the CRLR and RAMP1 components of CGRP R. The CGRP R binding proteins were found to inhibit, interfere with, or modulate at least one of the biological responses related to CGRP R, and as such, are useful for ameliorating the effects of CGRP R-related diseases or disorders. Binding of certain antigen-binding proteins to CGRP R can, therefore, have one or more of the following activities: inhibiting, interfering with, or modulating CGRP R, inhibiting vasodialation, decreasing neurogenic inflammation, and alleviating, ameliorating, treating, preventing, or reducing symptoms of chronic pain or migraine.

In one aspect, there is provided an antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof selectively inhibits the human CGRP receptor as compared with human AM1, AM2, or amylin receptors.

In one exemplary ~~aspect~~embodiment, the isolated antigen binding proteins selectively inhibit human CGRP receptor (as compared with the human AM1, AM2 or amylin receptors). In some embodiments, the isolated antigen binding protein selectively inhibits the human CGRP receptor with a selectivity ratio of 50 or more, 75 or more, 100 or more, 150 or more, 200 or more, 250 or more, 300 or more, 400 or more, 500 or more, 750 or more or 1,000 or more. The degree of selective inhibition may be determined using any suitable method, e.g., using a cAMP assay as described in the Examples herein. In some embodiments, the isolated antigen binding protein specifically binds to both human CRLR and human RAMP1, and does not specifically bind to human AM1, human AM2 or a human amylin receptor (e.g., AMY1 or AMY2). For example, the isolated antigen binding protein may specifically bind human CGRP R with a $K_D \leq 1$ μM, ≤100 nM, ≤10 nM, or ≤5 nM. In some embodiments, the isolated antigen binding protein specifically binds to human CGRP R with a $K_D \leq 100$ nM, ≤10 nM, or ≤5 nM as determined using a FACS binding assay and analyzed, for example, using methods described in Rathanaswami, *et al., Biochemical and Biophysical Research Communications* 334 (2005) 1004–1013. In some embodiments, the isolated antigen binding protein has a Ki of ≤100 nM, ≤10 nM, ≤1 nM, ≤0.5 nM or ≤0.1 nM in a CGRP binding competition assay. In some embodiments, the isolated antigen binding protein has a Ki of ≤100 nM, ≤50 nM, ≤20 nM, ≤10 nM, ≤1 nM, ≤0.5 nM or ≤0.1 nM in a radiolabeled ^{125}I-CGRP binding competition assay to membranes from cells expressing human CGRP R, for example, the assay described in Example 5 herein.

In another exemplary ~~aspect~~embodiment, the isolated antigen-binding proteins compete for binding to human CGRP R, e.g., the extracellular portion of CGRP R, with a reference antibody comprising a heavy chain variable region comprising a sequence selected from the group consisting of SEQ ID NO:158-170 and a light chain variable region comprising a sequence

selected from the group consisting of SEQ ID NO:137-153. In some embodiments, binding competition is assessed using a binning assays, e.g., using a Biacore analysis, for example, as described in Example 7 herein. In some embodiments, the isolated antigen binding protein

In any of the above-mentioned embodiments, the isolated antigen-binding protein that competes for binding to human CGRP R may be, for example, a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human (e.g., fully human) antibody, a humanized antibody, a chimeric antibody, a multi-specific antibody, or an antigen binding fragment thereof. Further, the antibody fragment of the isolated antigen-binding protein that competes for binding to human CGRP R can be a Fab fragment, and Fab' fragment, an $F(ab')_2$ fragment, an Fv fragment, a diabody or a single chain antibody molecule; and may be, for example, a human monoclonal antibody, e.g., an IgG1-, IgG2-, IgG3-, or IgG4-type antibody. In certain embodiments, the isolated antigen binding proteins that compete for binding to human CGRP R may be neutralizing antigen binding proteins.

