(SSc)/scleroderma is an autoimmune disease that begins with microvascular inflammation progressing to multi-organ connective tissue dysfunction involving tissues in skin, lung, heart, kidney, and intestine. TGFβ is involved in the dysregulation of vascular, connective tissue, and immune components in SSc (Lafyatis R. *Nat Rev Rheumatol.* 2014 Dec; 10(12):706-19).

TGFβ signaling also plays roles in cancer pathogenesis, particularly in peritumoral stroma and immune compartments, where it can inhibit productive anti-tumor immune responses both by promoting excessive ECM production that prevents T cell infiltration into tumor tissue and by promoting T regulatory cell differentiation and activation, which can suppress anti-tumor immunity. Taken together, these findings implicate TGFβ as a potential therapeutic target for fibrotic diseases and cancer. However, the multifarious homeostatic functions of TGFβ and complexity in context-dependent mechanisms of TGFβ activation have contributed to limitations in terms of both safety and efficacy to establish a favorable therapeutic index in interventional studies of TGFβ inhibitors in human fibrotic disorders. For example, pan-TGFβ inhibitors have been associated with undesirable safety signals. In particular, the small molecule ALK5 inhibitors AZ12601011 and AZ12799734 (Anderton *et al.* (2011) Toxicologic Pathology, 39: 916-924) caused microscopic heart valve lesions in rats, and the pan-TGFβ 1D11 antibody (Lonning *et al.* (2011) Current Pharmaceutical Biotechnology, 12, 2176-2189) caused mice treated with 1D11 to develop histologic lesions, weight loss, nonneoplastic cystic epithelial hyperplasia and inflammation of the tongue and dental dysplasia and epithelial hyperplasia of the gingiva and esophagus. Further, CAT-192 (metelimumab), an antibody predominantly selective for TGFβ1, had a high serious adverse event rate with multiple gastric hemorrhages observed in a phase 1-2 study in SSc (Denton *A&R* 56:323 (2007)).

Thus, there remains a need in the art for safe and efficacious molecules that target TGFβ. The present invention provides such molecules and related uses.

SUMMARY

The present disclosure provides isoform-selective anti-TGFβ antibodies and methods of using the same.

In one example, an isolated anti-TGFβ3 antibody is provided, wherein the antibody comprises: (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of one of SEQ ID NOs: 5 , 34, 35, and 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and

(ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9. In some examples, the antibody selectively neutralizes TGFβ3.

In another example, an isolated anti-TGFβ3 antibody is provided, wherein the antibody selectively neutralizes TGFβ3, and wherein the antibody comprises one or more of the following features: (a) the anti-TGFβ3 antibody specifically binds to the beta6/beta7 hairpin region of TGFβ3; (b) binding of the anti-TGFβ3 antibody sterically blocks the ability of TGFBR2, but not TGFBR1, to bind TGFβ3; (c) binding of the anti-TGFβ3 antibody to TGFβ3 blocks TGFBR2 binding and inhibits the TGFBR1/TGFBR2 signaling receptors from binding to TGFβ3; (d) the anti-TGFβ3 antibody directly contacts amino acid residue R394 in the beta6/beta7 hairpin region of human TGFβ3; (e) the anti-TGFβ3 antibody directly contacts amino acid residue R394 in the beta6/beta7 hairpin region of human TGFβ3 and residue R394 of TGFβ3 makes an ionic salt bridge with the anti-TGFβ3 antibody in the heavy chain CDR2; (f) isoform selectivity of the anti-TGFβ3 antibody for TGFβ3 over TGFβ1 is achieved by direct contact by the antigen binding domain of the anti-TGFβ3 antibody with amino acid residues T387, L389, and T395 of TGFβ3 (human TGFβ3 numbering); (g) the isoform selectivity of the anti-TGFβ3 antibody for TGFβ3 over TGFβ2 is achieved by direct contact by the antigen binding domain of the anti-TGFβ3 antibody with amino acid residues R325, R394, and V398 of TGFβ3 (human TGFβ3 numbering); (h) the anti-TGFβ3 antibody has reduced toxicity relative to the pan-TGFβ antibody 1D11; (i) the anti-TGFβ3 antibody has reduced toxicity in rodents or cynomolgus monkeys relative to the pan-TGFβ antibody 1D11; (j) the anti-TGFβ3 antibody has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; (k) the anti-TGFβ3 antibody has reduced toxicity in rodents relative to the pan-TGFβ small molecule inhibitor galunisertib; (l) the anti-TGFβ3 antibody has reduced toxicity relative to the anti-TGFβ1 antibody CAT-192; (m) the anti-TGFβ3 antibody has reduced toxicity relative to an isoform selective anti-TGFβ2 antibody and/or anti-TGFβ2/3 antibody; (n) the anti-TGFβ3 antibody comprises: (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of one of SEQ ID NOs: 5, 34, 35, and 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (o) the anti-TGFβ3 antibody comprises an antigen binding domain that directly contacts amino

acid residues R325, K331, W332, H334, E335, T387, I388, L389, Y391, V392, G393, R394, P396, K397, and V398 on human TGFβ3; and (p) the anti-TGFβ3 antibody as in (o), wherein the antigen binding domain is within 15-8, 8, 8-5, 7-5, 6-5, or 5 angstroms of the TGFβ3 amino acid residues.

In another example, an isolated anti-TGFβ3 antibody is provided, wherein the antibody selectively neutralizes TGFβ3, and wherein the antibody comprises one or more of the following features: (a) the anti-TGFβ3 antibody specifically binds to the beta6/beta7 hairpin region of TGFβ3; (b) binding of the anti-TGFβ3 antibody sterically blocks the ability of TGFBR2, but not TGFBR1, to bind TGFβ3; (c) binding of the anti-TGFβ3 antibody to TGFβ3 blocks TGFBR2 binding and inhibits the TGFBR1/TGFBR2 signaling receptors from binding to TGFβ3; (d) the anti-TGFβ3 antibody directly contacts amino acid residue R394 in the beta6/beta7 hairpin region of human TGFβ3; (e) the anti-TGFβ3 antibody directly contacts amino acid residue R394 in the beta6/beta7 hairpin region of human TGFβ3 and residue R394 of TGFβ3 makes an ionic salt bridge with the anti-TGFβ3 antibody in the heavy chain CDR2; (f) isoform selectivity of the anti-TGFβ3 antibody for TGFβ3 over TGFβ1 is achieved by direct contact by the antigen binding domain of the anti-TGFβ3 antibody with amino acid residues T387, L389, and T395 of TGFβ3 (human TGFβ3 numbering); (g) the isoform selectivity of the anti-TGFβ3 antibody for TGFβ3 over TGFβ2 is achieved by direct contact by the antigen binding domain of the anti-TGFβ3 antibody with amino acid residues R325, R394, and V398 of TGFβ3 (human TGFβ3 numbering); (h) the anti-TGFβ3 antibody has reduced toxicity relative to the pan-TGFβ antibody 1D11; (i) the anti-TGFβ3 antibody has reduced toxicity in rodents or cynomolgus monkeys relative to the pan-TGFβ antibody 1D11; (j) the anti-TGFβ3 antibody has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; (k) the anti-TGFβ3 antibody has reduced toxicity in rodents relative to the pan-TGFβ small molecule inhibitor galunisertib; (l) the anti-TGFβ3 antibody has reduced toxicity relative to the anti-TGFβ1 antibody CAT-192; (m) the anti-TGFβ3 antibody has reduced toxicity relative to an isoform selective anti-TGFβ2 antibody and/or anti-TGFβ2/3 antibody; (n) the anti-TGFβ3 antibody comprises: (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 5, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (o) the anti-TGFβ3 antibody comprises an antigen binding domain that directly contacts amino acid residues R325, K331,

