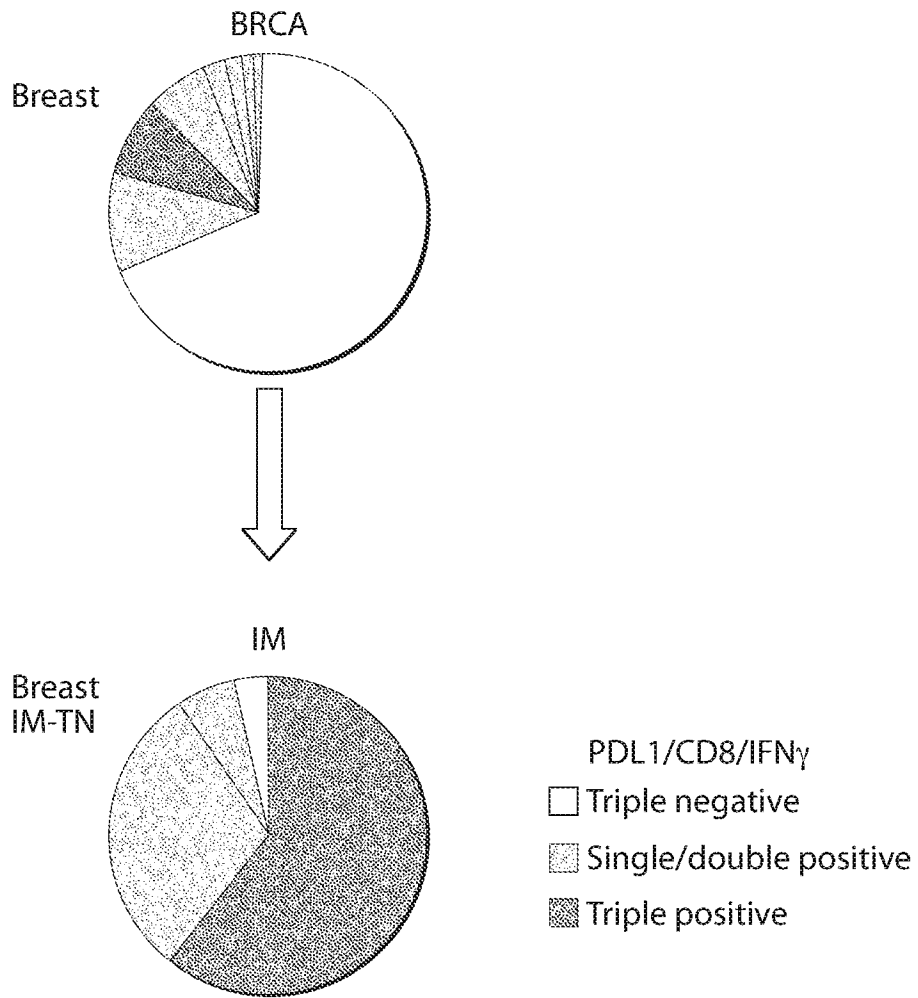


FIGURE 13

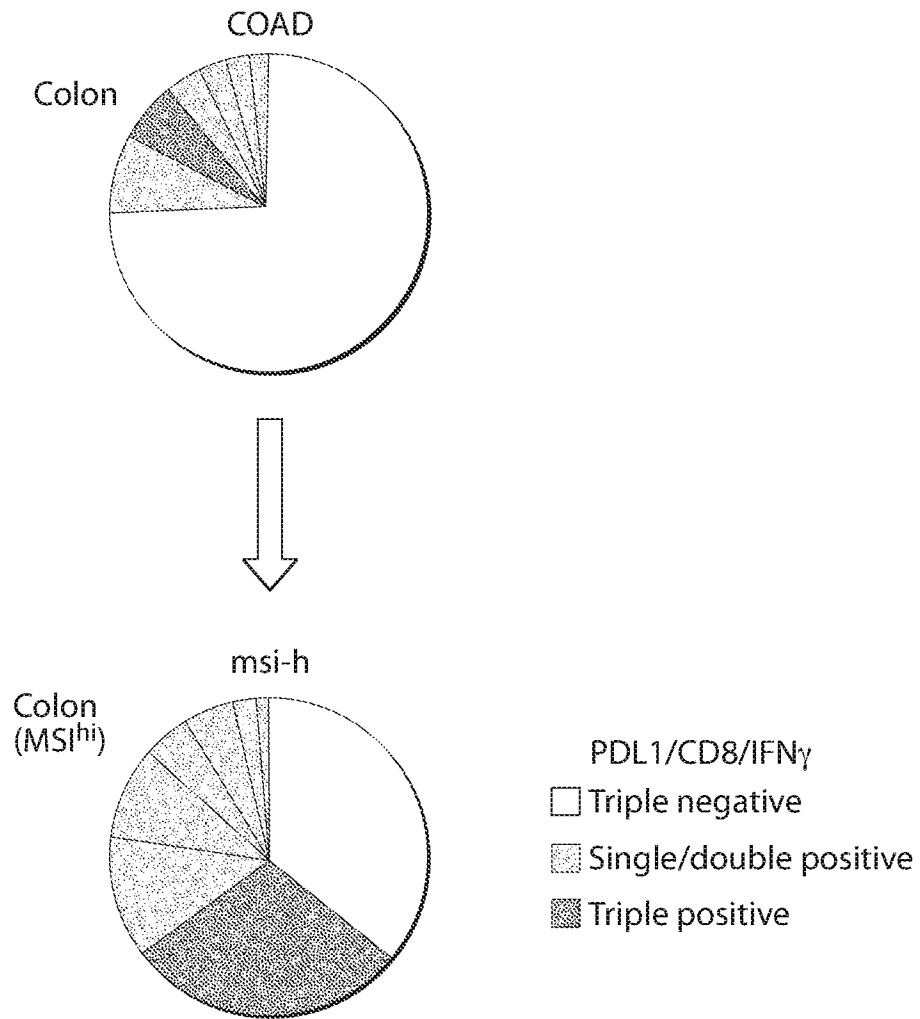


FIGURE 14

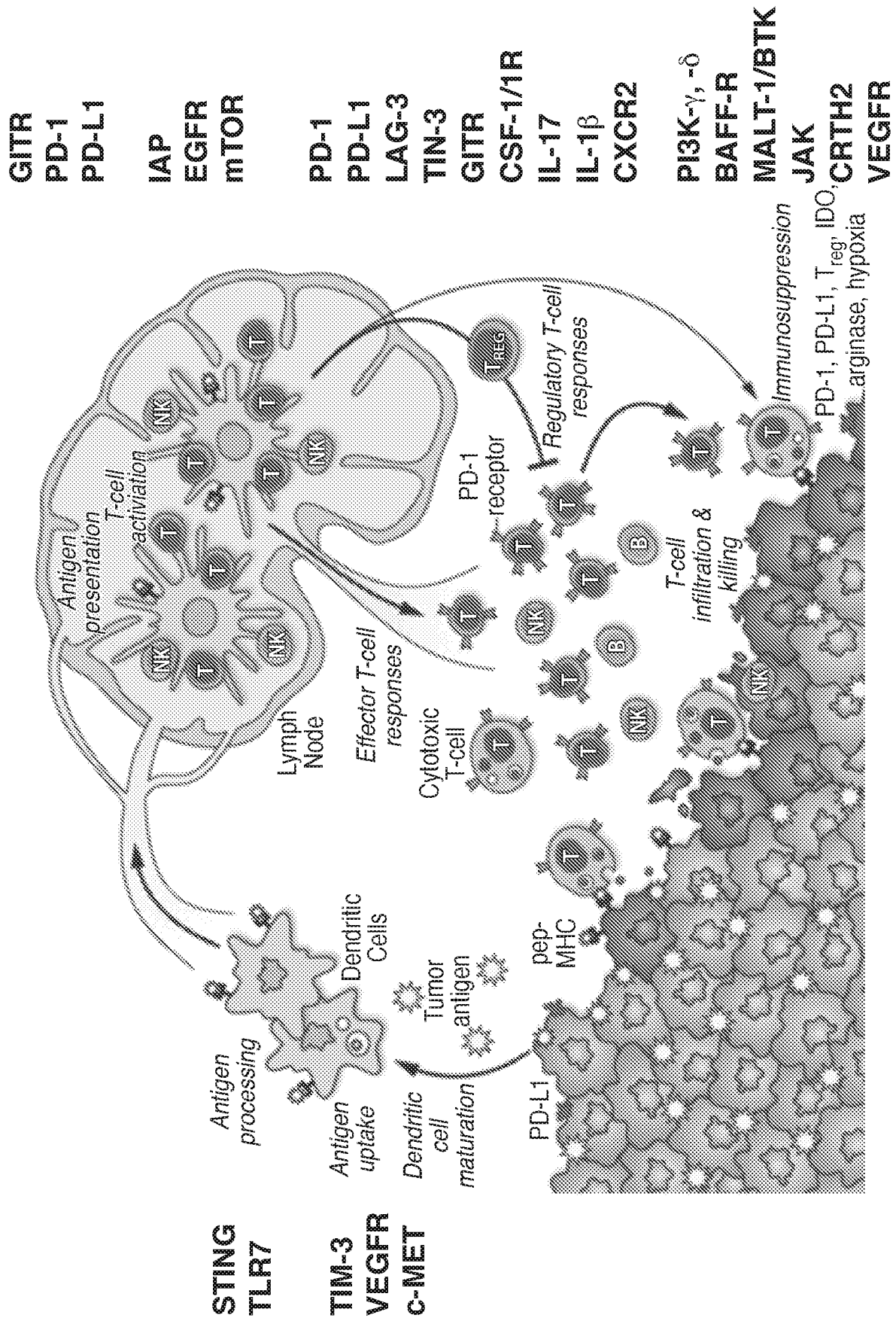


FIGURE 15

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2016/044545

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

a. forming part of the international application as filed:

in the form of an Annex C/ST.25 text file.

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b. furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

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3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/044545

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28
ADD. A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07K A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2010/019570 A2 (MEDAREX INC [US]; THUDIUM KENT B [US]; KORMAN ALAN J [US]; LEBLANC HEI) 18 February 2010 (2010-02-18) cited in the application whole document, especially Examples 1, 3, 4, 6; Tables 4, 7, 9	1-46
Y	DREW M. PARDOLL: "The blockade of immune checkpoints in cancer immunotherapy", NATURE REVIEWS CANCER, vol. 12, no. 4, 22 March 2012 (2012-03-22), pages 252-264, XP055150744, ISSN: 1474-175X, DOI: 10.1038/nrc3239 cited in the application whole document, especially page 261, left-hand column; paragraph bridging pages 261-262	1-46