In certain exemplary ~~aspects~~embodiments, the isolated antigen-binding proteins described, e.g., isolated antibodies or fragments thereof, comprise (A) one or more heavy chain complementary determining regions (CDRHs) selected from the group consisting of: (i) a CDRH1 having SEQ ID NO:134; (ii) a CDRH2 having SEQ ID NO:135; (iii) a CDRH3 having SEQ ID NO:136; and optionally (iv) a CDRH of (i), (ii) and (iii) that contains one or more amino acid substitutions (e.g., conservative amino acid substitutions), deletions or insertions that collectively total no more than four amino acids; (B) one or more light chain complementary determining regions (CDRLs) selected from the group consisting of: (i) a CDRL1 selected from the group consisting of SEQ ID NOs:107, 111 and 118; (ii) a CDRL2 selected from the group consisting of SEQ ID NOs: 108, 112 and 119; (iii) a CDRL3 selected from the group consisting of SEQ ID NOs: 109, 113 and 120; and optionally (iv) a CDRL of (i), (ii) and (iii) that contains one or more, e.g., one, two, three, four or more, amino acid substitutions (e.g., conservative amino acid substitutions), deletions or insertions that collectively total no more than four amino acids; or (C) one or more heavy chain CDRHs of (A) and one or more light chain CDRLs of (B).

In some embodiments, the CDRHs are further selected from the group consisting of: (i) a CDRH1 having SEQ ID NO:131; (ii) a CDRH2 having SEQ ID NO:132; (iii) a CDRH3 having SEQ ID NO:133; and optionally (iv) a CDRH of (i), (ii) and (iii) that contains one or more, e.g., one, two, three, four or more amino acid substitutions (e.g., conservative amino acid substitutions), deletions or insertions that collectively total no more than three amino acids. In related embodiments, the CDRHs are further selected from the group consisting of: (i) a CDRH1 selected from the group consisting of SEQ ID NO:76, 88, 100, 121, 125 and 128; (ii) a CDRH2 selected from the group consisting of SEQ ID NO: 89, 101, 122, 124, 126, and 129; (iii) a CDRH3 selected from the group consisting of SEQ ID NO: 78, 90, 102, 123, 127, and

deletions or insertions. In one embodiment, the total number of amino acid substitutions, deletions or insertions is no more than two amino acids per CDR. In another embodiment, the amino acid substitutions are conservative substitutions.

In another embodiment, the isolated antigen-binding protein comprises at least one or two CDRH of any of the above-mentioned (A) and at least one or two CDRL of any of the above-mentioned (B). In yet another embodiment, the isolated antigen-binding protein comprises (i) at least three CDRH of any of the above-mentioned (A), where the three CDRHs include CDRH1, a CDRH2 and a CDRH3, and (ii) at least three CDRL of any of the above-mentioned (B), where the three CDRLs include CDRL1, a CDRL2 and a CDRL3. In additional embodiments, the isolated antigen binding proteins described above comprise a first amino acid sequence comprising at least one CDRH and a second amino acid sequence comprising at least one CDRL. In one embodiment, the first and the second amino acid sequences are covalently bonded to each other.

