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(54) Title: ANTI-CGRP ANTIBODIES FOR TREATING MENSTRUAL-RELATED MIGRAINES

(57) Abstract: The invention provides for methods, treatments, and uses of anti-human calcitonin gene related peptide (CGRP) antibodies for the treatment of menstrual-related migraines.

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Anti-CGRP Antibodies For Treating Menstrual-Related Migraines

The present invention is in the field of medicine. More specifically, the present invention relates to methods and uses of antibodies directed to calcitonin gene-related peptide (CGRP) for the treatment of menstrual-related migraines.

Migraine is a common neurologic disease that affects more than 36 million people in the Unites States, being more prevalent in females of reproductive age. Migraine without aura in more than 50% of women correlates with menstrual cycle hormonal fluctuations, and has been recognized as more severe and difficult to manage with conventional therapies around the menstrual period. The latest edition of the International Classification of Headache Disorders (ICHD III beta) itself recognizes menstrual migraines. As such, a need exists for therapies directed to menstrual-related migraines.

The present invention derives from an exploratory analysis focused on the effect of galcanezumab, an anti-human calcitonin gene-related peptide (CGRP) antibody, studied for the prevention of chronic and episodic migraine, in the incidence and severity of migraine attacks during the perimenstrual period.

Antibodies directed to calcitonin gene-related peptide (CGRP) and methods of making the same are well known and have been previously described, for example, in WO2011/156324A1. "CGRP" or 'calcitonin gene related peptide" refers to a peptide having the sequence given in SEQ ID NO: 5. Non-limiting examples of anti-human calcitonin gene related peptide (CGRP) antibodies include eptinezumab, fremanezumab, and galcanezumab. In some embodiments, the anti-human calcitonin gene related peptide (CGRP) antibody comprises a heavy chain having a heavy chain variable region having the amino acid sequence of SEQ ID NO: 2 and a light chain having a light chain variable region having the amino acid sequence of SEQ ID NO: 1. In some embodiments, the anti-human calcitonin gene related peptide (CGRP) antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 4 and a light chain having the amino acid sequence of SEQ ID NO: 3. In some embodiments, the anti-human calcitonin gene related peptide antibody binds to an epitope on human CGRP comprising amino acids VTHRLAGLLSR of SEQ ID NO: 5, as determined by hydrogen-deuterium exchange. The antibodies disclosed herein are preferably formulated for parenteral administration, more preferably for subcutaneous delivery.

In some embodiments, a patient is a human who has been diagnosed as having a condition or disorder in need of treatment with an antibody or pharmaceutical composition described herein. In some embodiments, a patient is a human that is characterized as being at risk of a condition or disorder for which treatment or administration with a pharmaceutical composition described herein is indicated.

As used herein, the term “treating” (or “treat” or “treatment”) refers to processes involving a slowing, interrupting, arresting, controlling, stopping, reducing, or reversing the progression or severity of a symptom, disorder, condition, or disease, but does not necessarily involve a total elimination of all disease-related symptoms, conditions, or disorders associated with CGRP activity. As used herein, the term “prevention” (or “prevent” or “preventing”) refers to precluding, averting, obviating, forestalling, reducing the incidence of, stopping, or hindering the symptoms of a disease, disorder and/or condition. Prevention includes administration to a subject who does not exhibit symptoms of a disease, disorder, and/or condition at the time of administration.

As used herein, the term “therapeutically effective amount” refers to the amount or dose of an anti-human calcitonin gene related peptide (CGRP) antibody in a pharmaceutical composition, which upon single or multiple dose administration to the patient, provides the desired pharmacological effect in the patient. A dose can include a higher initial loading dose, followed by a lower dose. A “dose” refers to a predetermined quantity of a therapeutic drug calculated to produce the desired therapeutic effect in a patient. A therapeutically effective amount can be determined by the attending diagnostician.

