What is claimed is:

1. An isolated monoclonal antibody or an antigen-binding fragment thereof that specifically binds to GFRα3, having one or more of the following characteristics:

(i) exhibits a K_D ranging from about 10^{-8} M to about 10^{-13} M as measured by surface plasmon resonance;

(ii) demonstrates the ability to block about 50-100% of the binding of GFRα3 to its ligand, artemin, with an IC_{50} value ranging from about 40 pM to about 15 nM;

(iii) demonstrates the ability to block about 20% to about 100% of the binding of GFRα3 to a solid support coated with a mixture of artemin and RET;

(iv) blocks or inhibits artemin-dependent activation of RET with an IC_{50} ranging from about 200 pM to about 50 nM;

(v) inhibits or reduces one or more nociceptive responses in an *in vivo* model of bone cancer pain;

(vi) inhibits or reduces artemin-sensitized thermal hyperalgesia *in vivo*;

(vii) inhibits or reduces allodynia in an *in vivo* model of osteoarthritis;

(viii) does not cross-react with other GFR co-receptors for RET;

(ix) comprises a heavy chain variable region (HCVR) having an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 18, 34, 50, 66, 82, 98, 114, 130, 146, 162, 178, 194, 210, 226, 242, 258, 274, 290, 306, 322, 338, 354, 381 and 397; or

(x) comprises a light chain variable region (LCVR) having an amino acid sequence selected from the group consisting of SEQ ID NOs : 10, 26, 42, 58, 74, 90, 106, 122, 138, 154, 170, 186, 202, 218, 234, 250, 266, 282, 298, 314, 330, 346, 362, 389 and 405.

2. The isolated monoclonal antibody or an antigen-binding fragment thereof of claim 1, wherein the antibody is selected from the group consisting of a murine antibody, a chimeric antibody, a humanized antibody and a human antibody.

3. The isolated monoclonal antibody or an antigen-binding fragment thereof of either claim 1 or 2, wherein the antibody does not cross-react with human GFRα1 or human GFRα2

4. The isolated monoclonal antibody or an antigen-binding fragment thereof of any one of claims 1-3, wherein the antibody is a human monoclonal antibody comprising (a) a heavy chain variable region (HCVR) having an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 18, 34, 50, 66, 82, 98, 114, 130, 146, 162, 178, 194, 210, 226, 242, 258, 274,

290, 306, 322, 338, 354, 381 and 397 and (b) a light chain variable region (LCVR) having an amino acid sequence selected from the group consisting of SEQ ID NOs : 10, 26, 42, 58, 74, 90, 106, 122, 138, 154, 170, 186, 202, 218, 234, 250, 266, 282, 298, 314, 330, 346, 362, 389 and 405.

5. The isolated monoclonal antibody or an antigen-binding fragment thereof of any one of claims 1-4, wherein the antibody demonstrates the ability to block about 50-95% of the binding of human GFRα3 to its ligand, artemin, with an IC_{50} value ranging from about 40 pM to about 750 pM.

6. The isolated monoclonal antibody or an antigen-binding fragment thereof of any of claims 1-4, wherein the antibody or the antigen-binding fragment thereof blocks about 75-100% of the binding of human GFRα3 to its ligand, artemin, with an IC_{50} value ranging from about 400 pM to about 15 nM.

7. The isolated monoclonal antibody or an antigen-binding fragment thereof of any one of claims 1-4, wherein the antibody or the antigen-binding fragment thereof blocks or inhibits artemin-dependent activation of human RET with an IC_{50} ranging from about 300 pM to about 5 nM.

8. The isolated monoclonal antibody or an antigen-binding fragment thereof of any one of claims 1-4, wherein the antibody or the antigen-binding fragment thereof blocks or inhibits artemin-dependent activation of cynomolgus RET with an IC_{50} ranging from about 0.7 nM to about 2.5 nM.

9. An isolated antibody or antigen-binding fragment thereof that binds specifically to human GFRα3, wherein the antibody comprises the three heavy chain CDRs (HCDR1, HCDR2 and HCDR3) contained within a HCVR amino acid sequence selected from the group consisting of SEQ ID NO: 2, 18, 34, 50, 66, 82, 98, 114, 130, 146, 162, 178, 194, 210, 226, 242, 258, 274, 290, 306, 322, 338, 354, 381 and 397; and the three light chain CDRs (LCDR1, LCDR2 and LCDR3) contained within a LCVR amino acid sequence selected from the group consisting of SEQ ID NOs : 10, 26, 42, 58, 74, 90, 106, 122, 138, 154, 170, 186, 202, 218, 234, 250, 266, 282, 298, 314, 330, 346, 362, 389 and 405.