In another ~~aspect~~embodiment, the isolated antigen-binding protein includes a CDRH1, a CDRH2 and a CDRH3. In one embodiment, CDRH1 comprises SEQ ID NO:73, CDRH2 comprises SEQ ID NO:74 and CDRH3 comprises SEQ ID NO:75. In another embodiment, CDRH1 comprises SEQ ID NO:76, CDRH2 comprises SEQ ID NO:77 and CDRH3 comprises SEQ ID NO:78. In another embodiment, CDRH1 comprises SEQ ID NO:79, CDRH2 comprises SEQ ID NO:80 and CDRH3 comprises SEQ ID NO:81. In another embodiment, CDRH1 comprises SEQ ID NO:82, CDRH2 comprises SEQ ID NO:83 and CDRH3 comprises SEQ ID NO:84. In another embodiment, CDRH1 comprises SEQ ID NO:85, CDRH2 comprises SEQ ID NO:86 and CDRH3 comprises SEQ ID NO:87. In another embodiment, CDRH1 comprises SEQ ID NO:88, CDRH2 comprises SEQ ID NO:89 and CDRH3 comprises SEQ ID NO:90. In another embodiment, CDRH1 comprises SEQ ID NO:76, CDRH2 comprises SEQ ID NO:91 and CDRH3 comprises SEQ ID NO:78. In another embodiment, CDRH1 comprises SEQ ID NO:92, CDRH2 comprises SEQ ID NO:93 and CDRH3 comprises SEQ ID NO:94. In another embodiment, CDRH1 comprises SEQ ID NO:76, CDRH2 comprises SEQ ID NO:95 and CDRH3 comprises SEQ ID NO:78. In another embodiment, CDRH1 comprises SEQ ID NO:73, CDRH2 comprises SEQ ID NO:74 and CDRH3 comprises SEQ ID NO:96. In another embodiment, CDRH1 comprises SEQ ID NO:97, CDRH2 comprises SEQ ID NO:98 and CDRH3 comprises SEQ ID NO:99. In another embodiment, CDRH1 comprises SEQ ID NO:100, CDRH2 comprises SEQ ID NO:101 and CDRH3 comprises SEQ ID NO:102.

In another ~~aspect~~embodiment, the isolated antigen-binding protein includes a CDRL1 sequence, a CDRL2 sequence and a CDRL3 sequence. In one embodiment, CDRL1 comprises SEQ ID

NO:42, CDRL2 comprises SEQ ID NO:43 and CDRL3 comprises SEQ ID NO:44. In another embodiment, CDRL1 comprises SEQ ID NO:45, CDRL2 comprises SEQ ID NO:46 and CDRL3 comprises SEQ ID NO:47. In another embodiment, CDRL1 comprises SEQ ID NO:48, CDRL2 comprises SEQ ID NO:49 and CDRL3 comprises SEQ ID NO:50. In another embodiment, CDRL1 comprises SEQ ID NO:51, CDRL2 comprises SEQ ID NO:52 and CDRL3 comprises SEQ ID NO:53. In another embodiment, CDRL1 comprises SEQ ID NO:54, CDRL2 comprises SEQ ID NO:55 and CDRL3 comprises SEQ ID NO:56. In another embodiment, CDRL1 comprises SEQ ID NO:57, CDRL2 comprises SEQ ID NO:58 and CDRL3 comprises SEQ ID NO:59. In another embodiment, CDRL1 comprises SEQ ID NO:60, CDRL2 comprises SEQ ID NO:55 and CDRL3 comprises SEQ ID NO:56. In another embodiment, CDRL1 comprises SEQ ID NO:45, CDRL2 comprises SEQ ID NO:61 and CDRL3 comprises SEQ ID NO:47. In another embodiment, CDRL1 comprises SEQ ID NO:62, CDRL2 comprises SEQ ID NO:63 and CDRL3 comprises SEQ ID NO:64. In another embodiment, CDRL1 comprises SEQ ID NO:65, CDRL2 comprises SEQ ID NO:55 and CDRL3 comprises SEQ ID NO:56. In another embodiment, CDRL1 comprises SEQ ID NO:66, CDRL2 comprises SEQ ID NO:67 and CDRL3 comprises SEQ ID NO:68. In another embodiment, CDRL1 comprises SEQ ID NO:69, CDRL2 comprises SEQ ID NO:70 and CDRL3 comprises SEQ ID NO:71. In another embodiment, CDRL1 comprises SEQ ID NO:69, CDRL2 comprises SEQ ID NO:70 and CDRL3 comprises SEQ ID NO:72.