As used herein, the term “month,” “monthly,” or derivations thereof, refers to a time period that is from 28 to 31 consecutive days. The term "about" as used herein, means in reasonable vicinity of the stated numerical value, such as plus or minus 10% of the stated numerical value.

The present disclosure provides a method of treating menstrual-related migraines in a human patient comprising administering a therapeutically effective amount of an anti-human calcitonin gene related peptide (CGRP) antibody to the human patient in need thereof.

The present disclosure provides a method of treating menstrual-related migraines in a human patient comprising administering a therapeutically effective amount of an anti-

human calcitonin gene related peptide (CGRP) antibody to the human patient in need thereof; wherein the human patient has been diagnosed with episodic migraines prior to receiving the antibody.

The present disclosure provides a method of treating menstrual-related migraines in a human patient comprising administering a therapeutically effective amount of an anti-human calcitonin gene related peptide (CGRP) antibody to the human patient in need thereof; wherein the human patient has been diagnosed with chronic migraines prior to receiving the antibody.

The present disclosure provides a method of treating menstrual-related migraines in a human patient comprising administering a therapeutically effective amount of an anti-human calcitonin gene related peptide (CGRP) antibody to the human patient in need thereof, wherein the human patient experiences auras with their menstrual-related migraines.

The present disclosure provides a method of treating menstrual-related migraines in a human patient comprising administering a therapeutically effective amount of an anti-human calcitonin gene related peptide (CGRP) antibody to the human patient in need thereof; wherein the human patient does not experience auras with their menstrual-related migraines.

The present disclosure provides a method of treating menstrual-related migraines in a human patient comprising administering a therapeutically effective amount of an anti-human calcitonin gene related peptide (CGRP) antibody to the human patient in need thereof; wherein the antibody administered is eptinezumab.

The present disclosure provides a method of treating menstrual-related migraines in a human patient comprising administering a therapeutically effective amount of an anti-human calcitonin gene related peptide (CGRP) antibody to the human patient in need thereof; wherein the antibody administered is fremanezumab.

The present disclosure provides a method of treating menstrual-related migraines in a human patient comprising administering a therapeutically effective amount of an anti-human calcitonin gene related peptide (CGRP) antibody to the human patient in need thereof; wherein the antibody administered binds to an epitope comprising amino acids VTHRLAGLLSR of SEQ ID NO: 5.

The present disclosure provides a method of treating menstrual-related migraines in a human patient comprising administering a therapeutically effective amount of an anti-human calcitonin gene related peptide (CGRP) antibody to the human patient in need thereof; wherein the antibody comprises a heavy chain having a heavy chain variable region having the amino acid sequence of SEQ ID NO: 2 and a light chain having a light chain variable region having the amino acid sequence of SEQ ID NO: 1.

The present disclosure provides a method of treating menstrual-related migraines in a human patient comprising administering a therapeutically effective amount of an anti-human calcitonin gene related peptide (CGRP) antibody to the human patient in need thereof; wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 4 and a light chain having the amino acid sequence of SEQ ID NO: 3.

In some examples, the anti-human CGRP antibody is administered subcutaneously at a dose of about 120 mg to 240 mg; preferably wherein the anti-human CGRP antibody is galcanezumab. In some examples, the anti-human CGRP antibody is administered subcutaneously at a dose of about 120 mg; preferably wherein the anti-human CGRP antibody is galcanezumab. In some examples, the anti-human CGRP antibody is administered subcutaneously at a dose of about 240 mg; preferably wherein the anti-human CGRP antibody is galcanezumab. In some examples, the anti-human CGRP antibody is administered a first dose of about 240 mg and a second dose of 120 mg and wherein the first and second dose are administered about one month apart; preferably wherein the anti-human CGRP antibody is galcanezumab. In some examples, the anti-human CGRP antibody is administered once per month; preferably wherein the anti-human CGRP antibody is galcanezumab.

The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines.