W332, H334, E335, T387, I388, L389, Y391, V392, G393, R394, P396, K397, and V398 on human TGFβ3; and (p) the anti-TGFβ3 antibody as in (o), wherein the antigen binding domain is within 15-8, 8, 8-5, 7-5, 6-5, or 5 angstroms of the TGFβ3 amino acid residues. In some examples, the anti-TGFβ3 antibody comprises a heavy chain variable region (VH) amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 23, 37, and 42-50. In some examples, the anti-TGFβ3 antibody comprises a VH amino acid sequence selected from the group consisting of SEQ ID NOs: 23, 37, and 42-50. In some examples, the anti-TGFβ3 antibody comprises a complete heavy (H) chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 29, 59, 64, and 65-72. In some examples, the anti-TGFβ3 antibody comprises a complete heavy (H) chain amino acid sequence selected from the group consisting of SEQ ID NOs: 29, 59, 64, and 65-72. In further examples, the anti-TGFβ3 antibody comprises a light chain variable region (VL) amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity an amino acid sequence selected from the group consisting of SEQ ID NOs: 22, 36, and 38-41. In yet other examples, the anti-TGFβ3 antibody comprises a complete light (L) chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 28, 58, and 60-63. In some examples, the anti-TGFβ3 antibody comprises a complete L chain amino acid sequence selected from the group consisting of SEQ ID NOs: 28, 58, and 60-63. In some examples, the anti-TGFβ3 antibody comprises a VH/VL pair, the VH/VL pair comprising amino acid sequences (respectively) selected from the group consisting of SEQ ID NOs: 23/22 (rat 2A10), SEQ ID NOs: 37/36 (v1), SEQ ID NOs: 37/38 (v1.1), SEQ ID NOs: 37/39 (v1.2), SEQ ID NOs: 37/40 (v1.3), SEQ ID NOs: 37/41 (v1.4), SEQ ID NOs: 42/36 (v1.5), SEQ ID NOs: 43/36 (v1.6), SEQ ID NOs:44/36 (v1.7), SEQ ID NOs: 45/36 (v2), SEQ ID NOs: 45/38 (v2.1), SEQ ID NOs: 45/39 (v2.2), SEQ ID NOs: 45/40 (v2.3), SEQ ID NOs: 45/41 (v2.4), SEQ ID NOs: 46/36 (v2.5), SEQ ID NOs: 47/36 (v2.6), SEQ ID NOs: 48/36 (v2.7), SEQ ID NOs: 49/36 (v2.8), and SEQ ID NOs: 50/36 (v2.9). In some examples, the anti-TGFβ3 antibody comprises a complete H/L chain pair, the complete H/L chain pair comprising amino acid sequences (respectively) selected from the group consisting of SEQ ID NOs: 29/28 (rat 2A10), SEQ ID NOs: 59/58 (v1), SEQ ID NOs: 59/60 (v1.1), SEQ ID NOs: 59/61 (v1.2), SEQ ID NOs: 59/62 (v1.3), SEQ ID NOs: 59/63 (v1.4), SEQ ID NOs: 64/58 (v1.5), SEQ ID NOs: 65/58 (v1.6),

SEQ ID NOs: 66/58 (v1.7), SEQ ID NOs: 67/58 (v2), SEQ ID NOs: 67/60 (v2.1), SEQ ID NOs: 67/61 (v2.2), SEQ ID NOs: 67/62 (v2.3), SEQ ID NOs: 67/63 (v2.4), SEQ ID NOs: 68/58 (v2.5), SEQ ID NOs: 69/58 (v2.6), SEQ ID NOs: 70/58 (v2.7), SEQ ID NOs: 71/58 (v2.8), SEQ ID NOs: 72/58 (v2.9). In some examples, the anti-TGFβ3 antibody comprises a VL of SEQ ID NO: 22 comprising one or more framework modifications selected from the group consisting of: 4L or 4M, 38H or 38Q, 43A or 43Q, and 58V. In some examples, the anti-TGFβ3 antibody VL comprises a set of framework modifications selected from the group consisting of: (i) 4L in FR1, 38H and 43Q in FR2, 58I in FR3 (h2A10.v1 and h2A10.v2); (ii) 4M in FR1 (h2A10.v1.1 and h2A10.v2.1); (iii) 38Q in FR2 (h2A10.v1.2 and h2A10.v2.2); (iv) 43A in FR2 (h2A10.v1.3 and h2A10.v2.3); (v) 58V in FR3 (h2A10.v1.4 and h2A10.v2.4); (vi) 38Q, 43A in FR2, 58V in FR3 (h2A10.v3 and h2A10.v4); (vii) 58V in FR3 (h2A10.v1.4 and h2A10.v2.4); and (vi) 38Q, 43A in FR2, 58V in FR3 (h2A10.v3 and h2A10.v4), wherein the mutations are relative to the rat 2A10 VL having SEQ ID NO: 22. In other examples, the anti-TGFβ3 antibody comprises a VH of SEQ ID NO: 23 comprising one or more framework modifications selected from the group consisting of: 47L or 47W; 49A, 49S, or 49G; 73D or 73N; and 76N, 78D or 78L, 78A, or 78V. In some examples, the anti-TGFβ3 antibody VH comprises a set of framework modifications selected from the group consisting of: (i) 47L, 49A in FR2, 78V in FR3 (h2A10.v1); (ii) 47L, 49A in FR2, 73D, 76S, 78V in FR3 (h2A10.v2); (iii) 47W in FR2 (h2A10.v1.5); (iv): 49G in FR2 (h2A10.v1.6); (v) 78A in FR3 (h2A10.v1.7); (vi) 47W in FR2 (h2A10.v2.5); (vii) 49S in FR2 (h2A10.v2.6); (viii) 73N in FR3 (h2A10.v2.7); (ix) 76N in FR3 (h2A10.v2.8); (x) 78L in FR3 (h2A10.v2.9); and (xi) 49S in FR2, 76N, 78L in FR3 (h2A10.v3 and h2A10.v4), wherein the mutations are relative to the rat 2A10 VH having SEQ ID NO: 23.

In certain examples of the above anti-TGFβ3 antibodies, the VL of the anti-TGFβ3 antibody retains leucine (L) at position 4 in framework I and leucine (L) at position 47 in framework II (relative to the rat 2A10 VL having SEQ ID NO: 22). In some examples, the VH retains D at position 73 in framework III of VH from rat 2A10 (relative to the rat 2A10 VH having SEQ ID NO: 23).

In another example, an isolated anti-TGFβ3 antibody is provided, wherein the antibody selectively neutralizes TGFβ3, and wherein the antibody comprises one or more of the following features: (a) the anti-TGFβ3 antibody specifically binds to the beta6/beta7 hairpin region of TGFβ3; (b) binding of the anti-TGFβ3 antibody sterically blocks the ability of TGFBR2, but not TGFBR1, to bind TGFβ3; (c) binding of the anti-TGFβ3 antibody to TGFβ3 blocks TGFBR2 binding and inhibits the TGFBR1/TGFBR2 signaling receptors from binding

to TGFβ3; (d) the anti-TGFβ3 antibody directly contacts amino acid residue R394 in the beta6/beta7 hairpin region of human TGFβ3; (e) the anti-TGFβ3 antibody directly contacts amino acid residue R394 in the beta6/beta7 hairpin region of human TGFβ3 and residue R394 of TGFβ3 makes an ionic salt bridge with the anti-TGFβ3 antibody in the heavy chain CDR2; (f) isoform selectivity of the anti-TGFβ3 antibody for TGFβ3 over TGFβ1 is achieved by direct contact by the antigen binding domain of the anti-TGFβ3 antibody with amino acid residues T387, L389, and T395 of TGFβ3 (human TGFβ3 numbering); (g) the isoform selectivity of the anti-TGFβ3 antibody for TGFβ3 over TGFβ2 is achieved by direct contact by the antigen binding domain of the anti-TGFβ3 antibody with amino acid residues R325, R394, and V398 of TGFβ3 (human TGFβ3 numbering); (h) the anti-TGFβ3 antibody has reduced toxicity relative to the pan-TGFβ antibody 1D11; (i) the anti-TGFβ3 antibody has reduced toxicity in rodents or cynomolgus monkeys relative to the pan-TGFβ antibody 1D11; (j) the anti-TGFβ3 antibody has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; (k) the anti-TGFβ3 antibody has reduced toxicity in rodents relative to the pan-TGFβ small molecule inhibitor galunisertib; (l) the anti-TGFβ3 antibody has reduced toxicity relative to the anti-TGFβ1 antibody CAT-192; (m) the anti-TGFβ3 antibody has reduced toxicity relative to an isoform selective anti-TGFβ2 antibody and/or anti-TGFβ2/3 antibody; (n) the anti-TGFβ3 antibody comprises: (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (o) the anti-TGFβ3 antibody comprises an antigen binding domain that directly contacts amino acid residues R325, K331, W332, H334, E335, T387, I388, L389, Y391, V392, G393, R394, P396, K397, and V398 on human TGFβ3; and (p) the anti-TGFβ3 antibody as in (o), wherein the antigen binding domain is within 15-8, 8, 8-5, 7-5, 6-5, or 5 angstroms of the TGFβ3 amino acid residues. In some examples, the anti-TGFβ3 antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO: 52. In some examples, the anti-TGFβ3 antibody comprises the VH amino acid sequence of SEQ ID NO: 52. In some examples, the anti-TGFβ3 antibody comprises a complete H chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO: 74. In some examples, the anti-TGFβ3 antibody comprises the

complete H chain amino acid sequence of SEQ ID NO: 74. In some examples, the anti-TGFβ3 comprises a VL amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 22, 36, and 38-41. In some examples, the anti-TGFβ3 antibody comprises a VL amino acid sequence selected from the group consisting of SEQ ID NOs: 22, 36, and 38-41. In some examples, the anti-TGFβ3 antibody comprises a complete L chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 28, 58, and 60-63. In some examples, the anti-TGFβ3 comprises a complete L chain amino acid sequence selected from the group consisting of SEQ ID NOs: 28, 58, and 60-63. In further examples, the anti-TGFβ3 antibody comprises a VH/VL pair comprising the amino acid sequences (respectively) of SEQ ID NOs: 52/36. In some examples, the anti-TGFβ3 antibody comprises a complete H/L chain pair, the H/L chain pair comprising the amino acid sequences (respectively) of SEQ ID NOs: 74/58.