In another ~~aspect~~embodiment, the isolated antigen-binding protein includes a CDRL1 sequence, a CDRL2 sequence, a CDRL3 sequence, a CDRH1 sequence, a CDRH2 sequence and a CDRH3 sequence. In one embodiment, CDRL1 comprises SEQ ID NO:42, CDRL2 comprises SEQ ID NO:43, CDRL3 comprises SEQ ID NO:44, CDRH1 comprises SEQ ID NO:73, CDRH2 comprises SEQ ID NO:74 and CDRH3 comprises SEQ ID NO:75. In another embodiment, CDRL1 comprises SEQ ID NO:45, CDRL2 comprises SEQ ID NO:46, CDRL3 comprises SEQ ID NO:47, CDRH1 comprises SEQ ID NO:76, CDRH2 comprises SEQ ID NO:77 and CDRH3 comprises SEQ ID NO:78. In another embodiment, CDRL1 comprises SEQ ID NO:48, CDRL2 comprises SEQ ID NO:49, CDRL3 comprises SEQ ID NO:50, CDRH1 comprises SEQ ID NO:79, CDRH2 comprises SEQ ID NO:80 and CDRH3 comprises SEQ ID NO:81. In another embodiment, CDRL1 comprises SEQ ID NO:51, CDRL2 comprises SEQ ID NO:52, CDRL3 comprises SEQ ID NO:53, CDRH1 comprises SEQ ID NO:82, CDRH2 comprises SEQ ID NO:83 and CDRH3 comprises SEQ ID NO:84. In another embodiment, CDRL1 comprises SEQ ID NO:54, CDRL2 comprises SEQ ID NO:55, CDRL3 comprises SEQ ID NO:56, CDRH1 comprises SEQ ID NO:85, CDRH2 comprises SEQ ID NO:86 and

the isolated antigen binding protein may be a human monoclonal antibody, and may be, e.g., an IgG1-, IgG2-, IgG3-, or IgG4-type antibody. Further, the isolated antigen binding proteins may be neutralizing antigen binding proteins.

In any of the above-mentioned sequence-defined embodiments, the isolated antigen-binding protein may specifically bind to both human CRLR and human RAMP1 and not specifically bind to AM1, AM2 or a human amylin receptor (e.g., AMY1), for example, the isolated antigen binding protein may specifically bind to human CGRP R with a $K_D \leq 1$ μM, ≤100 nM, ≤10 nM, or ≤5 nM, e.g., as determined using a FACS binding assay and analyzed, for example, using methods described in Rathanaswami, *et al., Biochemical and Biophysical Research Communications* 334 (2005) 1004–1013. In any of the above-mentioned sequence-defined embodiments, the isolated antigen-binding protein may selectively inhibit human CGRP R, relative to the human the AM1, AM2 or AMY1 receptors, e.g., with a selectivity ratio of 100 or more, 250 or more, 500 or more, 750 or more, 1,000 or more, 2,500 or more, 5,000 or more or 10,000 or more, where the degree of selective inhibition may be determined using any suitable method, e.g., using a cAMP assay as described in the Examples herein. In any of the above-mentioned sequence-defined embodiments, the isolated antigen-binding protein may have a Ki of ≤100 nM, ≤10 nM, ≤1 nM, ≤0.5 nM or ≤0.1 nM in a CGRP binding competition assay, e.g., in a radiolabeled ^{125}I-CGRP binding competition assay to membranes from cells expressing human CGRP R, e.g., the assay described in Example 5 herein.

Another set of embodiment includes isolated antigen-binding proteins that include one or a combination of CDRs having the consensus sequences described below, and optionally, bind human CGRP R. The consensus sequences are derived from phylogenetically related CDR sequences. In one ~~aspect~~embodiment, the CDRs from the various groups may be mixed and matched in any particular isolated antigen-binding protein that binds human CGRP R. In another ~~aspect~~embodiment, the antigen binding protein comprises heavy and light chain CDRs that are derived from the same phylogenetically-related group of antibody clones. Exemplary CDR consensus sequences are as follows:

K1 Consensus

CDR1 RASQGIRX_1DLG (SEQ ID NO:103), wherein X_1 is selected from the group consisting of N and K.