The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the human patient has been diagnosed with episodic migraines prior to receiving the antibody.

The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related

migraines; the human patient has been diagnosed with chronic migraines prior to receiving the antibody.

The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the human patient experiences auras with their menstrual-related migraines.

The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the human patient does not experience auras with their menstrual-related migraines.

The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the antibody administered is eptinezumab.

The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the antibody administered is fremanezumab.

The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the antibody administered binds to an epitope comprising amino acids VTHRLAGLLSR of SEQ ID NO: 5.

The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the antibody comprises a heavy chain having a heavy chain variable region having the amino acid sequence of SEQ ID NO: 2 and a light chain having a light chain variable region having the amino acid sequence of SEQ ID NO: 1.

The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 4 and a light chain having the amino acid sequence of SEQ ID NO: 3.

The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the antibody is administered subcutaneously at a dose of 120 mg to

240 mg; preferably wherein the anti-human CGRP antibody is galcanezumab. The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the antibody is administered subcutaneously at a dose of 120 mg; preferably wherein the anti-human CGRP antibody is galcanezumab. The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the antibody is administered subcutaneously at a dose of 240 mg; preferably wherein the anti-human CGRP antibody is galcanezumab. The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the human patient is administered a first dose of 240 mg and a second dose of 120 mg and wherein the first and second dose are administered about one month apart; preferably wherein the anti-human CGRP antibody is galcanezumab. The present disclosure provides an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the antibody is administered once per month; preferably wherein the anti-human CGRP antibody is galcanezumab.

The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines.

The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the human patient has been diagnosed with episodic migraines prior to receiving the antibody.

The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the human patient has been diagnosed with chronic migraines prior to receiving the antibody.

The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-

related migraines; wherein the human patient experiences auras with their menstrual-related migraines.

The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the human patient does not experience auras with their menstrual-related migraines.

The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the antibody administered is eptinezumab.

The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the antibody administered is fremanezumab.

The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the antibody administered binds to an epitope comprising amino acids VTHRLAGLLSR of SEQ ID NO: 5.

The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the antibody comprises a heavy chain having a heavy chain variable region having the amino acid sequence of SEQ ID NO: 2 and a light chain having a light chain variable region having the amino acid sequence of SEQ ID NO: 1.

The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 4 and a light chain having the amino acid sequence of SEQ ID NO: 3.

The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the antibody is administered subcutaneously at a dose of 120 mg to 240 mg; preferably wherein the anti-human CGRP antibody is galcanezumab. The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-

related migraines; wherein the antibody is administered subcutaneously at a dose of 120 mg; preferably wherein the anti-human CGRP antibody is galcanezumab. The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the antibody is administered subcutaneously at a dose of 240 mg; preferably wherein the anti-human CGRP antibody is galcanezumab. The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the human patient is administered a first dose of 240 mg and a second dose of 120 mg of the antibody and wherein the first and second dose are administered about one month apart; preferably wherein the anti-human CGRP antibody is galcanezumab. The present disclosure provides a use of an anti-human calcitonin gene related peptide (CGRP) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines; wherein the antibody is administered once per month; preferably wherein the anti-human CGRP antibody is galcanezumab.

The present disclosure provides a pharmaceutical composition comprising an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines. The present disclosure provides a pharmaceutical composition comprising an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the antibody comprises a heavy chain having a heavy chain variable region having the amino acid sequence of SEQ ID NO: 2 and a light chain having a light chain variable region having the amino acid sequence of SEQ ID NO: 1. The present disclosure provides a pharmaceutical composition comprising an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines; wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 4 and a light chain having the amino acid sequence of SEQ ID NO: 3.

In embodiments that refer to a method of treatment as described herein, such embodiments are also further embodiments for use in that treatment, or alternatively for the use of the combination for the manufacture of a medicament for use in that treatment.