In another example, an isolated anti-TGFβ3 antibody is provided, wherein the antibody selectively neutralizes TGFβ3, and wherein the antibody comprises one or more of the following features: (a) the anti-TGFβ3 antibody specifically binds to the beta6/beta7 hairpin region of TGFβ3; (b) binding of the anti-TGFβ3 antibody sterically blocks the ability of TGFBR2, but not TGFBR1, to bind TGFβ3; (c) binding of the anti-TGFβ3 antibody to TGFβ3 blocks TGFBR2 binding and inhibits the TGFBR1/TGFBR2 signaling receptors from binding to TGFβ3; (d) the anti-TGFβ3 antibody directly contacts amino acid residue R394 in the beta6/beta7 hairpin region of human TGFβ3; (e) the anti-TGFβ3 antibody directly contacts amino acid residue R394 in the beta6/beta7 hairpin region of human TGFβ3 and residue R394 of TGFβ3 makes an ionic salt bridge with the anti-TGFβ3 antibody in the heavy chain CDR2; (f) isoform selectivity of the anti-TGFβ3 antibody for TGFβ3 over TGFβ1 is achieved by direct contact by the antigen binding domain of the anti-TGFβ3 antibody with amino acid residues T387, L389, and T395 of TGFβ3 (human TGFβ3 numbering); (g) the isoform selectivity of the anti-TGFβ3 antibody for TGFβ3 over TGFβ2 is achieved by direct contact by the antigen binding domain of the anti-TGFβ3 antibody with amino acid residues R325, R394, and V398 of TGFβ3 (human TGFβ3 numbering); (h) the anti-TGFβ3 antibody has reduced toxicity relative to the pan-TGFβ antibody 1D11; (i) the anti-TGFβ3 antibody has reduced toxicity in rodents or cynomolgus monkeys relative to the pan-TGFβ antibody 1D11; (j) the anti-TGFβ3 antibody has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; (k) the anti-TGFβ3 antibody has reduced toxicity in rodents relative to the pan-

TGFβ small molecule inhibitor galunisertib; (l) the anti-TGFβ3 antibody has reduced toxicity relative to the anti-TGFβ1 antibody CAT-192; (m) the anti-TGFβ3 antibody has reduced toxicity relative to an isoform selective anti-TGFβ2 antibody and/or anti-TGFβ2/3 antibody; (n) the anti-TGFβ3 antibody comprises: (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 34, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (o) the anti-TGFβ3 antibody comprises an antigen binding domain that directly contacts amino acid residues R325, K331, W332, H334, E335, T387, I388, L389, Y391, V392, G393, R394, P396, K397, and V398 on human TGFβ3; and (p) the anti-TGFβ3 antibody as in (o), wherein the antigen binding domain is within 15-8, 8, 8-5, 7-5, 6-5, or 5 angstroms of the TGFβ3 amino acid residues. In some examples, the anti-TGFβ3 antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO: 51 or 55. In some examples, the anti-TGFβ3 antibody comprises the VH amino acid sequence of SEQ ID NO: 51 or 55. In some examples, the anti-TGFβ3 antibody comprises a complete H chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO: 73 or 77. In some examples, the anti-TGFβ3 antibody comprises the complete H chain amino acid sequence of SEQ ID NO: 73. In some examples, the anti-TGFβ3 antibody comprises the complete H chain amino acid sequence of SEQ ID NO: 77. In some examples, the anti-TGFβ3 antibody comprises a VL amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 22, 36, and 38-41. In some examples, the anti-TGFβ3 antibody comprises a VL amino acid sequence selected from the group consisting of SEQ ID NOs: 22, 36, and 38-41. In some examples, the anti-TGFβ3 antibody comprises a complete L chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 28, 58, and 60-63. In some examples, the anti-TGFβ3 antibody comprises a complete L chain amino acid sequence selected from the group consisting of SEQ ID NOs: 28, 58, and 60-63. In some examples, the anti-TGFβ3 antibody comprises a VH/VL pair, the VH/VL pair comprising the amino acid sequences (respectively) of SEQ ID NOs: 51/36 or SEQ ID NOs: 55/54. In some examples, the anti-TGFβ3 antibody

comprises a complete H/L chain pair, the H/L chain pair comprising the amino acid sequences (respectively) of SEQ ID NOs: 73/58 or SEQ ID NOs: 77/76.

In another example, an isolated anti-TGFβ3 antibody is provided, wherein the antibody selectively neutralizes TGFβ3, and wherein the antibody comprises one or more of the following features: (a) the anti-TGFβ3 antibody specifically binds to the beta6/beta7 hairpin region of TGFβ3; (b) binding of the anti-TGFβ3 antibody sterically blocks the ability of TGFBR2, but not TGFBR1, to bind TGFβ3; (c) binding of the anti-TGFβ3 antibody to TGFβ3 blocks TGFBR2 binding and inhibits the TGFBR1/TGFBR2 signaling receptors from binding to TGFβ3; (d) the anti-TGFβ3 antibody directly contacts amino acid residue R394 in the beta6/beta7 hairpin region of human TGFβ3; (e) the anti-TGFβ3 antibody directly contacts amino acid residue R394 in the beta6/beta7 hairpin region of human TGFβ3 and residue R394 of TGFβ3 makes an ionic salt bridge with the anti-TGFβ3 antibody in the heavy chain CDR2; (f) isoform selectivity of the anti-TGFβ3 antibody for TGFβ3 over TGFβ1 is achieved by direct contact by the antigen binding domain of the anti-TGFβ3 antibody with amino acid residues T387, L389, and T395 of TGFβ3 (human TGFβ3 numbering); (g) the isoform selectivity of the anti-TGFβ3 antibody for TGFβ3 over TGFβ2 is achieved by direct contact by the antigen binding domain of the anti-TGFβ3 antibody with amino acid residues R325, R394, and V398 of TGFβ3 (human TGFβ3 numbering); (h) the anti-TGFβ3 antibody has reduced toxicity relative to the pan-TGFβ antibody 1D11; (i) the anti-TGFβ3 antibody has reduced toxicity in rodents or cynomolgus monkeys relative to the pan-TGFβ antibody 1D11; (j) the anti-TGFβ3 antibody has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; (k) the anti-TGFβ3 antibody has reduced toxicity in rodents relative to the pan-TGFβ small molecule inhibitor galunisertib; (l) the anti-TGFβ3 antibody has reduced toxicity relative to the anti-TGFβ1 antibody CAT-192; (m) the anti-TGFβ3 antibody has reduced toxicity relative to an isoform selective anti-TGFβ2 antibody and/or anti-TGFβ2/3 antibody; (n) the anti-TGFβ3 antibody comprises: (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (o) the anti-TGFβ3 antibody comprises an antigen binding domain that directly contacts amino acid residues R325, K331, W332, H334, E335, T387, I388, L389, Y391, V392, G393, R394, P396, K397, and V398 on human TGFβ3; and (p) the anti-TGFβ3 antibody as in (o), wherein the antigen binding domain

is within 15-8, 8, 8-5, 7-5, 6-5, or 5 angstroms of the TGFβ3 amino acid residues. In some examples, the anti-TGFβ3 antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO: 53 or 57. In some examples, the anti-TGFβ3 antibody comprises the VH amino acid sequence of SEQ ID NO: 53. In some examples, the anti-TGFβ3 antibody comprises the VH amino acid sequence of SEQ ID NO: 57. In some examples, the anti-TGFβ3 antibody comprises a complete H chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO: 75 or 79. In some examples, the anti-TGFβ3 antibody comprises the complete H chain amino acid sequence of SEQ ID NO: 75. In some examples, the anti-TGFβ3 antibody comprises a complete H chain amino acid sequence of SEQ ID NO: 79. In some examples, the anti-TGFβ3 antibody comprises a VL amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 22, 36, and 38-41. In some examples, the anti-TGFβ3 antibody comprises a VL amino acid sequence selected from the group consisting of SEQ ID NOs: 22, 36, and 38-41. In some examples, the anti-TGFβ3 antibody comprises a complete L chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 28, 58, and 60-63. In some examples, the anti-TGFβ3 antibody comprises a complete L chain amino acid sequence selected from the group consisting of SEQ ID NOs: 28, 58, and 60-63. In some examples, the anti-TGFβ3 antibody comprises a VH/VL pair comprising the amino acid sequences (respectively) of SEQ ID NOs: 53/36 or SEQ ID NOs: 57/56. In some examples, the anti-TGFβ3 antibody comprises a complete H/L chain pair, the H/L chain pair comprising the amino acid sequences (respectively) of SEQ ID NOs: 75/58 or SEQ ID NOs: 79/78.

In another example, an anti-TGFβ3 antibody is provided, the antibody comprising: (a) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (b) a VH/VL pair, the VH of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 57, and the VL of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 56; or (c) a complete H/L chain pair, the H chain of the H/L chain

pair comprising the amino acid sequence of SEQ ID NO: 79 and the L chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 78.

In another example, an isolated anti-TGFβ2/3 antibody is provided, wherein the antibody selectively neutralizes TGFβ2 and TGFβ3, and wherein the antibody comprises one or more of the following features: (a) selectivity of the anti-TGFβ2/3 antibody for TGFβ2 and TGFβ3 over human TGFβ1, with respect to selective neutralization, is achieved by direct contact of the antibody's antigen binding domain with amino acid residue E373 TGFβ2 or TGFβ3 (human TGFβ2 numbering); (b) the anti-TGFβ2/3 antibody neutralizes TGFβ2 and/or TGFβ3 via an allosteric mechanism; (c) the anti-TGFβ2/3 antibody induces a conformational change in TGFβ2 and/or TGFβ3 homodimer; (d) the anti-TGFβ2/3 antibody induces a conformational change in TGFβ2 and/or TGFβ3 homodimer, wherein the conformational change comprises the two monomers pinching together by several degrees; (e) the anti-TGFβ2/3 antibody is a divalent antibody or a monovalent antibody; (f) the anti-TGFβ2/3 antibody comprises (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 10, CDR-H2 has the amino acid sequence of SEQ ID NO: 11, and CDR-H3 has the amino acid sequence of SEQ ID NO: 12; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 13; CDR-L2 has the amino acid sequence of SEQ ID NO: 14, and CDR-L3 has the amino acid sequence of SEQ ID NO: 15; (g) the anti-TGFβ2/3 antibody specifically binds to TGFβ2 homodimer, the TGFβ2 homodimer having a first and a second TGFβ2 monomer, and wherein the anti-TGFβ2/3 antibody comprises an antigen binding domain that directly contacts (i) amino acid residues V313, Q314, D315, R320, L322, Y323, R328, D329, F345, and A347 of the first TGFβ2 monomer, and (ii) amino acid residues N368, T369, I370, N371, P372, E373, A374, S375, A376, and S377 of the second TGFβ2 monomer (human TGFβ2 numbering); (h) the anti-TGFβ2/3 antibody as in (g), wherein the antigen binding domain is within 5 angstroms of the TGFβ2 and/or TGFβ3 amino acid residues; (i) wherein the anti-TGFβ2/3 antibody specifically binds to the same epitope on TGFβ3 as in (g); and (j) the anti-TGFβ2/3 antibody does not neutralize TGFβ2 and/or TGFβ3 in monovalent form. In one example, the anti-TGFβ2/3 antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 27, 81, 83, 86-88, 93-100, and 102-105. In one example, the anti-TGFβ2/3 antibody comprises a VH amino acid sequence selected from the group consisting of SEQ ID NOs: 27, 81, 83, 86-88, 93-100, and 102-105. In one example, the anti-TGFβ2/3 antibody comprises a complete H chain amino acid sequence having at least

95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 33, 107, 109, 112-114, and 119-130. In one example, the anti-TGFβ2/3 comprises a VL amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 26, 80, 82, 84, 85, 89-92, and 101. In one example, the anti-TGFβ2/3 antibody comprises a VL amino acid sequence selected from the group consisting of SEQ ID NOs: 26, 80, 82, 84, 85, 89-92, and 101. In one example, the anti-TGFβ2/3 antibody comprises a complete L chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 32, 106, 108, 110, 111, 115-118, and 186. In one example, the anti-TGFβ2/3 antibody comprises a complete L chain amino acid sequence selected from the group consisting of SEQ ID NOs: 32, 106, 108, 110, 111, 115-118, and 186. In one example, the anti-TGFβ2/3 antibody comprises a VH/VL pair, the VH/VL pair comprising amino acid sequences (respectively) selected from the group consisting of SEQ ID NOs: 27/26 (rabbit 4A11), SEQ ID NOs: 81/80 (v1), SEQ ID NOs: 81/82 (v2), SEQ ID NOs: 83/80 (v3), SEQ ID NOs: 83/82 (v4), SEQ ID NOs: 81/84 (v5), SEQ ID NOs: 81/85 (v6), SEQ ID NOs: 83/84 (v7), SEQ ID NOs: 86/84 (v7/1), , SEQ ID NOs: 87/84 (v7.2), SEQ ID NOs: 88/84 (v7.3), SEQ ID NOs: 83/89 (v7.4), SEQ ID NOs: 83/90 (v7.5), SEQ ID NOs: 83/91 (v7.6), SEQ ID NOs: 83/92 (v7.7), SEQ ID NOs: 93/84 (v7.8), SEQ ID NOs: 94/84 (v7.9), SEQ ID NOs: 95/84 (v7.10), SEQ ID NOs: 96/84 (v7.11), SEQ ID NOs: 97/84 (v7.12), SEQ ID NOs: 98/84 (v7.13), SEQ ID NOs: 99/84 (v7.14), SEQ ID NOs: 100/84 (v7.15), SEQ ID NOs: 102/101 (v7.16), SEQ ID NOs: 103/101 (v7.17), SEQ ID NOs: 104/101 (v7.18), SEQ ID NOs: 105/101 (v7.19), and SEQ ID NOs: 83/85 (v8). In one example, the anti-TGFβ2/3 antibody comprises a complete H/L chain pair, the complete H/L chain pair comprising amino acid sequences (respectively) selected from the group consisting of SEQ ID NOs: 32/33 (rabbit 4A11), SEQ ID NOs: 107/106 (v1), SEQ ID NOs: 107/108 (v2), SEQ ID NOs: 109/106 (v3), SEQ ID NOs: 109/108 (v4), SEQ ID NOs: 107/110 (v5), SEQ ID NOs: 107/111 (v6), SEQ ID NOs: 109/110 (v7), SEQ ID NOs: 112/110 (v7.1), SEQ ID NOs: 113/110 (v7.2), SEQ ID NOs: 114/110 (v7.3), SEQ ID NOs: 114/115 (v7.4), SEQ ID NOs: 114/116 (v7.5), SEQ ID NOs: 114/117 (v7.6), SEQ ID NOs: 114/118 (v7.7), SEQ ID NOs: 119/110 (v7.8), SEQ ID NOs:120/110 (v7.9), SEQ ID NOs: 121/110 (v7.10), SEQ ID NOs: 122/110 (v7.11), SEQ ID NOs: 123/110 (v7.12), SEQ ID NOs: 124/110 (v7.13), SEQ ID NOs: 125/110 (v7.14), SEQ ID NOs: 126/110 (v7.15), SEQ ID NOs: 127/186 (v7.16), SEQ ID NOs: 128/186 (v7.17), SEQ ID NOs: 129/186 (v7.18), SEQ ID NOs: 130/186