CDR2 X_1ASSLQS (SEQ ID NO:104), wherein X_1 is selected from the group consisting of A and G.

CDR3 LQYNX_1X_2PWT (SEQ ID NO:105), wherein X_1 is selected from the group consisting of I and S, and X_2 is selected from the group consisting of Y and F.

Research Communications 334 (2005) 1004–1013. In any of the above-mentioned V_L and V_H sequence defined embodiments, the isolated antigen-binding protein may selectively inhibit human CGRP R, relative to the human the AM1, AM2 or AMY1 receptors, e.g., with a selectivity ratio of 100 or more, 250 or more, 500 or more, 750 or more, 1,000 or more, 2,500 or more, 5,000 or more or 10,000 or more, where the degree of selective inhibition may be determined using any suitable method, e.g., using a cAMP assay as described in the Examples herein. In any of the above-mentioned V_L and V_H sequence-defined embodiments, the isolated antigen-binding protein may have a Ki of ≤100 nM, ≤10 nM, ≤1 nM, ≤0.5 nM or ≤0.1 nM in a CGRP binding competition assay, e.g., in a radiolabeled ^{125}I-CGRP binding competition assay to membranes from cells expressing human CGRP R, e.g., the assay described in Example 5 herein.

In one ~~aspect~~embodiment, the isolated antigen-binding proteins comprise a heavy chain sequence that has at least 80%, 85%, 90% or 95% sequence identity with an amino acid sequence selected from the group consisting of SEQ ID NOs:29-41. Some of the isolated antigen-binding proteins described comprise a light chain sequence that has at least 80%, 85%, 90% or 95% sequence identity with an amino acid sequence selected from the group consisting of SEQ ID NOs:12-28. Some of the isolated antigen-binding proteins comprise a heavy chain sequence that has at least 80%, 85%, 90% or 95% sequence identity with an amino acid sequence selected from the group consisting of SEQ ID NOs: 29-41, and a light chain sequence that has at least 80%, 85%, 90% or 95% sequence identity with an amino acid sequence selected from the group consisting of SEQ ID NOs: 12-28. In some embodiments, the isolated antigen-binding proteins comprise (A) a heavy chain comprising a sequence (i) selected from the group consisting of SEQ ID NOs: 29-41, or (ii) as defined by (i) and containing one or more (e.g., five, ten, fifteen or twenty) amino acid substitutions (e.g., conservative amino acid substitutions), deletions or insertions; (B) a light chain comprising a sequence (iii) selected from the group consisting of SEQ ID NOs: 12-28, or (iv) as defined by (iii) containing one or more (e.g., five, ten, fifteen or twenty) amino acid substitutions (e.g., conservative amino acid substitutions), deletions or insertions; or (C) a heavy chain of (A) and a light chain of (B). In some embodiments, the isolated antigen-binding proteins comprise a heavy chain comprising a sequence selected from the group consisting of SEQ ID NOs: 29-41 and a light chain comprising a sequence selected from the group consisting of SEQ ID NOs: 12-28.

In one embodiment, the isolated antigen-binding protein comprises (A) a heavy chain comprising an amino acid sequence selected from the group consisting of (i) SEQ ID NO:29, (ii) a sequence that is at least 90% or 95% identical to the sequence defined by (i), and (iii) a sequence as defined by (i) containing up to ten amino acid substitutions (e.g., conservative

In any of the above-mentioned light and heavy chain sequence defined embodiments, the isolated antigen-binding protein may specifically bind to both human CRLR and human RAMP1 and not specifically bind to AM1, AM2 or a human amylin receptor (e.g., AMY1), for example, the isolated antigen binding protein may specifically bind to human CGRP R with a $K_D \leq 1$ μM, ≤100 nM, ≤10 nM, or ≤5 nM, e.g., as determined using a FACS binding assay and analyzed, for example, using methods described in Rathanaswami, *et al., Biochemical and Biophysical Research Communications* 334 (2005) 1004–1013. In any of the above-mentioned light and heavy chain sequence defined embodiments, the isolated antigen-binding protein may selectively inhibit human CGRP R, relative to the human the AM1, AM2 or AMY1 receptors, e.g., with a selectivity ratio of 100 or more, 250 or more, 500 or more, 750 or more, 1,000 or more, 2,500 or more, 5,000 or more or 10,000 or more, where the degree of selective inhibition may be determined using any suitable method, e.g., using a cAMP assay as described in the Examples herein. In any of the above-mentioned light and heavy chain sequence-defined embodiments, the isolated antigen-binding protein may have a Ki of ≤100 nM, ≤10 nM, ≤1 nM, ≤0.5 nM or ≤0.1 nM in a CGRP binding competition assay, e.g., in a radiolabeled ^{125}I-CGRP binding competition assay to membranes from cells expressing human CGRP R, e.g., the assay described in Example 5 herein.

In another aspect, there is provided an isolated nucleic acid polynucleotide that encodes an antibody or antigen-binding fragment as defined above.

In a further ~~aspect~~embodiment, also provided are isolated nucleic acid polynucleotides that encode any of the CGRP R antigen-binding proteins summarized above. In one embodiment, the isolated polynucleotide comprises a sequence selected from the group consisting of SEQ ID NOs:175, 176, 178, 179, 180, 181, 182, 183, 186, 187, 188, 189, 191, 192, 193, 194, 195, 196, 197, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209 and 210. In another embodiment, the isolated polynucleotide comprises a sequence selected from the group consisting of SEQ ID NOs:224-258. In another embodiment, the isolated polynucleotide comprises a sequence capable of hybridizing under stringent hybridization conditions with a sequence selected from the group consisting of SEQ ID NOs:224-258. In another embodiment, the isolated polynucleotide comprises a sequence that is about 80%, 85%, 90% or 95% or more identical to a sequence selected from the group consisting of SEQ ID NOs:224-258. In some instances, the isolated nucleic acid molecules are operably-linked to a control sequence.

In another aspect, there is provided an expression vector comprising an isolated polynucleotide as defined above.

In related embodiments, the isolated polynucleotides are incorporated into an expression vector.

In another aspect, there is provided a cell line transformed with expression vector as defined above.

Also included are cell lines transformed with expression vectors comprising isolated polynucleotide as described above. In a related ~~aspect~~embodiment, also provided are expression vectors and host cells transformed or transfected with the expression vectors that comprise the

aforementioned isolated nucleic acid molecules that encode CGRP R antigen-binding proteins described above

In another aspect, there is provided a method of making an antibody or antigen-binding fragment thereof as defined above, comprising preparing the antibody or antigen-binding fragment thereof from a host cell that secretes that antigen-binding protein.

In another ~~aspect~~embodiment, also provided is a method of preparing the antigen-binding proteins that includes the step of preparing the antigen binding protein from a host cell that secretes the antigen-binding protein. In some embodiments, the antigen binding protein is generated using an immunogen comprising soluble CGRP receptor. In some embodiments, such soluble CGRP receptor is obtained by co-expressing and purifying an N-terminal extracellular domain (ECD) of human CRLR and an ECD of human RAMP1, e.g., an ECD of human CRLR comprising SEQ ID NO: 6 and an ECD of RAMP1 comprising SEQ ID NO: 8, for example, as described in Examples 1 and 2 herein.

In another aspect, there is provided a pharmaceutical composition comprising an antibody or antigen-binding fragment thereof as defined above and a pharmaceutically acceptable excipient .

In yet another ~~aspect~~embodiment, a pharmaceutical composition is provided comprising at least one of the antigen-binding proteins summarized above and a pharmaceutically acceptable excipient. In one embodiment, the pharmaceutical composition may comprise an additional active agent that is selected from the group consisting of a radioisotope, radionuclide, a toxin, or a therapeutic and a chemotherapeutic group.

In another aspect, there is provided an antibody or antigen-binding fragment thereof as defined above for use in treatment of headache or migraine.

In one ~~aspect~~embodiment, the isolated antigen binding protein is effective to inhibit vasodialation and/or decrease neurogenic inflammation when administered to a patient. In one embodiment, the isolated antigen binding protein is effective to reduce the frequency and/or severity of headaches, for example, migraine headaches. For example, the antigen binding protein may be used as an acute treatment of migraine, and/or as a prophylactic treatment to prevent or reduce the frequency and/or severity of symptoms, particularly pain symptoms, associated with a migraine attack.

Other ~~aspects~~embodiments further provide method for treating or preventing a condition associated with CGRP R in a patient, comprising administering to a patient an effective amount of at least one isolated antigen-binding protein summarized above. In one embodiment, the condition is a headache, for example, a migraine headache or a cluster headache or another type of pain, e.g., a chronic pain; in another embodiment it is diabetes mellitus (type II) ; in another embodiment it is

inflammation, particularly neurogenic inflammation; in another embodiment it is a cardiovascular disorder; in another embodiment it is a hemodynamic derangement associated with endotoxemia and sepsis; in another embodiment it is vasodialation.

In another ~~aspect~~embodiment, also provided is a method of inhibiting binding of CGRP to human CGRP R, e.g., the extracellular portion of CGRP R, in a patient comprising administering an effective amount of at least one antigen-binding protein provided herein and/or summarized above.

These and other aspects will be described in greater detail herein. Each of the aspects provided can encompass various embodiments provided herein. It is therefore anticipated that each of the embodiments involving one element or combinations of elements can be included in each aspect described, and all such combinations of the above aspects and embodiments are expressly considered. Other features, objects, and advantages of the ~~invention~~disclosure are apparent in the detailed description that follows.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows an alignment of RAMP-1 sequences from human, cynomolgus monkey and rat.

Fig. 2 shows an alignment of CRLR sequences from human, cynomolgus monkey and rat.

Figs 3A and 3B show phylogenetically-based sequence alignments of light chain CDRs from the indicated anti-CGRP receptor antibody clones having kappa light chains, and certain corresponding consensus sequences.

Fig. 4 shows phylogenetically-based sequence alignments of light chain CDRs from the indicated anti-CGRP receptor antibody clones having lambda light chains, and certain corresponding consensus sequences.

Figs. 5A, 5B, 5C, 5D and 5E show phylogenetically-based sequence alignments of heavy chain CDRs from the indicated anti-CGRP receptor antibody clones, and certain corresponding consensus sequences.

Fig. 5F shows consensus sequences of exemplary anti-CGRP receptor antibody heavy chain CDRs disclosed herein.

Fig. 6 is a plot of data from two experiments showing percent inhibition of labeled ligand binding to CGRP R by 1092 anti-CGRP R hybridoma supernatants (diamonds) and 68 negative control supernatants (squares).

Figs. 7A-D show exemplary cAMP assay IC50 data from cells expressing hCGRP receptor (Fig. 7A), hAM1 (Fig. 7B), hAM2 (Fig. 7C) and human amylin receptors (Fig. 7D) for three indicated anti-CGRP R mAbs.

Fig. 8 shows an example of ^{125}I-CGRP binding data such as may be used to determine the Ki of mAbs to human CGRP receptor.

Figs. 9A-D show Biacore competition data for selected antibodies disclosed herein.

Fig. 10 shows a FACS Kd determination of mAb 12G8.

Fig. 11 shows an alignment of cynomolgus, human, human chimeras, rat, and rhesus RAMP1 sequences.