Effect of Anti-Human CGRP Antibodies on Menstrual-Related Migraine

Analyses were performed using data from 3 double-blind, placebo (PBO)-controlled, Phase 3 studies in patients aged 18-65 years with episodic (EVOLVE-1 & EVOLVE-2) or chronic migraine (REGAIN), specifically 2,886 patients (858 EVOLVE-1, 915 EVOLVE-2, 1113 REGAIN) randomly received 120 mg (with 240 mg loading dose at first month) or 240 mg galcanezumab (GMB) or PBO (placebo), which was administered subcutaneously once/month for 6 months in EVOLVE-1&2 and for 3 months in REGAIN.

For female patients, the perimenstrual period is defined as the day menstruation started, plus the previous and subsequent two days (i.e. a 5-day period around the start of menstruation). A menstrual-related migraine is defined as a migraine headache within the 5-day perimenstrual period. A menstrual-related migraine headache day (MRMHD) is defined as a migraine headache day within the 5-day perimenstrual period. Exploratory analysis included intent-to-treat (ITT) patients who had >0 MRMHD during a one-month baseline period. Using a negative binomial repeated measures model, the estimated number of MRMHD per 30-day period was estimated each month and overall across 6 months for pooled EVOLVE-1 & EVOLVE-2 data, and across 3 months for REGAIN.

For ITT patients with >0 MRMHD, baseline mean number of MRMHDs were 2.4, 2.4 and 2.6 for 120mg, 240mg and PBO group, respectively, for pooled EVOLVE-1 & EVOLVE-2 (n=650). Corresponding values were 4.0, 4.5, and 4.4 days, respectively, for REGAIN (n=407). Statistically significantly lower incidence of MRMHDs per 30 day period were observed for both GMB doses compared with PBO overall across 6 months for pooled EVOLVE-1 & EVOLVE-2 and across 3 months for REGAIN (see Table 1). This evidence suggests that galcanezumab given monthly is effective in reducing migraine headache days during the perimenstrual period.

Table 1. Estimated Number of Menstrual Migraine Headache Days							
Period	Treatment	N	Estimated Number of MMHDs per 30 day Period (SE)	95% CI	Rate Ratio per 30 day period	95% CI	P-value
ITT patients with baseline number of MRMHDs>0 for Episodic Migraine							
Average of Month 1 to 6	PBO	321	1.58 (0.13)	1.34, 1.86			
	120mg	170	1.16 (0.12)	0.96, 1.41	0.74	0.64, 0.85	<0.001
	240mg	159	1.12 (0.12)	0.90, 1.38	0.71	0.60, 0.83	<0.001
ITT patients with baseline number of MRMHDs>0 for Chronic Migraine							
Average of Month 1 to 3	PBO	198	3.52 (0.18)	3.18, 3.90			
	120mg	112	2.58 (0.21)	2.58, 3.40	0.84	0.73, 0.97	0.015
	240mg	97	3.01 (0.20)	2.64, 3.42	0.85	0.75, 0.98	0.021

CI = confidence interval; ITT = intent-to-treat; PBO=placebo; SE = standard error; MRMHD = Menstrual-Related Migraine Headache Days

5

Sequences

SEQ ID NO: 1 –LCVR of Galcanezumab (Artificial Sequence)

DIQMTQSPSSLSASVGDRVTITCRASKDISKYLNWYQQKPGKAPKLLIYYTSGYH
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGDALPPTFGGGTKVEIK

SEQ ID NO: 2 –HCVR of Galcanezumab (Artificial Sequence)

QVQLVQSGAEVKKPGSSVKVSCKASGYTFGNYWMQWVRQAPGQGLEWMGAI
YEGTGKTVYIQKFADRVTITADKSTSTAYMELSSLRSEDTAVYYCARLSDYVSGF
GYWGQGTTVTVSS

SEQ ID NO: 3 –LC of Galcanezumab (Artificial Sequence)

DIQMTQSPSSLSASVGDRVTITCRASKDISKYLNWYQQKPGKAPKLLIYYTSGYH
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGDALPPTFGGGTKVEIKRTVA
APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ
DSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 4 –HC of Galcanezumab (Artificial Sequence)

QVQLVQSGAEVKKPGSSVKVSCKASGYTFGNYWMQWVRQAPGQGLEWMGAI
YEGTGKTVYIQKFADRVTITADKSTSTAYMELSSLRSEDTAVYYCARLSDYVSGF
GYWGQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKR
VESKYGPPCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEV
QFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
KGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNH
YTQKSLSLSLG

SEQ ID NO: 5 – Human αCGRP Peptide (*Homo sapiens*)

ACDTATCVTHRLAGLLSRSGGVVKNNFVPTNVGSKAF

WE CLAIM:

1. A method of treating menstrual-related migraines in a human patient comprising administering a therapeutically effective amount of an anti-human calcitonin gene related peptide (SEQ ID NO: 5) antibody to the human patient in need thereof.
2. The method of Claim 1, wherein the human patient has been diagnosed with episodic migraines prior to receiving the antibody.
3. The method of Claim 1, wherein the human patient has been diagnosed with chronic migraines prior to receiving the antibody.
4. The method of any one of Claims 1-3, wherein the human patient experiences auras with their menstrual-related migraines.
5. The method of any one of Claims 1-3, wherein the human patient does not experience auras with their menstrual-related migraines.
6. The method of any one of Claims 1-5, wherein the antibody administered is eptinezumab.
7. The method of any one of Claims 1-5, wherein the antibody administered is fremanezumab.
8. The method of any one of Claims 1-5, wherein the antibody administered binds to an epitope comprising amino acids VTHRLAGLLSR of SEQ ID NO: 5.
9. The method of any one of Claims 1-5 and 8, wherein the antibody comprises a heavy chain having a heavy chain variable region having the amino acid sequence of SEQ ID NO: 2 and a light chain having a light chain variable region having the amino acid sequence of SEQ ID NO: 1.
10. The method of any one of Claims 1-5 and 8, wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 4 and a light chain having the amino acid sequence of SEQ ID NO: 3.
11. The method of any one of Claims 1-5 and 8-10, wherein the antibody is administered subcutaneously at a dose of about 120 mg to 240 mg.
12. The method of any one of Claims 1-5 and 8-10, wherein the antibody is administered subcutaneously at a dose of about 120 mg.
13. The method of any one of Claims 1-5 and 8-10, wherein the antibody is administered subcutaneously at a dose of about 240 mg.

14. The method of any one of Claims 1-5 and 8-10, wherein the human patient is administered a first dose of about 240 mg and a second dose of 120 mg and wherein the first and second dose are administered about one month apart.
15. The method of any one of Claims 1-5 and 8-13, wherein the antibody is administered once per month.
16. An anti-human calcitonin gene related peptide (SEQ ID NO: 5) antibody for use in the treatment of a human patient having menstrual-related migraines.
17. The antibody for use of Claim 16, wherein the human patient has been diagnosed with episodic migraines prior to receiving the antibody.
18. The antibody for use of Claim 16, wherein the human patient has been diagnosed with chronic migraines prior to receiving the antibody.
19. The antibody for use of any one of Claims 16-18, wherein the human patient experiences auras with their menstrual-related migraines.
20. The antibody for use of any one of Claims 16-18, wherein the human patient does not experience auras with their menstrual-related migraines.
21. The antibody for use of any one of Claims 16-20, wherein the antibody administered is eptinezumab.
22. The antibody for use of any one of Claims 16-20, wherein the antibody administered is fremanezumab.
23. The antibody for use of any one of Claims 16-20, wherein the antibody administered binds to an epitope comprising amino acids VTHRLAGLLSR of SEQ ID NO: 5.
24. The antibody for use of any one of Claims 16-20 and 23, wherein the antibody comprises a heavy chain having a heavy chain variable region having the amino acid sequence of SEQ ID NO: 2 and a light chain having a light chain variable region having the amino acid sequence of SEQ ID NO: 1.
25. The antibody for use of any one of Claims 16-20 and 23, wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 4 and a light chain having the amino acid sequence of SEQ ID NO: 3.
26. The antibody for use of any one of Claims 23-25, wherein the antibody is administered subcutaneously at a dose of 120 mg to 240 mg.
27. The antibody for use of any one of Claims 23-25, wherein the antibody is administered subcutaneously at a dose of 120 mg.

28. The antibody for use of any one of Claims 23-25, wherein the antibody is administered subcutaneously at a dose of 240 mg.
29. The antibody for use of any one of Claims 23-25, wherein the human patient is administered a first dose of 240 mg and a second dose of 120 mg and wherein the first and second dose are administered about one month apart.
30. The antibody for use of any one of Claims 23-28, wherein the antibody is administered once per month.
31. Use of an anti-human calcitonin gene related peptide (SEQ ID NO: 5) antibody for the manufacture of a medicament for the treatment of menstrual-related migraines.
32. The antibody for use of Claim 31, wherein the human patient has been diagnosed with episodic migraines prior to receiving the antibody.
33. The antibody for use of Claim 31, wherein the human patient has been diagnosed with chronic migraines prior to receiving the antibody.
34. The antibody for use of any one of Claims 31-33, wherein the human patient experiences auras with their menstrual-related migraines.
35. The antibody for use of any one of Claims 31-33, wherein the human patient does not experience auras with their menstrual-related migraines.
36. The antibody for use of any one of Claims 31-35, wherein the antibody administered is eptinezumab.
37. The antibody for use of any one of Claims 31-35, wherein the antibody administered is fremanezumab.
38. The antibody for use of any one of Claims 31-35, wherein the antibody administered binds to an epitope comprising amino acids VTHRLAGLLSR of SEQ ID NO: 5.
39. The antibody for use of any one of Claims 31-35 and 38, wherein the antibody comprises a heavy chain having a heavy chain variable region having the amino acid sequence of SEQ ID NO: 2 and a light chain having a light chain variable region having the amino acid sequence of SEQ ID NO: 1.
40. The antibody for use of any one of Claims 31-35 and 38, wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 4 and a light chain having the amino acid sequence of SEQ ID NO: 3.
41. The antibody for use of any one of Claims 38-40, wherein the antibody is administered subcutaneously at a dose of 120 mg to 240 mg.

42. The antibody for use of any one of Claims 38-40, wherein the antibody is administered subcutaneously at a dose of 120 mg.

43. The antibody for use of any one of Claims 38-40, wherein the antibody is administered subcutaneously at a dose of 240 mg.

44. The antibody for use of any one of Claims 38-40, wherein the human patient is administered a first dose of 240 mg and a second dose of 120 mg of the antibody and wherein the first and second dose are administered about one month apart.

45. The antibody for use of any one of Claims 38-43, wherein the antibody is administered once per month.

46. A pharmaceutical composition comprising an anti-human calcitonin gene related peptide (CGRP) antibody for use in the treatment of a human patient having menstrual-related migraines.

47. The pharmaceutical composition of Claim 46, wherein the antibody comprises a heavy chain having a heavy chain variable region having the amino acid sequence of SEQ ID NO: 2 and a light chain having a light chain variable region having the amino acid sequence of SEQ ID NO: 1.

48. The pharmaceutical composition of any one of Claims 46-47, wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 4 and a light chain having the amino acid sequence of SEQ ID NO: 3.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/033651

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/18 A61P25/06
ADD.

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

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, EMBASE, BIOSIS, WPI Data

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 August 2019	07/10/2019

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Marinoni J-C

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Form PCT/ISA/210 (second sheet) (April 2005)

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Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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