10. The isolated antibody or antigen-binding fragment thereof of claim 9, wherein the antibody or antigen-binding fragment comprises a heavy chain variable region (HCVR) having an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 18, 34, 50, 66, 82, 98, 114, 130, 146, 162, 178, 194, 210, 226, 242, 258, 274, 290, 306, 322, 338, 354, 381 and 397.

11. The isolated antibody or antigen-binding fragment thereof of either claim 9 or 10, wherein the antibody or antigen-binding fragment comprises a light chain variable region (LCVR) having an amino acid sequence selected from the group consisting of SEQ ID NOs : 10, 26, 42, 58, 74, 90, 106, 122, 138, 154, 170, 186, 202, 218, 234, 250, 266, 282, 298, 314, 330, 346, 362, 389 and 405.

12. The isolated antibody or antigen-binding fragment of any one of claims 9-11, comprising a HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NOs: SEQ ID NO: 2/10, 18/26, 34/42, 50/58, 66/74, 82/90, 98/106, 114/122, 130/138, 146/154, 162/170, 178/186, 194/202, 210/218, 226/234, 242/250, 258/266, 274/282, 290/298, 306/314, 322/330, 338/346, 354/362, 381/389 and 397/405.

13. The isolated antibody or antigen-binding fragment of claim 12, comprising a HCVR/LCVR amino acid sequence pair selected from the group consisting of SEQ ID NO: 50/58, 146/154, 210/218 and 290/298.

14. The isolated antibody or antigen-binding fragment of any one of claims 9-12, comprising:

(a) a HCDR1 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 4, 20, 36, 52, 68, 84, 100, 116, 132, 148, 164, 180, 196, 212, 228, 244, 260, 276, 292, 308, 324, 340, 356, 383 and 399;

(b) a HCDR2 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 6, 22, 38, 54, 70, 86, 102, 118, 134, 150, 166, 182, 198, 214, 230, 246, 262, 278, 294, 310, 326, 342, 358, 385 and 401;

(c) a HCDR3 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 8, 24, 40, 56, 72, 88, 104, 120, 136, 152, 168, 184, 200, 216, 232, 248, 264, 280, 296, 312, 328, 344, 360, 387 and 403;

(d) a LCDR1 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 12, 28, 44, 60, 76, 92, 108, 124, 140, 156, 172, 188, 204, 220, 236, 252, 268, 284, 300, 316, 332, 348, 364, 391 and 407;

(e) a LCDR2 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 30, 46, 62, 78, 94, 110, 126, 142, 158, 174, 190, 206, 222, 238, 254, 270, 286, 302, 318, 334, 350, 366, 393 and 409; and

(f) a LCDR3 domain having an amino acid sequence selected from the group consisting of SEQ ID NOs: 16, 32, 48, 64, 80, 96, 112, 128, 144, 160, 176, 192, 208, 224, 240, 256, 272, 288, 304, 320, 336, 352, 368, 395 and 411.

15. An isolated antibody or antigen-binding fragment thereof that competes for specific binding to human GFRα3 with an antibody or antigen-binding fragment comprising heavy and light chain sequence pairs selected from the group consisting of SEQ ID NOs: 2/10, 18/26, 34/42, 50/58, 66/74, 82/90, 98/106, 114/122, 130/138, 146/154, 162/170, 178/186, 194/202, 210/218, 226/234, 242/250, 258/266, 274/282, 290/298, 306/314, 322/330, 338/346 and 354/362, 381/389 and 397/405.

16. An isolated antibody or antigen-binding fragment thereof that binds the same epitope on human GFRα3 that is recognized by an antibody comprising heavy and light chain sequence pairs selected from the group consisting of SEQ ID NOs: 2/10, 18/26, 34/42, 50/58, 66/74, 82/90, 98/106, 114/122, 130/138, 146/154, 162/170, 178/186, 194/202, 210/218, 226/234, 242/250, 258/266, 274/282, 290/298, 306/314, 322/330, 338/346 and 354/362, 381/389 and 397/405.

17. An isolated nucleic acid molecule encoding the antibody or antigen-binding fragment of any of claims 9-14.

18. An expression vector comprising the nucleic acid molecule of claim 17.

19. A method of producing an anti-GFRα3 antibody or antigen-binding fragment thereof comprising the steps of introducing the expression vector of claim 18 into an isolated host cell, growing the cell under conditions permitting production of the antibody or fragment thereof, and recovering the antibody so produced.

20. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof according to any one of claims 1 through 16 and a pharmaceutically acceptable carrier or diluent.

21. A method for treating a GFRα3-related condition or disease, or the pain associated with the GFRα3-related condition or disease, the method comprising administering the antibody or antigen-binding fragment of any of claims 1-16, to a patient in need thereof, wherein the GFRα3-related condition or disease is prevented, ameliorated, or reduced in severity or frequency of occurrence, or the pain associated with the condition or disease is prevented, ameliorated, or reduced in severity or frequency of occurrence.

22. The method of claim 21, wherein the GFRα3-related condition or disease is selected from the group consisting of acute pain, chronic pain, neuropathic pain, inflammatory pain, a functional pain syndrome, arthritis, pancreatitis, osteoarthritis, cluster headaches, trigeminal neuralgia, herpetic neuralgia, general neuralgias, neurodegenerative disorders, movement

disorders, neuroendocrine disorders, ataxia, visceral pain, gout, post-herpetic neuralgia, diabetic neuropathy, sciatica, back pain, head or neck pain, severe or intractable pain, breakthrough pain, post-surgical pain, hereditary erythromelalgia, dental pain, rhinitis, cancer pain, complex regional pain syndrome (CRPS), inflammatory bowel disease (*e.g.* Crohn's disease or ulcerative colitis) and bladder disorders.

23. The method of claim 22, wherein the functional pain syndrome is selected from the group consisting of chronic low back pain, irritable bowel syndrome (IBS), fibromyalgia (FM), chronic fatigue syndrome, abdominal pain, temporomandibular joint disorder (TMJD), painful bladder syndrome (interstitial cystitis), functional gastrointestinal disorders/syndromes, functional chest pain syndrome, migraines and tension type headaches, chronic pelvic pain syndrome, painful prostate syndrome (chronic prostatitis), multiple chemical sensitivity syndrome and Gulf War syndrome.

24. The method of claim 22, wherein the cancer pain is associated with a cancer selected from the group consisting of endometrial cancer, prostate cancer, breast cancer, cervical cancer, liver cancer, pancreatic cancer, colon cancer, stomach cancer, uterine cancer, ovarian cancer, kidney cancer, non-small cell lung cancer, brain cancer, a leukemia, a lymphoma, bone cancer and pain associated with metastasis of a cancer.

23. The method of claim 21, wherein the antibody or antigen-binding fragment is administered to the patient in combination with a second therapeutic agent.

24. The method of claim 23, wherein the second therapeutic agent is selected from the group consisting of an opioid, a COX-2 inhibitor, a local anesthetic, an NMDA modulator, a cannabinoid receptor agonist, a P2X family modulator, a VR1 antagonist, a substance P antagonist, a second GFRα3 antagonist, a cytokine or cytokine receptor antagonist, a nerve growth factor (NGF) inhibitor (a small molecular inhibitor or an anti-NGF antibody), an inhibitor of BDNF, TrkA, TrkB or p75, aspirin, a NSAID, a steroid, morphine, a selective serotonin reuptake inhibitor (SSRI), a serotonin norepinephrine reuptake inhibitor (SNRI), a tricyclic, an inhibitor of a voltage-gated sodium channel (Na_v), a calcium channel inhibitor, a potassium channel inhibitor, a tumor necrosis factor (TNF) or TNF receptor inhibitor, an inhibitor of TWEAK (TNF-related WEAK inducer of apoptosis), a RET inhibitor, an inhibitor of a GDNF family ligand, an inhibitor of GFRα1, GFRα2 or GFRα4, an inhibitor of an acid sensing ion channel (ASIC1 or ASIC3), an anti-convulsant (gabapentin or pregabalin), an inhibitor of a prekineticin receptor (PROK1 and PROK2), a caspase inhibitor, a p38 inhibitor, an IKK1/2 inhibitor, CTLA-4Ig and a corticosteroid.

25. The method of claim 24, wherein the second GFRα3 antagonist is a small organic molecule, a polypeptide antagonist, a second antibody specific for GFRα3, a siRNA or an antisense molecule specific for GFRα3.

26. The method of claim 24, wherein the cytokine or cytokine receptor antagonist is an interleukin-1 (IL-1) antagonist, an IL-6 antagonist, or an IL-18 antagonist.

27. A pharmaceutical composition comprising an antibody or antigen-binding fragment thereof according to any one of claims 1 through 16 and a second therapeutic agent according to claim 24 and a pharmaceutically acceptable carrier or diluent.

28. The isolated antibody or antigen-binding fragment thereof according to any one of claims 1 through 16, or the pharmaceutical composition of either claim 20 or 27, for use in treating a GFRα3-related condition or disease, or the pain associated with the GFRα3-related condition or disease, wherein the GFRα3-related condition or disease is prevented, ameliorated, or reduced in severity or frequency of occurrence, or the pain associated with the condition or disease is prevented, ameliorated, or reduced in severity or frequency of occurrence.

29. The isolated antibody or antigen-binding fragment thereof for use according to claim 28, wherein the GFRα3-related condition or disease is selected from the group consisting of acute pain, chronic pain, neuropathic pain, inflammatory pain, a functional pain syndrome, arthritis, pancreatitis, osteoarthritis, cluster headaches, trigeminal neuralgia, herpetic neuralgia, general neuralgias, neurodegenerative disorders, movement disorders, neuroendocrine disorders, ataxia, visceral pain, gout, post-herpetic neuralgia, diabetic neuropathy, sciatica, back pain, head or neck pain, severe or intractable pain, breakthrough pain, post-surgical pain, hereditary erythromelalgia, dental pain, rhinitis, cancer pain, complex regional pain syndrome (CRPS), inflammatory bowel disease (*e.g.* Crohn's disease or ulcerative colitis) and bladder disorders.

30. Use of the isolated antibody or antigen-binding fragment thereof according to any one of claims 1 through 16, or the pharmaceutical composition of either of claim 20 or 27, in the manufacture of a medicament for treating a GFRα3-related condition or disease, or the pain associated with the GFRα3-related condition or disease, wherein the GFRα3-related condition or disease is prevented, ameliorated, or reduced in severity or frequency of occurrence, or the pain associated with the condition or disease is prevented, ameliorated, or reduced in severity or frequency of occurrence.

31. The use of the isolated antibody or antigen-binding fragment thereof according to claim 30, wherein the GFRα3-related condition or disease is selected from the group consisting of acute pain, chronic pain, neuropathic pain, inflammatory pain, a functional pain syndrome, arthritis,

pancreatitis, osteoarthritis, cluster headaches, trigeminal neuralgia, herpetic neuralgia, general neuralgias, neurodegenerative disorders, movement disorders, neuroendocrine disorders, ataxia, visceral pain, gout, post-herpetic neuralgia, diabetic neuropathy, sciatica, back pain, head or neck pain, severe or intractable pain, breakthrough pain, post-surgical pain, hereditary erythromelalgia, dental pain, rhinitis, cancer pain, complex regional pain syndrome (CRPS), inflammatory bowel disease (*e.g.* Crohn's disease or ulcerative colitis) and bladder disorders.

CLAIMS

What is claimed is:

1. An isolated monoclonal antibody or an antigen-binding fragment thereof that specifically binds to glial cell-line derived neurotrophic factor (GDNF) family receptor alpha 3 (GFRα3), wherein the antibody comprises:
(a) a heavy chain complementarity determining region (HCDR) 1 domain of SEQ ID NO: 148;
(b) a HCDR2 domain of SEQ ID NO: 150;
(c) a HCDR3 domain of SEQ ID NO: 152;
(d) a light chain complementarity determining region (LCDR) 1 domain of SEQ ID NO: 156;
(e) a LCDR2 domain of SEQ ID NO: 158; and
(f) a LCDR3 domain of SEQ ID NO: 160.

2. The isolated monoclonal antibody or an antigen-binding fragment thereof of claim 1, wherein the antibody does not cross-react with human GFRα1 or human GFRα2.

3. The isolated monoclonal antibody or an antigen-binding fragment thereof of claim 1, wherein the antibody comprises (a) a heavy chain variable region (HCVR) of SEQ ID NO: 146 and (b) a light chain variable region (LCVR) of SEQ ID NO: 154.

4. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment comprises a HCVR of SEQ ID NO: 146.

5. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment comprises a LCVR of SEQ ID NO: 154.

6. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of claim 1 and a pharmaceutically acceptable carrier or diluent.