(rebound) after drug withdrawal are not uncommon. Adverse events do occur and many patients eventually require rehabilitative surgery conducted when their condition has transitioned to inactive TAO. Accordingly, there is still a need to provide alternative therapies for TAO and its related symptoms.

SUMMARY

[0007] An antibody, or antigen binding fragment thereof, is provided herein. In one aspect, the present disclosure provides an antibody, or antigen binding fragment thereof that binds to insulin-like growth factor I receptor (IGF-1R), comprising: (i) a heavy chain complementarity-determining region (HCDR) sequence selected from the group consisting of SEQ ID NO: 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, and 170; and a light chain CDR (LCDR) sequence selected from the group consisting of SEQ ID NO: 171, 172, 173, 174, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, and 198; or (ii) a heavy chain variable region comprising HCDRl, HCDR2, and HCDR3 sequences, wherein the HCDR1 sequence has the amino acid sequence of SEQ ID NO: 138, 139, 140, 141, 142, 143, 144, 145, 146, or 147; the HCDR2 has the amino acid sequence of SEQ ID NO: 148, 149, 150, 151, 152, 153, or 154; and the HCDR3 sequence has the amino acid sequence of SEQ ID NO: 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, or 170; or variants of any of the foregoing; and a light chain variable region comprising LCDR1, LCDR2, and LCDR3 sequences, wherein the LCDR1 sequence has the amino acid sequence SEQ ID NO: 171, 172, 173, 174, 176, 177, 178, 179, 180, or 181; the LCDR2 sequence has the amino acid sequence of SEQ ID NO: 182, 183, 184, 185, 186, 187, 188, 189, or 190; and the LCDR3 sequence has the amino acid sequence of SEQ ID NO: 191, 192, 193, 194, 195, 196, 197, or 198; or variants of any of the foregoing. In some examples, the antibody, or antigen binding fragment thereof, comprises a heavy chain complementarity-determining region sequence selected from the group consisting of SEQ ID NO: 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, and 170; and a light chain CDR sequence selected from the group consisting of SEQ ID NO: 171, 172,

173, 174, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, and 198.

[0007a] In another aspect, the present disclosure provides an antibody, or antigen binding fragment thereof, comprising: (i) a heavy chain variable region (VH) sequence selected from the group consisting of SEQ ID NO: 1, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64 and 65; and a light chain variable region (VL) sequence selected from the group consisting of SEQ ID NO: 2, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, and 54; or (ii) a VH and VL pair comprising the amino acid sequence of SEQ ID NOs:66-137, or a variant thereof.

[0007b] In yet another aspect, the present disclosure provides a nucleic acid molecule encoding an antibody, or antigen binding fragment thereof, as described herein. In yet another aspect, the present disclosure provides a vector comprising the nucleic acid molecule as described herein. In yet another aspect, the present disclosure provides a cell comprising the nucleic comprising the nucleic acid molecule as described herein or the vector as described herein.

[0007c] In yet another aspect, the present disclosure provides a pharmaceutical composition comprising the antibody as described herein or a nucleic acid molecule encoding the same, wherein the composition is an injectable pharmaceutical composition, optionally wherein the pharmaceutically composition is to suitable to be administered (i) intravenously or subcutaneously; or (ii) directly to the eye, the anterior chamber of the eye, the vitreous chamber of the eye, the suprachoroidal space, or the retro-orbital sinus; further optionally wherein the injection is a intravitreal injection, intraorbital injection, retro-orbital injection, suprachoroidal injection, or intracameral injection.

[0007d] In yet another aspect, the present disclosure provides an antibody, or antigen binding fragment thereof, as described herein, or a pharmaceutical composition as described herein for use as a medicament. In yet another aspect, the present disclosure provides a use of an antibody, or antigen binding fragment thereof, as described herein, or a pharmaceutical composition as described herein in the manufacture of a medicament for treating or reducing the severity of, thyroid-associated ophthalmopathy (TAO), or a symptom thereof, said use optionally: (i) comprising reducing Clinical Activity Score (CAS) of thyroid-associated ophthalmopathy (TAO), such as reducing Clinical Activity Score (CAS) by at least 2 points or reducing Clinical Activity Score (CAS) to one (1) or reducing Clinical Activity Score (CAS) to zero (0); (ii) resulting in an

improvement of greater than or equal to 8 points on the Graves' Ophthalmopathy Quality of Life (GO-QoL) assessment, improvement on the Functioning subscale of the GO-QoL, or improvement of the Appearance subscale of the GO-QoL; or (iii) resulting in reducing proptosis in an eye in a subject with thyroid-associated ophthalmopathy (TAO), optionally wherein proptosis is reduced by at least 2 mm, 3 mm or 4 mm; or (iv) resulting in reducing the severity of diplopia in a subject with thyroid-associated ophthalmopathy (TAO), optionally wherein the diplopia is constant diplopia, inconstant diplopia or intermittent diplopia, further optionally wherein the improvement in or reduction in severity of diplopia is sustained at least 20 weeks or at least 50 weeks after discontinuation of antibody administration.

[0007e] In yet another aspect, the present disclosure provides a use of an antibody, or antigen binding fragment thereof, as described herein, or a pharmaceutical composition as described herein, in the manufacture of a medicament for treating thyroid eye disease in a subject, optionally wherein (i) the antibody has a serum concentration in the subject of at least, or about, 70 μg/ml, 75 μg/ml, 80 μg/ml, 85 μg/ml, 90 μg/ml, 95 μg/ml, 100 μg/ml, or 105 μg/ml at least 1, 2, or 3 week after administration, further optionally wherein the antibody or the pharmaceutical composition is to be administered intravenously, still further optionally wherein the antibody or the pharmaceutical composition is to be administered at a dose of about 20 mg/kg, yet further optionally wherein the antibody or the pharmaceutical composition is to be administered at least, or about, once a week, once every two weeks, once every 3 weeks, or once every 4 weeks; or (ii) said antibody is to be administered at a dosage of 1 mg/kg to 5 mg/kg antibody or 5 mg/kg to 10 mg/kg as a first dose; or (iii) said antibody is to be administered at a dosage of 5 mg/kg to 20 mg/kg in subsequent doses; or (iv) said antibody is to be administered at about 10 mg/kg antibody as a first dose; and about 20 mg/kg antibody in subsequent doses, optionally wherein said subsequent doses are to be administered every three weeks for at least 21 weeks.

[0007f] In yet another aspect, the present disclosure provides a use of an antibody, or antigen binding fragment thereof, as described herein, or a pharmaceutical composition as described herein, in the manufacture of a medicament for increasing the internalization of IGF-1R on a cell in a subject, optionally wherein the subject has or is at risk of thyroid eye disease (TED). In yet another aspect, the present disclosure provides a use of an antibody, or antigen binding fragment thereof, as described herein, or a pharmaceutical composition as described herein, in the manufacture of a medicament for inhibiting IGF-1 stimulated receptor phosphorylation on a cell

in a subject, optionally wherein the subject has or is at risk of thyroid eye disease (TED), further optionally wherein: (i) the antibody has an IC50 of less than, or equal to, about 0.2 nm, 0.15 nm, 0.10 nm, 0.09 nm, optionally wherein the IC50 is measured in an *in vitro* assay, such as an assay as provided for herein, and/or (ii) the cell is an A549 cell or a HOCF cell. In yet another aspect, the present disclosure provides a use of an antibody, or antigen binding fragment thereof, as described herein, or a pharmaceutical composition as described herein, in the manufacture of a medicament for inhibiting IGF-1 induced receptor autophosphorylation in a cell in a subject by at least 95%, 96%, 97%, 98%, or 99% or by 100%, wherein the inhibition of the IGF-1 induced receptor autophosphorylation is measured as compared to the induced receptor autophosphorylation in the absence of the antibody or the pharmaceutical composition, optionally wherein the subject has or is at risk of thyroid eye disease (TED).

[0008] In some examples, an antibody, or antigen binding fragment thereof, is provided herein comprising a heavy chain variable region (VH) sequence selected from the group consisting of SEQ ID NO: 1, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64 and 65; and a light chain variable region (VL) sequence selected from the group consisting of SEQ ID NO: 2, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, and 54.

[0009] In some examples, any antibody or antigen binding fragment thereof provided herein binds to insulin-like growth factor I receptor (IGF-1R). In some examples, the antibody is a monoclonal antibody. In some examples, the antibody is a humanized antibody. In some examples, the antibody is a scFv antibody.

[0010] In some examples, the antibody, or antigen binding fragment thereof, comprises a VH peptide comprising an amino acid sequence as set forth in SEQ ID NOs: 1, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64 or 65, or any variant thereof.

[0011] In some examples, the antibody, or antigen binding fragment thereof, comprises a VL peptide comprising an amino acid sequence as set forth in SEQ ID NOs: 2, 30, 31,

32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, or 54, or any variant thereof.

[0012] In some examples, an antibody, or antigen binding fragment thereof, is provided, comprising: (i) a heavy chain variable region comprising HCDRl, HCDR2, and HCDR3 sequences, wherein the HCDR1 sequence has the amino acid sequence of SEQ ID NO: 138, 139, 140, 141, 142, 143, 144, 145, 146, or 147; the HCDR2 has the amino acid sequence of SEQ ID NO: 148, 149, 150, 151, 152, 153, or 154; and the HCDR3 sequence has the amino acid sequence of SEQ ID NO: 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, or 170; or variants of any of the foregoing; and (ii) a light chain variable region comprising LCDR1, LCDR2, and LCDR3 sequences, wherein the LCDR1 sequence has the amino acid sequence SEQ ID NO: 171, 172, 173, 174, 176, 177, 178, 179, 180, or 181; the LCDR2 sequence has the amino acid sequence of SEQ ID NO: 182, 183, 184, 185, 186, 187, 188, 189, or 190; and the LCDR3 sequence has the amino acid sequence of SEQ ID NO: 191, 192, 193, 194, 195, 196, 197, or 198; or variants of any of the foregoing.

[0013] In some examples, an antibody, or antigen binding fragment thereof, is provided comprising a VH and VL pair comprising the amino acid sequence of SEQ ID NOs:66-137, or a variant thereof.

[0014] In some examples, a method of treating or reducing the severity of, thyroid-associated ophthalmopathy (TAO), or a symptom thereof is provided, comprising administering to a subject any antibody disclosed herein or any pharmaceutical composition disclosed herein.

[0015] In some examples, a method of reducing proptosis in an eye in a subject with thyroid-associated ophthalmopathy (TAO) is provided, comprising administering to a subject any antibody disclosed herein or any pharmaceutical composition disclosed herein.

[0016] In some examples, a method of treating thyroid eye disease in a subject is provided, comprising administering to a subject an administering to a subject any antibody disclosed herein or any pharmaceutical composition disclosed herein.

[0017] In some examples, a method of reducing Clinical Activity Score (CAS) of thyroid-associated ophthalmopathy (TAO) in a subject is provided, comprising administering to a subject any antibody disclosed herein or any pharmaceutical composition disclosed herein.

[0018] In some examples, a method of a) reducing proptosis by at least 2 mm and b) reducing the clinical activity score (CAS) in a subject with thyroid-associated ophthalmopathy

(TAO) is provided, comprising administering to a subject an administering to a subject any antibody disclosed herein or any pharmaceutical composition disclosed herein.

[0019] In some examples, a method of treating or reducing the severity of diplopia in a subject with thyroid-associated ophthalmopathy (TAO) is provided, comprising administering to a subject any antibody disclosed herein or any pharmaceutical composition disclosed herein.

[0020] In some examples, a method of increasing the internalization of IGF-1R on a cell is provided, the method comprising contacting the cell with any antibody disclosed herein or any pharmaceutical composition disclosed herein.

[0021] In some examples, a method of inhibiting IGF-1 stimulated receptor phosphorylation on a cell is provided, the method comprising contacting the cell with any antibody disclosed herein or any pharmaceutical composition disclosed herein.

[0022] In some examples, a method of treating thyroid eye disease in a subject is provided, the method comprising administering any antibody disclosed herein or any pharmaceutical composition disclosed herein to the subject, wherein the antibody has a serum concentration in the subject of at least, or about, 70 μg/ml, 75 μg/ml, 80 μg/ml, 85 μg/ml, 90 μg/ml, 95 μg/ml, 100 μg/ml, or 105 μg/ml at least 1, 2, or 3 week after administration.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] FIG. 1 illustrates the NHP (non-human primates) serum concentration of various antibodies and embodiments as provided for herein.

[0024] FIG. 2 illustrates various properties of antibodies as provided for herein.

[0025] FIG. 3 illustrates various properties of antibodies as provided for herein.

DETAILED DESCRIPTION

[0026] Provided herein are antibodies that bind and modulate the activity of IGF-1R. The antibodies can be used, for example, to treat thyroid eye disease.

[0027] As used herein, "Thyroid-associated Ophthalmopathy" (TAO), "Thyroid Eye Disease" (TED), "Graves' Ophthalmopathy" or "Graves' Orbitopathy" (GO) refer to the same disorder or condition and are used interchangeably. They all refer to the inflammatory orbital pathology associated with some autoimmune thyroid disorders, most commonly with "Graves' Disease" (GD), but sometimes with other diseases, e.g. Hashimoto's thyroiditis.

WHAT IS CLAIMED IS:

1. An antibody, or antigen binding fragment thereof that binds to insulin-like growth factor I receptor (IGF-1R), comprising:

(i) a heavy chain complementarity-determining region (HCDR) sequence selected from the group consisting of SEQ ID NO: 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, and 170; and

a light chain CDR (LCDR) sequence selected from the group consisting of SEQ ID NO: 171, 172, 173, 174, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, and 198; or

(ii) a heavy chain variable region comprising HCDRl, HCDR2, and HCDR3 sequences, wherein the HCDR1 sequence has the amino acid sequence of SEQ ID NO: 138, 139, 140, 141, 142, 143, 144, 145, 146, or 147; the HCDR2 has the amino acid sequence of SEQ ID NO: 148, 149, 150, 151, 152, 153, or 154; and the HCDR3 sequence has the amino acid sequence of SEQ ID NO: 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, or 170; or variants of any of the foregoing; and

a light chain variable region comprising LCDR1, LCDR2, and LCDR3 sequences, wherein the LCDR1 sequence has the amino acid sequence SEQ ID NO: 171, 172, 173, 174, 176, 177, 178, 179, 180, or 181; the LCDR2 sequence has the amino acid sequence of SEQ ID NO: 182, 183, 184, 185, 186, 187, 188, 189, or 190; and the LCDR3 sequence has the amino acid sequence of SEQ ID NO: 191, 192, 193, 194, 195, 196, 197, or 198; or variants of any of the foregoing.

2. An antibody, or antigen binding fragment thereof, comprising:

(i) a heavy chain variable region (VH) sequence selected from the group consisting of SEQ ID NO: 1, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64 and 65; and

a light chain variable region (VL) sequence selected from the group consisting of SEQ ID NO: 2, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, and 54; or

(ii) a VH and VL pair comprising the amino acid sequence of SEQ ID NOs:66-137, or a variant thereof.

3. The antibody of any one of claims 1-2, wherein the antibody comprises

(i) a monoclonal antibody, and/or a humanized antibody, and/or a scFv antibody; or

(ii) human antibody, a monoclonal antibody, a human monoclonal antibody, a purified antibody, a diabody, a single-chain antibody, a multi-specific antibody, Fab, Fab', F(ab')2, Fv or scFv; or

(iii) a variant thereof comprising 1-10 substitutions, deletions, or insertions, optionally wherein the variant has 1-10 conservative substitutions and/or (ii) has at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% homology to a sequence of SEQ ID NOs: 1-65 or to a sequence of SEQ ID NOs: 66-137 or to a sequence of SEQ ID NO: 138-198.

4. The antibody of any one of claims 1-5, wherein (i) the heavy chain variable region and the light chain variable region are not linked by a linker or (ii) the heavy chain variable region and the light chain variable region are linked with a peptide linker, optionally, wherein the peptide linker comprises a sequence of: $(GGGGS)_n$ (SEQ ID NO: 211) $(GGGGA)_n$ (SEQ ID NO: 212), or any combination thereof, wherein each n is independently 1-5.

5. The antibody of any one of the preceding claims, wherein the antibody comprises a Fc region, optionally wherein:

(i) the Fc region is selected from the group consisting of SEQ ID NO: 199, 200, 201, 202, 203, 204, 205, and 206, and/or

(ii) the Fc region comprises a mutation that extends the half-life of the antibody when linked to the Fc region, optionally wherein the Fc region comprises a S228P, L235E, M252Y, S254T, T256E, M428L, N434S, L234F, P331S mutation, or any combination thereof.

6. A nucleic acid molecule encoding an antibody, or antigen binding fragment thereof, of any one of claims 1-5.

7. A vector comprising the nucleic acid molecule of claim 6.

8. A cell comprising the nucleic comprising the nucleic acid molecule of claim 6 or the vector of claim 7.

9. A pharmaceutical composition comprising the antibody of any one of claims 1-5 or a nucleic acid molecule encoding the same, wherein the composition is an injectable pharmaceutical composition, optionally wherein the pharmaceutically composition is to suitable to be administered

(i) intravenously or subcutaneously; or

(ii) directly to the eye, the anterior chamber of the eye, the vitreous chamber of the eye, the suprachoroidal space, or the retro-orbital sinus;

further optionally wherein the injection is a intravitreal injection, intraorbital injection, retro-orbital injection, suprachoroidal injection, or intracameral injection.

10. An antibody, or antigen binding fragment thereof, according to any one of claims 1 to 5, or a pharmaceutical composition according to claim 9 for use as a medicament.

11. Use of an antibody, or antigen binding fragment thereof, according to any one of claims 1 to 5, or a pharmaceutical composition according to claim 9 in the manufacture of a medicament for treating or reducing the severity of, thyroid-associated ophthalmopathy (TAO), or a symptom thereof, said use optionally:

(i) comprising reducing Clinical Activity Score (CAS) of thyroid-associated ophthalmopathy (TAO), such as reducing Clinical Activity Score (CAS) by at least 2 points or reducing Clinical Activity Score (CAS) to one (1) or reducing Clinical Activity Score (CAS) to zero (0); or

(ii) resulting in an improvement of greater than or equal to 8 points on the Graves' Ophthalmopathy Quality of Life (GO-QoL) assessment, improvement on the Functioning subscale of the GO-QoL, or improvement of the Appearance subscale of the GO-QoL; or

(iii) resulting in reducing proptosis in an eye in a subject with thyroid-associated ophthalmopathy (TAO), optionally wherein proptosis is reduced by at least 2 mm, 3 mm or 4 mm; or

(iv) resulting in reducing the severity of diplopia in a subject with thyroid-associated ophthalmopathy (TAO), optionally wherein the diplopia is constant diplopia, inconstant diplopia or intermittent diplopia, further optionally wherein the improvement in or reduction in severity of diplopia is sustained at least 20 weeks or at least 50 weeks after discontinuation of antibody administration.

12. Use of an antibody, or antigen binding fragment thereof, according to any one of claims 1 to 5, or a pharmaceutical composition according to claim 9, in the manufacture of a medicament for treating thyroid eye disease in a subject, optionally wherein

(i) the antibody has a serum concentration in the subject of at least, or about, 70 μg/ml, 75 μg/ml, 80 μg/ml, 85 μg/ml, 90 μg/ml, 95 μg/ml, 100 μg/ml, or 105 μg/ml at least 1, 2, or 3 week after administration, further optionally wherein the antibody or the pharmaceutical composition is to be administered intravenously, still further optionally wherein the antibody or the pharmaceutical composition is to be administered at a dose of about 20 mg/kg, yet further optionally wherein the antibody or the pharmaceutical composition is to be administered at least, or about, once a week, once every two weeks, once every 3 weeks, or once every 4 weeks; or

(ii) said antibody is to be administered at a dosage of 1 mg/kg to 5 mg/kg antibody or 5 mg/kg to 10 mg/kg as a first dose; or

(iii) said antibody is to be administered at a dosage of 5 mg/kg to 20 mg/kg in subsequent doses; or

(iv) said antibody is to be administered at about 10 mg/kg antibody as a first dose; and about 20 mg/kg antibody in subsequent doses, optionally wherein said subsequent doses are to be administered every three weeks for at least 21 weeks.

13. The use according to any one of claims 11 to 12, wherein the pharmaceutical composition additionally comprises a pharmaceutically acceptable diluent or excipient or carrier, optionally wherein the pharmaceutical composition further comprises:
(i) one or more pharmaceutically active compounds for the treatment of TAO, and/or
(ii) corticosteroids; rituximab or other anti-CD20 antibodies; tocilizumab or other anti-IL-6 antibodies; or selenium, infliximab or other anti-TNFalpha antibodies or a thyroid-stimulating hormone receptor (TSHR) inhibitor.

14. Use of an antibody, or antigen binding fragment thereof, according to any one of claims 1 to 5, or a pharmaceutical composition according to claim 9, in the manufacture of a medicament for increasing the internalization of IGF-1R on a cell in a subject, optionally wherein the subject has or is at risk of thyroid eye disease (TED).

15. Use of an antibody, or antigen binding fragment thereof, according to any one of

claims 1 to 5, or a pharmaceutical composition according to claim 9, in the manufacture of a medicament for inhibiting IGF-1 stimulated receptor phosphorylation on a cell in a subject, optionally wherein the subject has or is at risk of thyroid eye disease (TED), further optionally wherein:
(i) the antibody has an IC50 of less than, or equal to, about 0.2 nm, 0.15 nm, 0.10 nm, 0.09 nm, optionally wherein the IC50 is measured in an *in vitro* assay, such as an assay as provided for herein, and/or
(ii) the cell is an A549 cell or a HOCF cell.

16. Use of an antibody, or antigen binding fragment thereof, according to any one of claims 1 to 5, or a pharmaceutical composition according to claim 9, in the manufacture of a medicament for inhibiting IGF-1 induced receptor autophosphorylation in a cell in a subject by at least 95%, 96%, 97%, 98%, or 99% or by 100%, wherein the inhibition of the IGF-1 induced receptor autophosphorylation is measured as compared to the induced receptor autophosphorylation in the absence of the antibody or the pharmaceutical composition, optionally wherein the subject has or is at risk of thyroid eye disease (TED).