(v7.19), and SEQ ID NOs: 114/111 (v8). In one example, the anti-TGFβ2/3 antibody comprises a VL comprising the amino acid sequence of SEQ ID NO: 26 comprising one or more framework modifications selected from the group consisting of: 2A or 2I, 4L, 36F or 36Y, 43P or 43A, and 58V or 58I. In one example, the anti-TGFβ2/3 antibody VL comprises a set of framework modifications selected from the group consisting of: (i) 2A and 4L in FR1 and 36F in FR2 (h4A11.v1 and h4A11.v3); (ii) 2A and 4L in FR1 and 36F and 43P in FR2 (h4A11.v2 and h4A11.v4); (iii) 2A in FR1, 36F and 43P in FR2 and 58V in FR3 (h4A11.v5 and h4A11.v7); (iv) 2A and 4L in FR1 and 36F in FR2 (h4A11.v6 and h4A11.v8); (v) 2I in FR1 (h4A11.v7.4); (vi) 36Y in FR2 (h4A11.v7.5); (vii) 43A in FR2 (h4A11.v7.6); (viii) 58I in FR3 (h4A11.v7.7); and (ix) 2I in FR1, 43A in FR2, 58I in FR3 (h4A11.v7.16-19), wherein the mutations are relative to the VL comprising the amino acid sequence of SEQ ID NO: 26. In one example, the anti-TGFβ2/3 antibody comprises a VH comprising the amino acid sequence of SEQ ID NO: 27 comprising one or more framework modifications selected from the group consisting of: deletion of 1E, 2Q or 2V, 24V, 37V or 37I, 48I, 49G, 67F or 67V, 71K or 71V, 73S or 73T, deletion of 75K and 76N, 78V or 78F, 91F or 91Y, 105P or 105Q. In one example, the anti-TGFβ2/3 antibody VL comprises a set of framework modifications selected from the group consisting of: (i) 2Q and 24V in FR1, 48I and 49G in FR2, 71K, 73S, 78V and 91F in FR3 and 105P in FR4 (h4A11.v1, h4A11.v2, h4A11.v5, h4A11.v6); (ii) 2Q in FR1, 37V in FR2, 67F, 71K, 73S, 78V and 91F in FR3 and 105P in FR4 (h4A11.v3, h4A11.v4, h4A11.v7, h4A11.v8); (iii) delete 1E in FR1 (h4A11.v7.1); (iv) delete 75K and 76N in FR3 (h4A11.v7.2); (v) delete 1E in FR1 and 75K76N in FR3 (h4A11.v7.3); (vi) 2V in FR1 (h4A11.v7.8); (vi) 37I in FR2 (h4A11.v7.9); (vii) 67V in FR3 (h4A11.v7.10); (viii) 71V in FR3 (h4A11.v7.11); (ix) 73T in FR3 (h4A11.v7.12); (x) 78F in FR3 (h4A11.v7.13); (xi) 91Y in FR3 (h4A11.v7.14); (xii) 105Q in FR4 (h4A11.v7.15); (xiii) 2V in FR1, 37I in FR2, 67V, 73T, 78F in FR3, 105Q in FR4 ((h4A11.v7.16); (xiv) 2V in FR1, 37I in FR2, 67V, 73T, 91Y in FR3, 105Q in FR4 (h4A11.v7.17); (xv) 2V in FR1, 37I in FR2, 67V, 73T in FR3, 105Q in FR4 (h4A11.v7.18); and (xvi) 2V in FR1, 37I in FR2, 67V, 73T, deletion of 75K and 76N in FR3, 105Q in FR4 (h4A11.v7.19), wherein the mutations are relative to the VH comprising the amino acid sequence of SEQ ID NO: 27.

In a first aspect of the present disclosure, an isolated anti-TGFβ2 antibody is provided, wherein the antibody comprises: (a) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 16, CDR-H2 has the amino acid sequence of SEQ ID NO: 17, and CDR-H3 has the amino acid sequence of SEQ ID NO: 18; and (b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of

SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21. In one example, the anti-TGFβ2 antibody selectively neutralizes TGFβ2. In some examples, the anti-TGFβ2 antibody: (a) has reduced toxicity relative to the pan-TGFβ antibody 1D11; (b) has reduced toxicity in rodents relative to the pan-TGFβ antibody 1D11; (c) has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; and/or (d) has reduced toxicity in rodents relative to the pan-TGFβ small molecule inhibitor galunisertib. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142. In one example, the anti-TGFβ2 antibody comprises a complete H chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 31, 146, and 152-156. In one example, the anti-TGFβ2 antibody comprises a complete H chain amino acid sequence selected from the group consisting of SEQ ID NOs: 31, 146, and 152-156. In one example, the anti-TGFβ2 antibody comprises a VL amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 24, 131, 133-137, 143, and 144. In another example, the anti-TGFβ2 antibody comprises a VL amino acid sequence selected from the group consisting of SEQ ID NOs: 24, 131, 133-137, 143, and 144. In one example, the anti-TGFβ2 antibody comprises a complete L chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 30,145, 147-151, 157, and 158. In one example, the anti-TGFβ2 antibody comprises a complete L chain amino acid sequence selected from the group consisting of SEQ ID NOs: 30,145, 147-151, 157, and 158. In one example, the anti-TGFβ2 antibody comprises a VH/VL pair, the VH/VL pair comprising amino acid sequences selected from the group consisting of SEQ ID NOs: 25/24 (rabbit 6F12), SEQ ID NOs: 132/131 (v1), SEQ ID NOs: 132/133 (v1.1), SEQ ID NOs: 132/134 (v1.2), SEQ ID NOs: 132/135 (v1.3), SEQ ID NOs: 132/136 (v1.4), SEQ ID NOs: 132/137 (v1.5), SEQ ID NOs: 138/131 (v1.6), SEQ ID NOs: 139/131 (v1.7), SEQ ID NOs: 140/131 (v1.8), SEQ ID NOs: 141/131 (v1.9), SEQ ID NOs: 142/131 (v2), SEQ ID NOs: 132/143 (v3), and SEQ ID NOs: 142/144 (v4). In another aspect of the present disclosure, there is provided an isolated anti-TGFβ2 antibody, wherein the antibody comprises a VH/VL pair, the VH/VL pair comprising the amino acid sequences of SEQ ID NOs: 132/143. In one example, the anti-TGFβ2 comprises a complete H/L chain pair, the complete H/L chain pair comprising amino acid

sequences selected from the group consisting of SEQ ID NOs: 31/30 (rabbit 6F12), SEQ ID NOs: 146/145 (v1), SEQ ID NOs: 146/147 (v1.1), SEQ ID NOs: 146/148 (v1.2), SEQ ID NOs: 146/149 (v1.3), SEQ ID NOs: 146/150 (v1.4), SEQ ID NOs: 146/151 (v1.5), SEQ ID NOs: 152/145 (v1.6), SEQ ID NOs: 153/145 (v1.7), SEQ ID NOs: 154/145 (v1.8), SEQ ID NOs: 155/145 (v1.9), SEQ ID NOs: 156/145 (v2), SEQ ID NOs: 146/157 (v3), and SEQ ID NOs: 156/158 (v4). In yet another aspect of the present disclosure, there is provided an isolated anti-TGFβ2 antibody, wherein the antibody comprises a complete H/L chain pair, the complete H/L chain pair comprising the amino acid sequences of SEQ ID NOs: 146/157. In one example, the anti-TGFβ2 antibody comprises a VL comprising the amino acid sequence of SEQ ID NO: 24 comprising one or more framework mutations selected from the group consisting of 43S or 43A, 66G, 69T, 71F, and 87Y. In one example, the anti-TGFβ2 antibody VL comprises a set of framework mutations selected from the group consisting of: (i) 43S in FR2 and 66E, 69P, 71Y and 87F in FR3 (h6F12.v1 and h6F12.v2); (ii) 43S in FR2 and 58V, 66E, 69P, 71Y and 87F in FR3 (h6F12.v3 and h6F12.v4); (iii) 43A in FR2 (h6F12.v1.1); (iv) 66G in FR3 (h6F12.v1.2); (v) 69T in FR3 (h6F12.v1.3); (vi) 71F in FR3 (h6F12.v1.4); and (vii) 87Y in FR3 (h6F12.v1.5), wherein the mutations are relative to the VL comprising the amino acid sequence of SEQ ID NO: 24. In one example, the anti-TGFβ2 antibody comprises a VH comprising the amino acid sequence of SEQ ID NO: 25 comprising one or more framework mutations selected from the group consisting of 37V or 37I, 48M or 48L, 49G or 49A, 67L, 71K and 78V, and 105P or 105R. In one example, the anti-TGFβ2 antibody VH comprises a set of framework mutations selected from the group consisting of: (i) 37V, 48M and 49G in FR2 and 105P in FR4 (h6F12.v1 and h6F12.v3); (ii) 37V and 48M in FR2, 67L, 71K and 78V in FR3 and 105P in FR4 (h6F12.v2 and h6F12.v4); (iii) 37I in FR2 (h6F12.v1.6); (iv) 48L in FR2 (h6F12.v1.7); (v) 49A in FR2 (h6F12.v1.8); (vi) 105R in FR4 (h6F12.v1.9); (vii) 37V, 48M and 49G in FR2 and 105P in FR4 (h6F12.v1 and h6F12.v3); (viii) 37V and 48M in FR2, 67L, 71K and 78V in FR3 and 105P in FR4 (6F12.v2 and h6F12.v4); (ix) 37I in FR2 (h6F12.v1.6); (x) 48L in FR2 (h6F12.v1.7); (xi) : 49A in FR2 (h6F12.v1.8); and (xii) 105R in FR4 (h6F12.v1.9), wherein the mutations are relative to the VH comprising the amino acid sequence of SEQ ID NO: 25.

In certain examples, the anti-TGFβ3 antibody and/or the anti-TGFβ2/3 antibody specifically binds to human TGFβ3. In some examples, the anti-TGFβ3 antibody specifically binds to both the immature and mature forms of TGFβ3. In some examples, the anti-TGFβ2/3 antibody and/or the anti-TGFβ2 specifically binds to human TGFβ2. In some examples, the antibody is a monoclonal antibody. In some examples, the antibody is a human, humanized, or chimeric antibody. In some examples, the antibody is an antibody fragment. In some

examples, the antibody comprises a human Fc region that is an IgG1 or IgG4 isotype. In some examples, the antibody comprises a human Fc region that is an IgG1 isotype. In some examples, the Fc region of the antibody is modified to remove effector function. In some examples, the Fc region comprises a modification to remove the glycosylation site at amino acid residue position N297 (EU numbering as in Kabat). In some examples, the modification is a mutation selected from N297G or N297A. In some examples, the modification is the mutation N297G. In some examples, the antibody has a Cmax of about 230-260 μg/ml and/or a half life ($t_{½}$) of about 15 to 16 days.

Also provided are isolated nucleic acids encoding the antibody according to any of the above examples, and host cells comprising the nucleic acids. In another aspect of the present disclosure, there is provided an isolated nucleic acid encoding the antibody as disclosed herein. In yet another aspect of the present disclosure, there is provided a host cell comprising the nucleic acid as disclosed herein. In some examples, a method of producing an antibody is provided. The method can include culturing the host cell provided herein so that the antibody is produced. In a further aspect of the present disclosure, there is provided a method of producing an antibody comprising culturing the host cell as disclosed herein, so that the antibody is produced. In some examples, the method further comprises recovering the antibody from the host cell. Also provided is an antibody produced by the method of producing the antibody. In another aspect of the present disclosure, there is provided an antibody produced by the method as disclosed herein.

In another example, an immunoconjugate comprising an antibody, such as any of the antibodies as described above, and a cytotoxic agent is provided. In a further aspect of the present disclosure, there is provided an immunoconjugate comprising the antibody as disclosed herein and a cytotoxic agent. In some examples, the antibody is an anti-TGFβ3 antibody comprising: (a1) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 5, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a2) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 34, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a3) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (a4) (i) heavy chain CDRs comprising CDR-H1, -

H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (b) a VH/VL pair, the VH of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 57, and the VL of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 56; or (c) a complete H/L chain pair, the H chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 79 and the L chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 78. In some examples, the antibody is an anti-TGFβ2 antibody, wherein the antibody comprises: (a) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 16, CDR-H2 has the amino acid sequence of SEQ ID NO: 17, and CDR-H3 has the amino acid sequence of SEQ ID NO: 18; and (b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21. In some examples, the antibody is an anti-TGFβ2/3 antibody comprising (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 10, CDR-H2 has the amino acid sequence of SEQ ID NO: 11, and CDR-H3 has the amino acid sequence of SEQ ID NO: 12; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 13; CDR-L2 has the amino acid sequence of SEQ ID NO: 14, and CDR-L3 has the amino acid sequence of SEQ ID NO: 15.

In another example, a pharmaceutical formulation or immunoconjugate comprising the antibody of any one of the above examples and a pharmaceutically acceptable carrier is provided. In another aspect of the present disclosure, there is provided a pharmaceutical formulation comprising the antibody as disclosed herein and a pharmaceutically acceptable carrier. In yet another aspect of the present disclosure, there is provided a pharmaceutical formulation comprising the antibody as disclosed herein, or the immunoconjugate as disclosed herein and a pharmaceutically acceptable carrier. In some examples, the antibody is an anti-TGFβ3 antibody comprising: (a1) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 5, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a2) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 34, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid

sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a3) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (a4) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (b) a VH/VL pair, the VH of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 57, and the VL of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 56; or (c) a complete H/L chain pair, the H chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 79 and the L chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 78. In some examples, the antibody is an anti-TGFβ2 antibody, wherein the antibody comprises: (a) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 16, CDR-H2 has the amino acid sequence of SEQ ID NO: 17, and CDR-H3 has the amino acid sequence of SEQ ID NO: 18; and (b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21. In some examples of the pharmaceutical formulation or conjugate, the antibody is an anti-TGFβ2/3 antibody comprising (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 10, CDR-H2 has the amino acid sequence of SEQ ID NO: 11, and CDR-H3 has the amino acid sequence of SEQ ID NO: 12; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 13; CDR-L2 has the amino acid sequence of SEQ ID NO: 14, and CDR-L3 has the amino acid sequence of SEQ ID NO: 15.

In some examples, the pharmaceutical formulation further comprises an additional therapeutic agent. In some examples, the additional therapeutic agent is selected from the group consisting of pirfenidone, nintedanib, mycophenylate mofetil, an IL-6 inhibitor (e.g.,

tocilizumab), an anti-CTFG antibody (e.g., FG-3019), an autotaxin inhibitor, a JAK inhibitor, an IL-11 inhibitor, and PTX2.

Also provided is an antibody according to any of the above examples for use as a medicament. In a further aspect of the present disclosure, there is provided the antibody as disclosed herein, for use as a medicament. In some examples, the antibody for use as a medicament is an anti-TGFβ3 antibody comprising: (a1) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 5, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a2) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 34, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a3) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (a4) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21. In some examples, the antibody for use as a medicament is an anti-TGFβ2/3 antibody comprising (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 10, CDR-H2 has the amino acid sequence of SEQ ID NO: 11, and CDR-H3 has the amino acid sequence of SEQ ID NO: 12; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3,

wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 13; CDR-L2 has the amino acid sequence of SEQ ID NO: 14, and CDR-L3 has the amino acid sequence of SEQ ID NO: 15.

Also provided is an antibody according to any of the above examples for use in treating a TGFβ-related disorder. In some examples, the antibody for use in treating a TGFβ-related disorder is an anti-TGFβ3 antibody comprising: (a1) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 5, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a2) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 34, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a3) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (a4) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (b) a VH/VL pair, the VH of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 57, and the VL of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 56; or (c) a complete H/L chain pair, the H chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 79 and the L chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 78. In some examples, the antibody for use in treating a TGFβ-related disorder is an anti-TGFβ2 antibody, wherein the antibody comprises: (a) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 16, CDR-H2 has the amino acid

sequence of SEQ ID NO: 17, and CDR-H3 has the amino acid sequence of SEQ ID NO: 18; and (b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21. In some examples, the antibody for use in treating a TGFβ-related disorder is an anti-TGFβ2/3 antibody comprising (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 10, CDR-H2 has the amino acid sequence of SEQ ID NO: 11, and CDR-H3 has the amino acid sequence of SEQ ID NO: 12; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 13; CDR-L2 has the amino acid sequence of SEQ ID NO: 14, and CDR-L3 has the amino acid sequence of SEQ ID NO: 15.

In one example, an anti-TGFβ3 antibody according to any of the above examples is provided and an anti-TGFβ2 antibody according to any of the above examples is provided for use in combination to treat a TGFβ-related disorder. In one example, the anti-TGFβ3 antibody for use in such combination comprises: (a1) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 5, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a2) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 34, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a3) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (a4) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs

comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (b) a VH/VL pair, the VH of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 57, and the VL of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 56; or (c) a complete H/L chain pair, the H chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 79 and the L chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 78. In another example, the anti-TGFβ2 antibody comprises: (a) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 16, CDR-H2 has the amino acid sequence of SEQ ID NO: 17, and CDR-H3 has the amino acid sequence of SEQ ID NO: 18; and (b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21. In one example, the anti-TGFβ2 antibody selectively neutralizes TGFβ2. In some examples, the anti-TGFβ2 antibody: (a) has reduced toxicity relative to the pan-TGFβ antibody 1D11; (b) has reduced toxicity in rodents relative to the pan-TGFβ antibody 1D11; (c) has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; and/or (d) has reduced toxicity in rodents relative to the pan-TGFβ small molecule inhibitor galunisertib. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142.

Also provided is an antibody according to any of the examples for use in the manufacture of a medicament for treating a TGFβ-related disorder, for inhibiting TGFBR-dependent SMAD signaling, for inhibiting the assembly of TGFβ-TGFBR signaling complexes, for inhibiting TGFβ signaling through the TGFBR1/R2 complex, for inhibiting TGFβ signaling through the TGFBR2/ALK1 complex facilitated by endoglin, and/or for inhibiting new collagen synthesis. In another aspect of the present disclosure, there is provided a use of an antibody as disclosed herein in the manufacture of a medicament for treating a TGFβ-related disorder in a subject. In yet another aspect of the present disclosure, there is provided a use of an as disclosed herein in the manufacture of a medicament for inhibiting TGFBR-dependent SMAD signaling, for inhibiting the assembly of TGFβ-TGFBR signaling complexes, for inhibiting TGFβ signaling through the TGFBR1/R2 complex, for inhibiting TGFβ signaling through the TGFBR2/ALK1 complex facilitated by endoglin, and/or for inhibiting new collagen synthesis. In one example, the antibody for such medicament is an anti-TGFβ3 antibody comprising: (a1) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 5, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and

CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a2) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 34, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a3) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (a4) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (b) a VH/VL pair, the VH of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 57, and the VL of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 56; or (c) a complete H/L chain pair, the H chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 79 and the L chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 78. In another example, the antibody for such medicament is an anti-TGFβ2 antibody comprising: (a) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 16, CDR-H2 has the amino acid sequence of SEQ ID NO: 17, and CDR-H3 has the amino acid sequence of SEQ ID NO: 18; and (b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21. In one example, the anti-TGFβ2 antibody selectively neutralizes TGFβ2. In some examples, the anti-TGFβ2 antibody: (a) has reduced toxicity relative to the pan-TGFβ antibody 1D11; (b) has reduced toxicity in rodents relative to the pan-TGFβ antibody 1D11; (c) has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; and/or (d) has reduced toxicity in rodents relative to the pan-TGFβ small molecule inhibitor galunisertib. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at

least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142. In another example, the antibody is an anti-TGFβ2/3 antibody comprising (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 10, CDR-H2 has the amino acid sequence of SEQ ID NO: 11, and CDR-H3 has the amino acid sequence of SEQ ID NO: 12; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 13; CDR-L2 has the amino acid sequence of SEQ ID NO: 14, and CDR-L3 has the amino acid sequence of SEQ ID NO: 15.

In some examples of the above uses and medicaments for treating TGFβ-related disorders, the TGFβ-related disorder is fibrosis. In some examples, the fibrosis is a fibrotic condition of the lung, liver, heart, kidney, pancreas, eye, and/or skin. In some examples, the fibrosis is a lung fibrosis selected from the group consisting of idiopathic pulmonary fibrosis (IPF), idiopathic pulmonary upper lobe fibrosis (Amitani disease), familial pulmonary fibrosis, pulmonary fibrosis (e.g., pulmonary fibrosis secondary to systemic inflammatory diseases such as, rheumatoid arthritis, scleroderma, lupus, cryptogenic fibrosing alveolitis, chronic obstructive pulmonary disease (COPD) or chronic asthma), cystic fibrosis, non-specific interstitial pneumonia (NSIP), cryptogenic organizing pneumonia (COP), progressive massive fibrosis, scleroderma/systemic sclerosis (SSc, including limited cutaneous (lcSSc) and diffuse cutaneous (dcSSc) forms and SSc-associated interstitial lung disease (SSc-ILD)), bronchiolitis obliterans-organizing pneumonia, connective tissue disease-associated ILD (CT-ILD), hypersensitivity pneumonitis, pulmonary hypertension, pulmonary tuberculosis, silicosis, asbestosis, acute lung injury, and acute respiratory distress (ARD, including bacterial pneumonia induced, trauma-induced, and viral pneumonia-induced, ventilator-induced, non-pulmonary sepsis induced). In some examples, the fibrosis is a fibrotic condition of the liver selected from the group consisting of liver cirrhosis, congenital hepatic fibrosis, obesity, fatty liver, alcohol induced liver fibrosis, non-alcoholic steatohepatitis (NASH), biliary duct injury, primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), infection- or viral-induced liver fibrosis (e.g., chronic hepatitis B and C virus infections), cystic fibrosis, autoimmune hepatitis, necrotizing hepatitis, primary sclerosing cholangitis, hemochromatosis, disorders of the biliary tree, and hepatic dysfunction attributable to infections. In some examples, the fibrosis is a fibrotic condition of the heart and/or pericardium selected from the group consisting of endomyocardial fibrosis, cardiac allograft vasculopathy (CAV), myocardial

infarction, atrial fibrosis, congestive heart failure, arterioclerosis, atherosclerosis, vascular stenosis, myocarditis, congestive cardiomyopathy, coronary infarcts, varicose veins, coronary artery stenosis and other post-ischemic conditions, and idiopathic retroperitoneal fibrosis. In some examples, the fibrosis is a fibrotic condition of the kidney selected from the group consisting of glomerulonephritis (including membranoproliferative, diffuse proliferative, rapidly progressive or sclerosing, post-infectious and chronic forms), diabetic glomerulosclerosis, focal segmental glomerulosclerosis, IgA nephropathy, diabetic nephropathy, ischemic nephropathy, tubulointerstitial kidney fibrosis, HIV-associated nephropathy, membrane nephropathy, glomerulonephritis secondary to systemic inflammatory diseases such as lupus, scleroderma and diabetes glomerulonephritis, idiopathic membranoproliferative glomerular nephritis, mesangial proliferative glomerulonephritis, crescentic glomerulonephritis, amyloidosis (which affects the kidney among other tissues), autoimmune nephritis, renal tubuloinsterstitial fibrosis, renal arteriosclerosis, Alport's syndrome, nephrotic syndrome, chronic renal failure, chronic kidney disease, periglomerular fibrosis/atubular glomeruli, combined apical emphysema and basal fibrosis syndrome (emphysema/fibrosis syndrome), glomerular hypertension, nephrogenic fibrosing dermatopathy, polycystic kidney disease, Fabry's disease, and renal hypertension. In some examples, the fibrosis is a fibrotic condition of the pancreas selected from the group consisting of stromal remodeling pancreatitis and stromal fibrosis. In some examples, the fibrosis is a fibrotic condition of the gastrointestinal tract selected from the group consisting of Crohn's disease, ulcerative colitis, collagenous colitis, colorectal fibrosis, villous atrophy, crypt hyperplasia, polyp formation, healing gastric ulcer, and microscopic colitis. In some examples, the fibrosis is a fibrotic condition of the eye selected from the group consisting of ocular fibrosis, ophthalmic fibrosis, proliferative vitreoretinopathy, vitreoretinopathy of any etiology, fibrosis associated with retinal dysfunction, fibrosis associated with wet or dry macular degeneration, scarring in the cornea and conjunctiva, fibrosis in the corneal endothelium, anterior subcapsular cataract and posterior capsule opacification, anterior segment fibrotic diseases of the eye, fibrosis of the corneal stroma (e.g., associated with corneal opacification), fibrosis of the trabecular network (e.g., associated with glaucoma), posterior segment fibrotic diseases of the eye, fibrovascular scarring (e.g., in retinal or choroidal vasculature of the eye), retinal fibrosis, epiretinal fibrosis, retinal gliosis, subretinal fibrosis (e.g., associated with age related macular degeneration), tractional retinal detachment in association with contraction of the tissue in diabetic retinopathy, congenital orbital fibrosis, lacrimal gland fibrosis, corneal subepithelial fibrosis, and Grave's ophthalmopathy. In some examples, the fibrosis is selected

from fibrosis resulting from spinal cord injury/fibrosis or central nervous system fibrosis such as fibrosis after a stroke, Duchenne muscular dystrophy, fibrosis associated with neurodegenerative disorder such as Alzheimer's disease or multiple sclerosis, vascular restenosis, uterine fibrosis, endometriosis, ovarian fibroids, Peyronie's disease, polycystic ovarian syndrome, disease related pulmonary apical fibrosis in ankylosing spondylitis, scarring, and fibrosis incident to microbial infections (e.g., bacterial, viral, parasitic, fungal). In a specific example, the fibrosis is SSc. In a specific example, the fibrosis is IPF. In a specific example, the fibrosis is chronic obstructive pulmonary disease (COPD). In a specific example, the fibrosis is progressive-fibrosing interstitial lung disease (PF-ILD). In a specific example, the PF-ILD is a disease or condition selected from the group consisting of non-specific interstitial pneumonia (NSIP), cryptogenic organizing pneumonia (COP), progressive massive fibrosis, a complication of coal worker's pneumoconiosis, scleroderma/systemic sclerosis, bronchiolitis obliterans-organizing pneumonia; connective tissue disease-associated ILD (CT-ILD), and hypersensitivity pneumonitis. In a specific example, the fibrosis is liver cirrhosis or chronic hepatic fibrosis. In a specific example, the fibrosis is GI tract fibrosis. In a specific example, the fibrosis is a fibrotic condition of the eye, fibrosis resulting from spinal cord injury, fibrosis or central nervous system fibrosis, or fibrosis associated with a neurodegenerative disorder.

In another example, a method of treating a subject having a TGFβ-related disorder is provided. In some examples, the method comprises administering an effective amount of an antibody or pharmaceutical formulation according to any of the above examples and examples to a subject in need thereof. In another example a method for inhibiting TGFBR-dependent SMAD signaling, inhibiting the assembly of TGFβ-TGFBR signaling complexes, inhibiting TGFβ signaling through the TGFBR1/R2 complex, inhibiting TGFβ signaling through the TGFBR2/ALK1 complex facilitated by endoglin, and/or for inhibiting new collagen synthesis in a subject is provided. In some examples, the method includes administering to a subject in need thereof an effective amount of the antibody according to any of the above examples and examples to inhibit TGFBR-dependent SMAD signaling, to inhibit the assembly of TGFβ-TGFBR signaling complexes, to inhibit TGFβ signaling through the TGFBR1/R2 complex, to inhibit TGFβ signaling through the TGFBR2/ALK1 complex facilitated by endoglin and/or to inhibit new collagen synthesis in the subject. In some examples, the method includes administering an additional therapeutic agent to the subject. In some examples, the additional therapeutic agent is selected from the group consisting of pirfenidone, nintedanib, mycophenylate mofetil, an IL-6 inhibitor (e.g., tocilizumab, sarilumab), an anti-

CTFG antibody (e.g., FG-3019), an autotaxin inhibitor, and PTX2. In one example of such methods, the antibody is an anti-TGFβ3 antibody comprising: (a1) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 5, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a2) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 34, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a3) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (a4) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (b) a VH/VL pair, the VH of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 57, and the VL of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 56; or (c) a complete H/L chain pair, the H chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 79 and the L chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 78. In another example of such methods, the antibody is an anti-TGFβ2 antibody comprising: (a) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 16, CDR-H2 has the amino acid sequence of SEQ ID NO: 17, and CDR-H3 has the amino acid sequence of SEQ ID NO: 18; and (b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21. In one example, the anti-

TGFβ2 antibody selectively neutralizes TGFβ2. In some examples, the anti-TGFβ2 antibody: (a) has reduced toxicity relative to the pan-TGFβ antibody 1D11; (b) has reduced toxicity in rodents relative to the pan-TGFβ antibody 1D11; (c) has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; and/or (d) has reduced toxicity in rodents relative to the pan-TGFβ small molecule inhibitor galunisertib. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142. In another example of such methods, the antibody is an anti-TGFβ2/3 antibody comprising (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 10, CDR-H2 has the amino acid sequence of SEQ ID NO: 11, and CDR-H3 has the amino acid sequence of SEQ ID NO: 12; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 13; CDR-L2 has the amino acid sequence of SEQ ID NO: 14, and CDR-L3 has the amino acid sequence of SEQ ID NO: 15.

In a further example of the above methods, the method can include administering to the subject an effective amount of an anti-TGFβ3 antibody and an effective amount of an anti-TGFβ2 antibody. In one example, the anti-TGFβ3 antibody for use in such combination comprises: (a1) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 5, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a2) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 34, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a3) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid

sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (a4) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (b) a VH/VL pair, the VH of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 57, and the VL of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 56; or (c) a complete H/L chain pair, the H chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 79 and the L chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 78. In another example, the anti-TGFβ2 antibody comprises: (a) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 16, CDR-H2 has the amino acid sequence of SEQ ID NO: 17, and CDR-H3 has the amino acid sequence of SEQ ID NO: 18; and (b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21. In one example, the anti-TGFβ2 antibody selectively neutralizes TGFβ2. In some examples, the anti-TGFβ2 antibody: (a) has reduced toxicity relative to the pan-TGFβ antibody 1D11; (b) has reduced toxicity in rodents relative to the pan-TGFβ antibody 1D11; (c) has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; and/or (d) has reduced toxicity in rodents relative to the pan-TGFβ small molecule inhibitor galunisertib. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142.

In further examples of the above methods for treating TGFβ-related disorders, the TGFβ-related disorder can be fibrosis. In some examples, the fibrosis is a fibrotic condition of the lung, liver, heart, kidney, pancreas, eye, and/or skin. In some examples, the fibrosis is a lung fibrosis selected from the group consisting of idiopathic pulmonary fibrosis (IPF), idiopathic pulmonary upper lobe fibrosis (Amitani disease), familial pulmonary fibrosis, pulmonary fibrosis (e.g., pulmonary fibrosis secondary to systemic inflammatory diseases such as, rheumatoid arthritis, scleroderma, lupus, cryptogenic fibrosing alveolitis, chronic

obstructive pulmonary disease (COPD) or chronic asthma), cystic fibrosis, non-specific interstitial pneumonia (NSIP), cryptogenic organizing pneumonia (COP), progressive massive fibrosis, scleroderma/systemic sclerosis (SSc, including limited cutaneous (lcSSc) and diffuse cutaneous (dcSSc) forms and SSc-associated interstitial lung disease (SSc-ILD)), bronchiolitis obliterans-organizing pneumonia, connective tissue disease-associated ILD (CT-ILD), hypersensitivity pneumonitis, pulmonary hypertension, pulmonary tuberculosis, silicosis, asbestosis, acute lung injury, and acute respiratory distress (ARD, including bacterial pneumonia induced, trauma-induced, and viral pneumonia-induced, ventilator-induced, non-pulmonary sepsis induced). In some examples, the fibrosis is a fibrotic condition of the liver selected from the group consisting of liver cirrhosis, congenital hepatic fibrosis, obesity, fatty liver, alcohol induced liver fibrosis, non-alcoholic steatohepatitis (NASH), biliary duct injury, primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), infection- or viral-induced liver fibrosis (e.g., chronic hepatitis B and C virus infections), cystic fibrosis, autoimmune hepatitis, necrotizing hepatitis, primary sclerosing cholangitis, hemochromatosis, disorders of the biliary tree, and hepatic dysfunction attributable to infections. In some examples, the fibrosis is a fibrotic condition of the heart and/or pericardium selected from the group consisting of endomyocardial fibrosis, cardiac allograft vasculopathy (CAV), myocardial infarction, atrial fibrosis, congestive heart failure, arterioclerosis, atherosclerosis, vascular stenosis, myocarditis, congestive cardiomyopathy, coronary infarcts, varicose veins, coronary artery stenosis and other post-ischemic conditions, and idiopathic retroperitoneal fibrosis. In some examples, the fibrosis is a fibrotic condition of the kidney selected from the group consisting of glomerulonephritis (including membranoproliferative, diffuse proliferative, rapidly progressive or sclerosing, post-infectious and chronic forms), diabetic glomerulosclerosis, focal segmental glomerulosclerosis, IgA nephropathy, diabetic nephropathy, ischemic nephropathy, tubulointerstitial kidney fibrosis, HIV-associated nephropathy, membrane nephropathy, glomerulonephritis secondary to systemic inflammatory diseases such as lupus, scleroderma and diabetes glomerulonephritis, idiopathic membranoproliferative glomerular nephritis, mesangial proliferative glomerulonephritis, crescentic glomerulonephritis, amyloidosis (which affects the kidney among other tissues), autoimmune nephritis, renal tubuloinsterstitial fibrosis, renal arteriosclerosis, