

Claims

1. An isolated antibody, or an antigen binding fragment thereof, which binds to interleukin-11 receptor subunit α (IL-11R α), wherein the at least one antibody, or antigen binding fragment thereof, comprises:

a heavy chain variable region (V_H) that comprises complementary determining region V_H CDR1, V_H CDR2, and V_H CDR3 sequences selected from **Table A1** and variants thereof which specifically bind to IL-11R α ; and

a light chain variable region (V_L) that comprises complementary determining region V_L CDR1, V_L CDR2, and V_L CDR3 sequences selected from **Table A1** and variants thereof which specifically bind to IL-11R α .

2. The isolated antibody, or antigen binding fragment thereof, of claim 1, wherein:

the V_H CDR1, V_H CDR2, and V_H CDR3 sequences comprise SEQ ID NOs: 1-3, respectively, and the V_L CDR1, V_L CDR2, and V_L CDR3 sequences comprise SEQ ID NOs: 4-6, respectively;

the V_H CDR1, V_H CDR2, and V_H CDR3 sequences comprise SEQ ID NOs: 7-9, respectively, and the V_L CDR1, V_L CDR2, and V_L CDR3 sequences comprise SEQ ID NOs: 10-12, respectively;

the V_H CDR1, V_H CDR2, and V_H CDR3 sequences comprise SEQ ID NOs: 13-15, respectively, and the V_L CDR1, V_L CDR2, and V_L CDR3 sequences comprise SEQ ID NOs: 16-18, respectively;

the V_H CDR1, V_H CDR2, and V_H CDR3 sequences comprise SEQ ID NOs: 19-21, respectively, and the V_L CDR1, V_L CDR2, and V_L CDR3 sequences comprise SEQ ID NOs: 22-24, respectively;

the V_H CDR1, V_H CDR2, and V_H CDR3 sequences comprise SEQ ID NOs: 25-27, respectively, and the V_L CDR1, V_L CDR2, and V_L CDR3 sequences comprise SEQ ID NOs: 28-30, respectively;

the V_H CDR1, V_H CDR2, and V_H CDR3 sequences comprise SEQ ID NOs: 31-33, respectively, and the V_L CDR1, V_L CDR2, and V_L CDR3 sequences comprise SEQ ID NOs: 34-36, respectively;

the V_H CDR1, V_H CDR2, and V_H CDR3 sequences comprise SEQ ID NOs: 34-39, respectively, and the V_L CDR1, V_L CDR2, and V_L CDR3 sequences comprise SEQ ID NOs: 40-42, respectively;

the V_H CDR1, V_H CDR2, and V_H CDR3 sequences comprise SEQ ID NOs: 43-45, respectively, and the V_L CDR1, V_L CDR2, and V_L CDR3 sequences comprise SEQ ID NOs: 46-48, respectively;

the V_H CDR1, V_H CDR2, and V_H CDR3 sequences comprise SEQ ID NOs: 49-51, respectively, and the V_L CDR1, V_L CDR2, and V_L CDR3 sequences comprise SEQ ID NOs: 52-54, respectively;

the V_H CDR1, V_H CDR2, and V_H CDR3 sequences comprise SEQ ID NOs: 55-57, respectively, and the V_L CDR1, V_L CDR2, and V_L CDR3 sequences comprise SEQ ID NOs: 58-60, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 61-63, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 64-66, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 67-69, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 70-72, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 73-75, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 76-78, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 79-81, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 82-84, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 85-87, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 88-90, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 91-93, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 94-96, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 97-99, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 100-102, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 103-105, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 106-108, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 109-111, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 112-114, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 115-117, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 118-120, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 121-123, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 124-126, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 127-129, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 130-132, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 133-135, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 136-138, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 139-141, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 142-144, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 145-147, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 148-150, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 151-153, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 154-156, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 157-159, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 160-162, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 163-165, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 166-168, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 169-171, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 172-174, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 175-177, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 178-180, respectively;

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 181-183, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 184-186, respectively; or

the V_HCDR1, V_HCDR2, and V_HCDR3 sequences comprise SEQ ID NOs: 187-189, respectively, and the V_LCDR1, V_LCDR2, and V_LCDR3 sequences comprise SEQ ID NOs: 190-192, respectively.

3. The isolated antibody, or antigen binding fragment thereof, of claim 1 or 2, wherein the V_H comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to a sequence selected from **Table A2**, optionally wherein the V_H has 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 alterations in the framework regions.

4. The isolated antibody, or antigen binding fragment thereof, of any one of claims 1-3, wherein the V_L comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to a sequence selected from **Table A2**, optionally wherein the V_L has 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 alterations in the framework regions.

5. The isolated antibody, or antigen binding fragment thereof, of any one of claims 1-4, wherein:

the V_H comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 193, and the V_L comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 194;

the V_H comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 195, and the V_L comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 196;

the V_H comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 197, and the V_L comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 198;

the V_H comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 243, and the V_L comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 244;

the V_H comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 245, and the V_L comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 246;

the V_H comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 247, and the V_L comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 248;

the V_H comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 249, and the V_L comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 250;

the V_H comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 251, and the V_L comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 252;

the V_H comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 253, and the V_L comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 254; or

the V_H comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 255, and the V_L comprises a sequence at least 80, 85, 90, 95, 97, 98, 99, or 100% identical to SEQ ID NO: 256.

6. The isolated antibody, or antigen binding fragment thereof, of any one of claims 1-5, which binds to human IL-11R α (see **Table B1**).

7. The isolated antibody, or antigen binding fragment thereof, of claim 6, which binds to a fibronectin domain III of human IL-11R α , or approximately residues 112-219 of SEQ ID NO: 257.

8. The isolated antibody, or antigen binding fragment thereof, of any one of claims 1-7, which has one or more of the following characteristics:

has a binding affinity for human IL-11R α of less than about 500, 400, 300, 200, 100, 90, 80, 70, 60, 50, 40, or 30 pM, and optionally has increased binding affinity for human IL-11R α relative to that of the TS7 and 8E2 antibodies;

antagonizes the binding and/or signaling activity between IL-11R α and IL-11, and optionally has increased potency as an IL-11 signaling antagonist relative to that of the TS7 and 8E2 antibodies;
reduces IL-11R α /gp130 dimerization or complex formation, optionally in a cell-based assay;
and/or
has reduced N-linked glycosylation in V_LCDR3, optionally relative to the TS7 and 8E2 antibodies.

9. The isolated antibody, or antigen binding fragment thereof, of any one of claims 1-8, comprising an IgA (including subclasses IgA1 and IgA2), IgD, IgE, IgG (including subclasses IgG1, IgG2, IgG3, and IgG4), or IgM Fc domain, optionally a human Fc domain, or a hybrid and/or variant thereof.

10. The isolated antibody, or antigen binding fragment thereof, of any one of claims 1-9, comprising an IgG Fc domain with high effector function in humans, optionally an IgG1 or IgG3 Fc domain.

11. The isolated antibody, or antigen binding fragment thereof, of any one of claims 1-9, comprising an IgG Fc domain with low effector function in humans, optionally an IgG2 or IgG4 Fc domain.

12. The isolated antibody, or antigen binding fragment thereof, of any one of claims 1-9, comprising a human IgG1 or IgG4 Fc domain, optionally selected from **Table F1**.

13. The isolated antibody, or antigen binding fragment thereof, of any one of claims 1-12, which is a monoclonal antibody.

14. The isolated antibody, or antigen binding fragment thereof, of any one of claims 1-13, which is a humanized antibody,

optionally wherein the antibody, or antigen binding fragment thereof, is a humanized monoclonal antibody that comprises a human IgG4 Fc domain with an S228P mutation (EU numbering).

15. The isolated antibody, or antigen binding fragment thereof, of any one of claims 1-14, which is selected from an Fv fragment, a single chain Fv (scFv) polypeptide, an adnectin, an anticalin, an

aptamer, an avimer, a camelid antibody, a designed ankyrin repeat protein (DARPin), a minibody, a nanobody, and a unibody.

16. An isolated polynucleotide encoding the isolated antibody, or antigen binding fragment thereof, according to any one of claims 1-15, an expression vector comprising the isolated polynucleotide, or an isolated host cell comprising the vector.

17. A pharmaceutical composition, comprising the isolated antibody, or antigen binding fragment thereof, of any one of claims 1-15, and a pharmaceutically-acceptable carrier.

18. The pharmaceutical composition of claim 17, wherein the composition has a purity of at least about 80%, 85%, 90%, 95%, 98%, or 99% on a protein basis with respect to the at least one antibody or antigen binding fragment, and is substantially aggregate- and endotoxin-free.

19. The pharmaceutical composition of claim 17 or 18, wherein the composition has reduced or undetectable heterogeneity of N-linked glycosylation (optionally relative to the TS7 and 8E2 antibodies), optionally in the V_LCDR3 sequence.

20. The pharmaceutical composition of any one of claims 17-19, wherein the composition is a sterile, injectable solution, optionally suitable for intravenous, intramuscular, subcutaneous, or intraperitoneal administration.

21. A method of treating a disease or condition in a subject in need thereof, comprising administering to the subject a pharmaceutical composition of any one of claims 17-20.

22. The method of claim 21, wherein the disease or condition is an IL-11-associated or IL-11-mediated disease or condition.

23. The method of claim 21 or 22, wherein the disease or condition is a cancer, an inflammatory disease, an autoimmune disease, a wasting disease, a bone disease, or fibrosis.

24. The method of claim 23, wherein the disease is a cancer, optionally a cancer that expresses or overexpresses IL-11R α and/or IL-11, optionally wherein the cancer displays IL-11R α /IL-11-dependent growth, adhesion, migration, invasion, and/or chemoresistance.

25. The method of claim 24, wherein the cancer is selected from one or more of bone cancer, prostate cancer, melanoma (e.g., metastatic melanoma), pancreatic cancer, small cell lung cancer, non-small cell lung cancer (NSCLC), mesothelioma, leukemia (e.g., lymphocytic leukemia, chronic myelogenous leukemia, acute myeloid leukemia, relapsed acute myeloid leukemia, hairy cell leukemias, acute lymphoblastic leukemias), lymphoma (e.g., non-Hodgkin's lymphomas, Hodgkin's lymphoma), hepatoma (hepatocellular carcinoma), sarcoma, B-cell malignancy, breast cancer, ovarian cancer, colorectal cancer, glioma, glioblastoma multiforme, meningioma, pituitary adenoma, vestibular schwannoma, primary CNS lymphoma, primitive neuroectodermal tumor (medulloblastoma), kidney cancer (e.g., renal cell carcinoma), bladder cancer, uterine cancer, esophageal cancer, brain cancer, head and neck cancers, cervical cancer, testicular cancer, thyroid cancer, and stomach cancer.

26. The method of claim 24 or 25, wherein the cancer is a metastatic cancer, optionally a metastatic cancer which has metastasized to the bone.

27. The method of claim 23, wherein the inflammatory disease is selected from one or more of airway or lung inflammation (e.g., inflammatory lung disease), asthma, rhinitis, chronic obstructive pulmonary disorder (COPD), dermatitis, psoriasis, hepatitis, gastric inflammation, irritable bowel syndrome (IBS), ulcerative colitis, Crohn's disease, colitis, diverticulitis, lupus erythematosus, nephritis, Parkinson's disease, multiple sclerosis (MS), Alzheimer's disease, arthritis, rheumatoid arthritis, sepsis, infection-induced inflammation, cardiovascular diseases such as atherosclerosis and vasculitis, diabetes, and gout.

28. The method of claim 23, wherein the autoimmune disease is selected from one or more of arthritis (including rheumatoid arthritis, reactive arthritis), systemic lupus erythematosus (SLE), psoriasis, inflammatory bowel disease (IBD), ulcerative colitis, Crohn's disease, encephalomyelitis, uveitis, myasthenia gravis, multiple sclerosis, insulin dependent diabetes, Addison's disease, celiac disease, chronic fatigue syndrome, autoimmune hepatitis, autoimmune alopecia, ankylosing spondylitis, fibromyalgia, pemphigus vulgaris, Sjogren's syndrome, Kawasaki's Disease, hyperthyroidism/Graves' disease, hypothyroidism/Hashimoto's disease, endometriosis, scleroderma, pernicious anemia, Goodpasture syndrome, Guillain-Barré syndrome, Wegener's disease, glomerulonephritis, aplastic anemia (including multiply transfused aplastic anemia patients), paroxysmal nocturnal hemoglobinuria, myelodysplastic syndrome, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, Evan's syndrome, Factor VIII inhibitor syndrome, systemic vasculitis, dermatomyositis, polymyositis, rheumatic

fever, autoimmune lymphoproliferative syndrome (ALPS), autoimmune bullous pemphigoid, Parkinson's disease, sarcoidosis, vitiligo, primary biliary cirrhosis, and autoimmune myocarditis.

29. The method of claim 23, wherein the wasting disease is selected from one or more of cachexia, optionally cachexia associated with cancer or renal failure, and sarcopenia.

30. The method of claim 23, wherein the bone disease is selected from osteoporosis (including post-menopausal osteoporosis), bone fracture, Paget's disease of bone, and bone resorption/damage associated with cancer or cancer therapy, including chemotherapy, hormone ablation, and hormone inhibition.

31. The method of claim 23, wherein the fibrosis is selected from fibrosis of the lungs, cardiovascular system, liver, brain, joints (optionally knee, hip, ankle, foot joints, shoulder, elbow, wrist, hand joints, or spinal vertebrae), intestine, skin, kidney, liver, thyroid, bone marrow, retroperitoneum, and eye.

32. The method of claim 31, wherein the fibrosis of the lungs is selected from fibrothorax, pulmonary fibrosis (optionally cystic fibrosis or interstitial lung disease (ILD)), autosomal recessive genetic disease optionally Hermansky-Pudlak syndrome, and radiation-induced lung injury.

33. The method of claim 32, wherein the ILD is idiopathic ILD, optionally selected from idiopathic pulmonary fibrosis (IPF), desquamative interstitial pneumonia (DIP), acute interstitial pneumonia (AIP) or Hamman-Rich syndrome, nonspecific interstitial pneumonia (NSIP), respiratory bronchiolitis-associated interstitial lung disease (RB-ILD), cryptogenic organizing pneumonia (COP), and lymphoid interstitial pneumonia (LIP).

34. The method of claim 32, wherein the ILD is secondary ILD, optionally selected from ILD related to connective tissue and autoimmune diseases (optionally sarcoidosis, rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, polymyositis, dermatomyositis, or antisynthetase syndrome), inhaled substances (optionally silicosis, asbestosis, berylliosis, industrial printing chemicals, or chronic hypersensitivity pneumonitis), drugs (optionally antibiotics, chemotherapeutics, or anti-arrhythmic agents), infections (optionally SARS CoV-2, atypical pneumonia, pneumocystis pneumonia, tuberculosis, Chlamydia trachomatis, or respiratory syncytial virus), malignancies (optionally lymphangitic carcinomatosis), and pediatric ILDs (optionally developmental disorders, growth

abnormalities deficient alveolarization, infant conditions of undefined cause, and ILD related to alveolar surfactant region).

35. The method of claim 31, wherein the fibrosis of the cardiovascular system is myocardial fibrosis (optionally interstitial fibrosis or replacement fibrosis).

36. An isolated antibody, or an antigen binding fragment thereof, which binds to interleukin-11 receptor subunit α (IL-11R α), wherein the antibody, or antigen binding fragment thereof, comprises a heavy chain variable region (VH) comprising an amino acid sequence at least 80% identical to SEQ ID NO: 233 and a light chain variable region (VL) comprising an amino acid sequence at least 80% identical to SEQ ID NO: 234, wherein the antibody, or antigen binding fragment thereof, binds to human IL-11R α with a binding affinity (KD) of less than about 100pM.

37. The isolated antibody, or an antigen binding fragment thereof, of claim 36, wherein the VH comprises complementary determining region VHCDR1, VHCDR2, and VHCDR3 sequences and the VL comprises complementary determining region VLCDR1, VLCDR2, and VLCDR3 sequences, wherein:

- a. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 25-27, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 28-30, respectively;
- b. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 121-123, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 124-126, respectively;
- c. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 133-135, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 136-138, respectively;
- d. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 169-171, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 172-174, respectively; or
- e. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 181-183, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 184-186, respectively.

38. The isolated antibody, or antigen binding fragment thereof, of claim 36 or 37, which binds to a fibronectin domain III of human IL-11R α , or approximately residues 112-219 of SEQ ID NO: 257.

39. The isolated antibody, or antigen binding fragment thereof, of any one of claims 36-38, comprising an IgA (including subclasses IgA1 and IgA2), IgD, IgE, IgG (including subclasses IgG1, IgG2, IgG3, and IgG4), or IgM Fc domain, optionally a human Fc domain, a hybrid and/or variant thereof.

40. The isolated antibody, or antigen binding fragment thereof, of any one of claims 36-39, comprising a human IgG1 or IgG4 Fc domain, optionally wherein the human IgG4 Fc domain comprises SEQ ID NO: 258 or 259.

41. The isolated antibody, or antigen binding fragment thereof, of any one of claims 36-40, which is a monoclonal antibody.

42. The isolated antibody, or antigen binding fragment thereof, of any one of claims 36-41, which is a humanized antibody, optionally wherein the antibody, or antigen binding fragment thereof, is a humanized monoclonal antibody that comprises a human IgG4 Fc domain with an S228P mutation (EU numbering).

43. The isolated antibody, or antigen binding fragment thereof, of any one of claims 36-40, which is selected from an Fv fragment, a single chain Fv (scFv) polypeptide, an adnectin, an anticalin, an aptamer, an avimer, a camelid antibody, a designed ankyrin repeat protein (DARPin), a minibody, a nanobody, and a unibody.

44. An isolated polynucleotide encoding the isolated antibody, or antigen binding fragment thereof, of any one of claims 36-43.

45. A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and the isolated antibody, or antigen binding fragment thereof, of any one of claims 36-43.

46. An isolated antibody, or an antigen binding fragment thereof, which binds to interleukin-11 receptor subunit α (IL-11R α), wherein the antibody, or antigen binding fragment thereof, comprises a

heavy chain variable region (VH) comprising an amino acid sequence at least 80% identical to SEQ ID NO: 209 and a light chain variable region (VL) comprising an amino acid sequence at least 80% identical to SEQ ID NO: 210 and wherein the antibody, or antigen binding fragment thereof, inhibits IL-11 signaling with a half-maximal inhibitory concentration (IC₅₀) of about 0.25µg/mL or less using a cell-based reporter assay.

47. The isolated antibody, or an antigen binding fragment thereof, of claim 46, wherein the VH comprises complementary determining region VHCDR1, VHCDR2, and VHCDR3 sequences and the VL comprises complementary determining region VLCDR1, VLCDR2, and VLCDR3 sequences, wherein:

- a. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 25-27, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 28-30, respectively;
- b. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 49-51, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 52-54, respectively; or
- c. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 73-75, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 76-78, respectively.

48. The isolated antibody, or antigen binding fragment thereof, of claim 46 or 47, which binds to a fibronectin domain III of human IL-11R α , or approximately residues 112-219 of SEQ ID NO: 257.

49. The isolated antibody, or antigen binding fragment thereof, of any one of claims 46-48, comprising an IgA (including subclasses IgA1 and IgA2), IgD, IgE, IgG (including subclasses IgG1, IgG2, IgG3, and IgG4), or IgM Fc domain, optionally a human Fc domain, a hybrid and/or variant thereof.

50. The isolated antibody, or antigen binding fragment thereof, of any one of claims 46-49, comprising a human IgG1 or IgG4 Fc domain, optionally wherein the human IgG4 Fc domain comprises SEQ ID NO: 258 or 259.

51. The isolated antibody, or antigen binding fragment thereof, of any one of claims 46-50, which is a monoclonal antibody.

52. The isolated antibody, or antigen binding fragment thereof, of any one of claims 46-51, which is a humanized antibody, optionally wherein the antibody, or antigen binding fragment thereof, is a humanized monoclonal antibody that comprises a human IgG4 Fc domain with an S228P mutation (EU numbering).

53. The isolated antibody, or antigen binding fragment thereof, of any one of claims 46-50, which is selected from an Fv fragment, a single chain Fv (scFv) polypeptide, an adnectin, an anticalin, an aptamer, an avimer, a camelid antibody, a designed ankyrin repeat protein (DARPin), a minibody, a nanobody, and a unibody.

54. An isolated polynucleotide encoding the isolated antibody, or antigen binding fragment thereof, of any one of claims 46-53.

55. A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and the isolated antibody, or antigen binding fragment thereof, of any one of claims 46-53.

56. A method of treating a disease or condition in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising a pharmaceutically-acceptable carrier and an isolated antibody, or antigen binding fragment thereof, which binds to interleukin-11 receptor subunit α (IL-11R α), wherein the antibody, or antigen binding fragment thereof, comprises a heavy chain variable region (VH) comprising an amino acid sequence at least 80% identical to SEQ ID NO: 233 and a light chain variable region (VL) comprising an amino acid sequence at least 80% identical to SEQ ID NO: 234, wherein the antibody, or antigen binding fragment thereof, binds to human IL-11R α with a binding affinity (KD) of less than about 100pM.

57. The method of claim 56, wherein the VH comprises complementary determining region VHCDR1, VHCDR2, and VHCDR3 sequences and the VL comprises complementary determining region VLCDR1, VLCDR2, and VLCDR3 sequences, wherein:

- a. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 25-27, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 28-30, respectively;

b. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 121-123, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 124-126, respectively;

c. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 133-135, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 136-138, respectively;

d. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 169-171, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 172-174, respectively; or

e. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 181-183, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 184-186, respectively.

58. The method of claim 56 or 57, wherein the disease or condition is an IL-11-associated or IL-11-mediated disease or condition.

59. The method of any one of claims 56-58, wherein the disease or condition is a cancer, an inflammatory disease, an autoimmune disease, a wasting disease, a bone disease, or a fibrotic disease.

60. A method of treating a disease or condition in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising a pharmaceutically-acceptable carrier and an isolated antibody, or antigen binding fragment thereof, which binds to interleukin-11 receptor subunit α (IL-11R α), wherein the antibody, or antigen binding fragment thereof, comprises a heavy chain variable region (VH) comprising an amino acid sequence at least 80% identical to SEQ ID NO: 209 and a light chain variable region (VL) comprising an amino acid sequence at least 80% identical to SEQ ID NO: 210, wherein the antibody, or antigen binding fragment thereof, inhibits IL-11 signaling with a half-maximal inhibitory concentration (IC₅₀) of about 0.25 μ g/mL or less using a cell-based reporter assay.

61. The method of claim 60, wherein the VH comprises complementary determining region VHCDR1, VHCDR2, and VHCDR3 sequences and the VL comprises complementary determining region VLCDR1, VLCDR2, and VLCDR3 sequences, wherein:

a. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 25-27, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 28-30, respectively;

b. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 49-51, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 52-54, respectively; or

c. the VHCDR1, VHCDR2, and VHCDR3 sequences comprise SEQ ID NOs: 73-75, respectively, and the VLCDR1, VLCDR2, and VLCDR3 sequences comprise SEQ ID NOs: 76-78, respectively.

62. The method of claim 60 or 61, wherein the disease or condition is an IL-11-associated or IL-11-mediated disease or condition.

63. The method of any one of claims 60-62, wherein the disease or condition is a cancer, an inflammatory disease, an autoimmune disease, a wasting disease, a bone disease, or a fibrotic disease.