

CLAIMS

1. Use of a humanized anti-PACAP (Pituitary Adenylate Cyclase-Activating Polypeptide) antibody or antigen binding fragment thereof in the manufacture of a medicament for blocking, inhibiting or neutralizing one or more biological effects associated with pituitary adenylate cyclase-activating peptide ("PACAP") and/or inhibiting PACAP-induced vasodilation and/or treating a condition associated with elevated PACAP, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises:

heavy chain variable region polypeptide having at least 90% identity to SEQ ID NO: 1322 and a light chain variable region polypeptide having at least 90% identity to SEQ ID NO: 1342, wherein said heavy chain variable region comprises the heavy chain complementarity-determining region (CDR) 1 polypeptide of SEQ ID NO: 1324, the heavy chain CDR2 polypeptide of SEQ ID NO: 1326, and the heavy chain CDR3 polypeptide of SEQ ID NO: 1328, and said light chain variable region comprises the light chain CDR1 polypeptide of SEQ ID NO: 1344, the light chain CDR2 polypeptide of SEQ ID NO: 1346, and the light chain CDR3 polypeptide of SEQ ID NO: 1348, , and wherein the humanized anti-PACAP antibody or antigen binding fragment thereof is to be administered to a subject in need thereof.

2. Use of a humanized anti-Pituitary Adenylate Cyclase-Activating Polypeptide ("PACAP") antibody or antigen binding fragment thereof in the manufacture of a medicament for treating or preventing the onset, frequency, severity or duration of headache or migraine in a subject, wherein an effective amount of the anti-PACAP antibody or antigen binding fragment thereof is to be administered to a subject in need thereof, wherein the anti-PACAP antibody or antigen binding fragment thereof comprises a heavy chain variable region polypeptide having at least 90% identity to SEQ ID NO: 1322 and a light chain variable region polypeptide having at least 90% identity to SEQ ID NO: 1342, wherein said heavy chain variable region comprises the heavy chain complementarity-determining region (CDR) 1 polypeptide of SEQ ID NO: 1324, the heavy chain CDR2 polypeptide of SEQ ID NO: 1326, and the heavy chain CDR3 polypeptide of SEQ ID NO: 1328, and said light chain variable region comprises the light chain CDR1 polypeptide of SEQ ID NO: 1344, the light chain CDR2 polypeptide of SEQ ID NO: 1346, and the light chain CDR3 polypeptide of SEQ ID NO: 1348.

3. Use of a humanized anti-PACAP antibody or antigen binding fragment thereof in the manufacture of a medicament for treating a human subject having an acute, episodic or chronic condition associated with at least one of increased vasodilation, photophobia, mast cell degranulation and neuronal activation or a combination of any of the foregoing and further condition which is further associated with Pituitary Adenylate Cyclase-Activating Polypeptide ("PACAP"),

wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises a heavy chain variable region polypeptide heavy chain variable region polypeptide having at least 90% identity to SEQ ID NO: 1322 and a light chain variable region polypeptide having at least 90% identity to SEQ ID NO: 1342, wherein said heavy chain variable region comprises the heavy chain complementarity-determining region (CDR) 1 polypeptide of SEQ ID NO: 1324, the heavy chain CDR2 polypeptide of SEQ ID NO: 1326, and the heavy chain CDR3 polypeptide of SEQ ID NO: 1328, and said light chain variable region comprises the light chain CDR1 polypeptide of SEQ ID NO: 1344, the light chain CDR2 polypeptide of SEQ ID NO: 1346, and the light chain CDR3 polypeptide of SEQ ID NO: 1348.

4. The use of claim 1, wherein the subject has a condition selected from (i) migraine with aura, migraine without aura, hemiplegic migraines, cluster headaches, migrainous neuralgia, chronic headaches, chronic migraine, medication overuse headache, tension headaches, general headaches, hot flush, photophobia, chronic paroxysmal hemicrania, secondary headaches due to an underlying structural problem in the head, secondary headaches due to an underlying structural problem in the neck, cranial neuralgia, sinus headaches, headache associated with sinusitis, allergy-induced headaches, allergy-induced migraines, trigeminal neuralgia, postherpetic neuralgia, phantom limb pain, fibromyalgia, reflex sympathetic dystrophy, pain, chronic pain, inflammatory pain, post-operative incision pain, post-surgical pain, trauma-related pain, lower back pain, eye pain, tooth pain, complex regional pain syndrome, cancer pain, primary or metastatic bone cancer pain, fracture pain, osteoporotic fracture pain, pain resulting from burn, gout joint pain, pain associated with sickle cell crises, pain associated with temporomandibular disorders, cirrhosis, hepatitis, neurogenic pain, neuropathic pain, nociceptive pain, visceral pain, menstrual pain, ovarialgia, osteoarthritis pain, rheumatoid arthritis pain, diabetic neuropathy, sciatica, dyspepsia, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease, ileitis, ulcerative colitis, renal colic, dysmenorrhea, cystitis, interstitial cystitis, menstrual period, labor, menopause, pancreatitis, schizophrenia, depression, post-traumatic stress disorder ("PTSD"), anxiety disorders, autoimmune diabetes, Sjogren's syndrome, multiple sclerosis, overactive bladder, bronchial hyperreactivity, asthma, stroke, bronchitis, bronchodilation, emphysema, chronic obstructive pulmonary disease ("COPD"), inflammatory dermatitis, acne vulgaris, atopic dermatitis, urticaria, keloids, hypertrophic scars and rosacea, endothelial dysfunction, Raynaud's syndrome, coronary heart disease ("CHD"), coronary artery disease ("CAD"), heart failure, peripheral arterial disease ("PAD"), diabetes, pulmonary hypertension ("PH"), connective tissue disorder, allergic dermatitis, psoriasis, pruritus, neurogenic cutaneous redness,

erythema, sarcoidosis, shock, sepsis, opiate withdrawal syndrome, morphine tolerance, and epilepsy;

(ii) migraine, headache or a pain associated disease or condition, wherein the headache or migraine is selected from the group consisting of migraine with aura, migraine without aura, hemiplegic migraine, cluster headache, migrainous neuralgia, chronic headache, chronic migraine, medication overuse headache, and tension headache;

(iii) an ocular disorder associated with photophobia selected from the group consisting of achromatopsia, aniridia, photophobia caused by an anticholinergic drug, aphakia, buphthalmos, cataracts, cone dystrophy, congenital abnormalities of the eye, viral conjunctivitis, corneal abrasion, corneal dystrophy, corneal ulcer, disruption of the corneal epithelium, ectopia lentis, endophthalmitis, eye trauma caused by disease, eye trauma caused by injury, eye trauma caused by infection, chalazion, episcleritis, glaucoma, keratoconus, optic nerve hypoplasia, hydrophthalmos, congenital glaucoma iritis, optic neuritis, pigment dispersion syndrome, pupillary dilation, retinal detachment, scarring of the cornea, sclera and uveitis;

(iv) a nervous system-related or neurological condition associated with photophobia selected from the group consisting of autism spectrum disorders, Chiari malformation, dyslexia, encephalitis, meningitis, subarachnoid hemorrhage, tumor of the posterior cranial fossa, ankylosing spondylitis, albinism, ariboflavinosis, benzodiazepines, chemotherapy, chikungunya, cystinosis, Ehlers-Danlos syndrome, hangover, influenza, infectious mononucleosis, magnesium deficiency, mercury poisoning, migraine, rabies, and tyrosinemia type II; or

(v) a photophobia associated disorder selected from the group consisting of migraine with aura, migraine without aura, iritis, uveitis, meningitis, depression, bipolar disorder, cluster headache or another trigeminal autonomic cephalalgia ("TAC") or blepharospasm, depression, agoraphobia, and bipolar disorder.

5. The use of claim 1, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the heavy chain variable region polypeptide of SEQ ID NO: 1322.

6. The use of claim 2, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the heavy chain variable region polypeptide of SEQ ID NO: 1322.

7. The use of claim 3, wherein the humanized anti-PACAP antibody or antigen

binding fragment thereof comprises the heavy chain variable region polypeptide of SEQ ID NO: 1322.

8. The use of claim 1, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the light chain variable region polypeptide of SEQ ID NO: 1342.

9. The use of claim 2, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the light chain variable region polypeptide of SEQ ID NO: 1342.

10. The use of claim 3, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the light chain variable region polypeptide of SEQ ID NO: 1342.

11. The use of claim 1, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the heavy chain variable region polypeptide of SEQ ID NO: 1322 and the light chain variable region polypeptide of SEQ ID NO: 1342.

12. The use of claim 2, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the heavy chain variable region polypeptide of SEQ ID NO: 1322 and the light chain variable region polypeptide of SEQ ID NO: 1342.

13. The use of claim 3, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the heavy chain variable region polypeptide of SEQ ID NO: 1322 and the light chain variable region polypeptide of SEQ ID NO: 1342.

14. The use of claim 1, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises a heavy chain polypeptide having at least 90% identity to SEQ ID NO: 1321.

15. The use of claim 2, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises a heavy chain polypeptide having at least 90% identity to SEQ ID NO: 1321.

16. The use of claim 3, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises a heavy chain polypeptide having at least 90% identity to SEQ ID NO: 1321.

17. The use of claim 1, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises a light chain polypeptide having at least 90% identity to SEQ ID NO: 1341.

18. The use of claim 2, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises a light chain polypeptide having at least 90% identity to SEQ ID NO: 1341.

19. The use of claim 3, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises a light chain polypeptide having at least 90% identity to SEQ ID NO: 1341.

20. The use of claim 1, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises a heavy chain polypeptide having at least 90% identity to SEQ ID NO: 1321 and a light chain polypeptide having at least 90% identity to SEQ ID NO: 1341.

21. The use of claim 2, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises a heavy chain polypeptide having at least 90% identity to SEQ ID NO: 1321 and a light chain polypeptide having at least 90% identity to SEQ ID NO: 1341.

22. The use of claim 3, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises a heavy chain polypeptide having at least 90% identity to SEQ ID NO: 1321 and a light chain polypeptide having at least 90% identity to SEQ ID NO: 1341.

23. The use of claim 1, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the heavy chain polypeptide of SEQ ID NO: 1321.

24. The use of claim 2, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the heavy chain polypeptide of SEQ ID NO: 1321.

25. The use of claim 3, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the heavy chain polypeptide of SEQ ID NO: 1321.

26. The use of claim 1, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the light chain polypeptide of SEQ ID NO: 1341.

27. The use of claim 2, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the light chain polypeptide of SEQ ID NO: 1341.

28. The use of claim 3, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the light chain polypeptide of SEQ ID NO: 1341.

29. The use of claim 1, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the heavy chain polypeptide of SEQ ID NO: 1321 and the light chain polypeptide of SEQ ID NO: 1341.

30. The use of claim 2, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the heavy chain polypeptide of SEQ ID NO: 1321 and the light chain polypeptide of SEQ ID NO: 1341.

31. The use of claim 3, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof comprises the heavy chain polypeptide of SEQ ID NO: 1321 and the light chain polypeptide of SEQ ID NO: 1341.

32. The use of claim 1, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof is expressed from the heavy chain encoding polynucleotide of SEQ ID NO: 1331 and the light chain encoding polynucleotide of SEQ ID NO: 1351.

33. The use of claim 32, wherein said heavy chain encoding polynucleotide and said light chain encoding polynucleotide are expressed in a CHO cell.

34. The use of claim 1, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof is to be intravenously or subcutaneously administered.

35. The use of claim 2, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof is to be intravenously or subcutaneously administered.

36. The use of claim 3, wherein the humanized anti-PACAP antibody or antigen binding fragment thereof is to be intravenously or subcutaneously administered.

37. The use of claim 2, wherein another active agent which comprises an anti-headache or anti-migraine drug or an analgesic is to be further administered.

38. The use of claim 1, wherein the humanized anti-Pituitary Adenylate Cyclase-

Activating Polypeptide ("PACAP") antibody or antigen binding fragment thereof comprises a heavy chain variable region polypeptide having at least 95% identity to SEQ ID NO: 1322 and a light chain variable region polypeptide having at least 95% identity to SEQ ID NO: 1342, wherein said heavy chain variable region comprises the heavy chain complementarity-determining region (CDR) 1 polypeptide of SEQ ID NO: 1324, the heavy chain CDR2 polypeptide of SEQ ID NO: 1326, and the heavy chain CDR3 polypeptide of SEQ ID NO: 1328, and said light chain variable region comprises the light chain CDR1 polypeptide of SEQ ID NO: 1344, the light chain CDR2 polypeptide of SEQ ID NO: 1346, and the light chain CDR3 polypeptide of SEQ ID NO: 1348.

39. The use of claim 2, wherein the humanized anti-Pituitary Adenylate Cyclase-Activating Polypeptide ("PACAP") antibody or antigen binding fragment thereof comprises a heavy chain variable region polypeptide having at least 95% identity to SEQ ID NO: 1322 and a light chain variable region polypeptide having at least 95% identity to SEQ ID NO: 1342, wherein said heavy chain variable region comprises the heavy chain complementarity-determining region (CDR) 1 polypeptide of SEQ ID NO: 1324, the heavy chain CDR2 polypeptide of SEQ ID NO: 1326, and the heavy chain CDR3 polypeptide of SEQ ID NO: 1328, and said light chain variable region comprises the light chain CDR1 polypeptide of SEQ ID NO: 1344, the light chain CDR2 polypeptide of SEQ ID NO: 1346, and the light chain CDR3 polypeptide of SEQ ID NO: 1348.

40. The use of claim 3, wherein the humanized anti-Pituitary Adenylate Cyclase-Activating Polypeptide ("PACAP") antibody or antigen binding fragment thereof comprises a heavy chain variable region polypeptide having at least 95% identity to SEQ ID NO: 1322 and a light chain variable region polypeptide having at least 95% identity to SEQ ID NO: 1342, wherein said heavy chain variable region comprises the heavy chain complementarity-determining region (CDR) 1 polypeptide of SEQ ID NO: 1324, the heavy chain CDR2 polypeptide of SEQ ID NO: 1326, and the heavy chain CDR3 polypeptide of SEQ ID NO: 1328, and said light chain variable region comprises the light chain CDR1 polypeptide of SEQ ID NO: 1344, the light chain CDR2 polypeptide of SEQ ID NO: 1346, and the light chain CDR3 polypeptide of SEQ ID NO: 1348.