Further documents are listed in the continuation of Box C.

See patent family annex.

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- "E" earlier application or patent but published on or after the international filing date
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- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

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- "&" document member of the same patent family

Date of the actual completion of the international search 21 October 2016	Date of mailing of the international search report 28/10/2016
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Luyten, Kattie

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2016/044545

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>DMITRIY ZAMARIN ET AL: "Immune checkpoint modulation: Rational design of combination strategies", PHARMACOLOGY AND THERAPEUTICS., vol. 150, 10 January 2015 (2015-01-10), pages 23-32, XP055218491, GB ISSN: 0163-7258, DOI: 10.1016/j.pharmthera.2015.01.003 whole document, especially page 25, right-hand column, lines 16-18; page 28, left-hand column, first full paragraph; page 28, right-hand column, second full paragraph</p> <p style="text-align: center;">-----</p>	1-46
Y	<p>KHALIL DANNY N ET AL: "The New Era of Cancer Immunotherapy: Manipulating T-Cell Activity to Overcome Malignancy", IMMUNOTHERAPY OF CANCER IN: ADVANCES IN CANCER RESEARCH; ISSN 0065-230X; VOL. 128; [ADVANCES IN CANCER RESEARCH; ISSN 0065-230X; VOL], ACADEMIC PRESS, US, vol. 128, 1 January 2015 (2015-01-01), pages 1-68, XP009190991, ISSN: 0065-230X, DOI: 10.1016/BS.ACR.2015.04.010 whole document, especially sectiona 2.3, 5.3; pages 42-43</p> <p style="text-align: center;">-----</p>	1-46
Y	<p>Rothe M.D.C., Schnorfeil F.M., Lichtenegger F.S., Schlüter M., Neitz J., Hiddemann W., Subklewe M.: "Enhancing dendritic cell-induced T-cell responses by immunomodulating molecules", 13th CIMT Annual Meeting</p> <p>11 May 2015 (2015-05-11), page 74, XP055280210, Retrieved from the Internet: URL:http://www.meeting.cimt.eu/cms/diskfiles/download/6/44f802fe32fbdc40d17db6cbf0fc0c9d/CIMT_Abstracts_2015.pdf [retrieved on 2016-06-14] page 74, labelled "053 Therapeutic Vaccination"</p> <p style="text-align: center;">-----</p>	1-46
Y,P	<p>WO 2015/138920 A1 (NOVARTIS AG [CH]; IMMUTEP S A [FR]; TRIEBEL FREDERIC [FR]; BRIGNONE CH) 17 September 2015 (2015-09-17) whole document, especially Examples 1,3; sequences</p> <p style="text-align: center;">-----</p>	1-46

INTERNATIONAL SEARCH REPORT

Information on patent family members

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