

as pain refractory to two or more prior monotherapy and/or dual therapy treatment regimens.

In one aspect of the present disclosure, there is provided a use of an antibody in the manufacture of a medicament for treating chronic pain in a subject in need thereof, wherein the antibody comprises a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

In another aspect of the present disclosure, there is provided a use of an antibody in the manufacture of a medicament for treating chronic osteoarthritis pain in a subject in need thereof, wherein the antibody comprises a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

In a further aspect of the present disclosure, there is provided a use of an antibody in the manufacture of a medicament for treating chronic diabetic peripheral neuropathy pain in a subject in need thereof, wherein the antibody comprises a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

In another aspect of the present disclosure, there is provided a use of an antibody in the manufacture of a medicament for treating chronic low back pain in a subject in

need thereof, wherein the antibody comprises a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

In a further aspect of the present disclosure, there is provided an antibody comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3, for use in the treatment of chronic pain.

The present ~~invention~~disclosure provides antibodies against TGF-alpha and Epiregulin for the treatment of chronic pain, including nociceptive, neuropathic, and mixed pain, and in particular treatment of chronic osteoarthritis (OA) pain, or chronic diabetic peripheral neuropathy pain (DPNP), or chronic low back pain. Furthermore, the present ~~invention~~disclosure provides antibodies against TGF-alpha and Epiregulin for the treatment of chronic osteoarthritis (OA) pain, or chronic diabetic peripheral neuropathy pain (DPNP), or chronic low back pain refractory to two or more prior monotherapy and/or dual therapy treatment regimens.

In an ~~embodiment~~example the present ~~invention~~disclosure provides a method of treating chronic pain in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of an antibody comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

In an ~~embodiment~~example the present ~~invention~~disclosure provides a method of treating chronic osteoarthritis pain in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of an antibody comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

In an ~~embodiment~~example the present ~~invention~~disclosure provides a method of treating chronic diabetic peripheral neuropathy pain in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of an antibody comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region

(LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

In an embodimentexample the present inventiondisclosure provides a method of treating chronic low back pain in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of an antibody comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

In an embodimentexample the present inventiondisclosure provides the method according to any one of embodimentexamples above, wherein the amino acid sequence of the LCVR is SEQ ID NO:9 or SEQ ID NO:10.

In an embodimentexample the present inventiondisclosure provides the method according to any one of the embodimentexamples above, wherein the amino acid sequence of the HCVR is SEQ ID NO:7.

In an embodimentexample the present inventiondisclosure provides the method according to any one of the embodimentexamples above, wherein the amino acid sequence of the LCVR is SEQ ID NO:9 and the amino acid sequence of the HCVR is SEQ ID NO:7.

In an embodimentexample the present inventiondisclosure provides the method according to any one of the embodimentexamples above, wherein the amino acid sequence of the light chain is SEQ ID NO:13 or SEQ ID NO:14.

In an embodimentexample the present inventiondisclosure provides the method according to any one of the embodimentexamples above, wherein the amino acid sequence of the heavy chain is SEQ ID NO:12.

In an embodimentexample the present inventiondisclosure provides the method according to any one of the embodimentexamples above, comprising two light chains wherein the amino acid sequence

of each light chain is SEQ ID NO:13, and two heavy chains wherein the amino acid sequence of each heavy chain is SEQ ID NO:12.

In an embodimentexample the present inventiondisclosure provides the method according to any one of the embodimentexamples above, comprising two light chains wherein the amino acid sequence of each light chain is SEQ ID NO:14, and two heavy chains wherein the amino acid sequence of each heavy chain is SEQ ID NO:12.

In an embodimentexample the present inventiondisclosure provides the method according to any one of the embodimentexamples above, wherein the dose of antibody is a 750 mg starting dose, followed by a 500 mg dose every 2 weeks, for as long as the patient needs treatment for pain.

In an embodimentexample the present inventiondisclosure provides the method according to any one of the embodimentexamples above wherein the chronic pain is refractory to two or more prior monotherapy and/or dual therapy treatment regimens.

In an embodimentexample the present inventiondisclosure provides an antibody comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3, for use in the treatment of chronic pain. In an embodimentexample the present inventiondisclosure further provides the above use wherein the chronic pain is selected from the group consisting of chronic osteoarthritis pain, chronic diabetic neuropathy pain, and chronic low back pain. In an embodimentexample the present inventiondisclosure further provides the above use, wherein the amino acid sequence of the LCVR is SEQ ID NO:9 or SEQ ID NO:10. In an embodimentexample the present inventiondisclosure further provides the above use wherein the amino acid sequence of the HCVR is SEQ ID NO:7. In an embodimentexample the present inventiondisclosure further provides the above use wherein the amino acid sequence of the LCVR is SEQ ID NO:9 and the amino acid sequence of the HCVR is SEQ ID NO:7. In an embodimentexample the present inventiondisclosure further provides the above use wherein the amino acid sequence of the light chain is SEQ ID NO:13 or SEQ ID NO:14. In an embodimentexample the present inventiondisclosure further provides the above use wherein the amino acid sequence of the heavy chain is SEQ ID NO:12. In an embodimentexample

the present [inventiondisclosure](#) further provides the above use comprising two light chains, wherein the amino acid sequence of each light chain is SEQ ID NO:13, and two heavy chains, wherein the amino acid sequence of each heavy chain is SEQ ID NO:12. In an [embodimentexample](#) the present [inventiondisclosure](#) further provides the above use comprising two light chains wherein the amino acid sequence of each light chain is SEQ ID NO:14, and two heavy chains wherein the amino acid sequence of each heavy chain is SEQ ID NO:12. In an [embodimentexample](#) the present [inventiondisclosure](#) further provides the above use wherein the chronic pain is chronic osteoarthritis pain. In an [embodimentexample](#) the present [inventiondisclosure](#) further provides the above use wherein the chronic pain is chronic diabetic peripheral neuropathy pain. In an [embodimentexample](#) the present [inventiondisclosure](#) further provides the above use wherein the chronic pain is chronic low back pain. In an [embodimentexample](#) the present [inventiondisclosure](#) further provides the above use wherein the dose of antibody is a 750mg starting dose, followed by a 500 mg dose every 2 weeks, for as long as the patient needs treatment for pain. In an [embodimentexample](#) the present [inventiondisclosure](#) further provides the above use wherein the chronic pain is refractory to two or more prior monotherapy and/or dual therapy treatment regimens. In an [embodimentexample](#) the [inventiondisclosure](#) provides for the use of an antibody according to the [embodimentexamples](#) above for the manufacture of a medicament for the treatment of chronic pain. In an [embodimentexample](#) the [inventiondisclosure](#) provides for the use of an antibody according to the [embodimentexamples](#) above for the manufacture of a medicament for the treatment of chronic pain, wherein the chronic pain is selected from chronic osteoarthritis pain, chronic diabetic neuropathy pain, and chronic low back pain.

Brief Description of Figures:

Figure 1. Pain efficacy of Antibody III in the rat meniscal tear model. Data are presented as mean $\pm$ SEM where group size is n=6. Statistical comparisons: ANOVA and Dunnett's test for comparison to control IgG1 (*p<0.001) and Tukey's for comparison between 1 and 10mg/kg Antibody III (*p<.05). Abbreviations: ANOVA = analysis of variance; IgG1 = immunoglobulin G1; SEM = standard error of the mean.

WE CLAIM:

1. ~~Use of A method of treating chronic pain in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of~~ an antibody in the manufacture of a medicament for treating chronic pain in a subject in need thereof, wherein the antibody comprisesing a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.
2. ~~Use of A method of treating chronic osteoarthritis pain in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of~~ an antibody in the manufacture of a medicament for treating chronic osteoarthritis pain in a subject in need thereof, wherein the antibody comprisesing a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.
3. ~~Use of A method of treating chronic diabetic peripheral neuropathy pain in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of~~ an antibody in the manufacture of a medicament for treating chronic diabetic peripheral neuropathy pain in a subject in need thereof, wherein the antibody comprisesing a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region

(HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.

4. ~~Use of A method of treating chronic low back pain in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of~~ an antibody in the manufacture of a medicament for treating chronic low back pain in a subject in need thereof, wherein the antibody comprisesing a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3.
5. The ~~usemethod~~ according to any one of Claims 1-4, wherein the amino acid sequence of the LCVR is SEQ ID NO:9 or SEQ ID NO:10.
6. The ~~usemethod~~ according to any one of Claims 1-4, wherein the amino acid sequence of the HCVR is SEQ ID NO:7.
7. The ~~usemethod~~ according to any one of Claims 1-4, wherein the amino acid sequence of the LCVR is SEQ ID NO:9 and the amino acid sequence of the HCVR is SEQ ID NO:7.
8. The ~~usemethod~~ according to any one of Claims 1-4, wherein the amino acid sequence of the light chain is SEQ ID NO:13 or SEQ ID NO:14.
9. The ~~usemethod~~ according to any one of Claims 1-4, wherein the amino acid sequence of the heavy chain is SEQ ID NO:12.

10. The ~~usemethod~~ according to any one of Claims 1-4, wherein the antibody comprises two light chains wherein the amino acid sequence of each light chain is SEQ ID NO:13, and two heavy chains wherein the amino acid sequence of each heavy chain is SEQ ID NO:12.
11. The ~~usemethod~~ according to any one of Claims 1-4, wherein the antibody comprises two light chains wherein the amino acid sequence of each light chain is SEQ ID NO:14, and two heavy chains wherein the amino acid sequence of each heavy chain is SEQ ID NO:12.
12. The ~~usemethod~~ according to any one of Claims 1-4, wherein the dose of antibody is a 750mg starting dose, followed by a 500 mg dose every 2 weeks, for as long as the ~~patientsubject~~ needs treatment for pain.
13. The ~~usemethod~~ according to any one of Claims 1-4 wherein the chronic pain is refractory to two or more prior monotherapy and/or dual therapy treatment regimens.
14. An antibody comprising a light chain and a heavy chain, wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is SEQ ID NO:4, LCDR2 is SEQ ID NO:5, LCDR3 is SEQ ID NO:6, HCDR1 is SEQ ID NO:1, HCDR2 is SEQ ID NO:2, and HCDR3 is SEQ ID NO:3, for use in the treatment of chronic pain.
15. The antibody for use according to claim 14 wherein the chronic pain is selected from the group consisting of chronic osteoarthritis pain, chronic diabetic neuropathy pain, and chronic low back pain.
16. The ~~antibody for~~ use according to Claims 14 or 15, wherein the amino acid sequence of the LCVR is SEQ ID NO:9 or SEQ ID NO:10.

17. The antibody for use according to Claims 14 or 15, wherein the amino acid sequence of the HCVR is SEQ ID NO:7.
18. The antibody for use according to Claims 14 or 15, wherein the amino acid sequence of the LCVR is SEQ ID NO:9 and the amino acid sequence of the HCVR is SEQ ID NO:7.
19. The antibody for use according to Claims 14, wherein the amino acid sequence of the light chain is SEQ ID NO:13 or SEQ ID NO:14.
20. The antibody for use according to Claims 14, wherein the amino acid sequence of the heavy chain is SEQ ID NO:12.
21. The antibody for use according to Claims 14, comprising two light chains, wherein the amino acid sequence of each light chain is SEQ ID NO:13, and two heavy chains, wherein the amino acid sequence of each heavy chain is SEQ ID NO:12.
22. The antibody for use according to Claims 14, comprising two light chains wherein the amino acid sequence of each light chain is SEQ ID NO:14, and two heavy chains wherein the amino acid sequence of each heavy chain is SEQ ID NO:12.
23. The antibody for use according to ~~any one claim and~~ of claims 14-22, wherein the chronic pain is chronic osteoarthritis pain.
24. The antibody for use according to ~~any one claim and~~ of claims 14-22, wherein the chronic pain is chronic diabetic peripheral neuropathy pain.
25. The antibody for use according to ~~any one claim and~~ of claims 14-22, wherein the chronic pain is chronic low back pain.

26. The antibody for use according to any one of claims 14 – 25, wherein the dose of antibody is a 750mg starting dose, followed by a 500 mg dose every 2 weeks, for as long as the patient~~subject~~ needs treatment for pain.
27. The antibody for use according to any one of claims 14 – 25, wherein the chronic pain is refractory to two or more prior monotherapy and/or dual therapy treatment regimens.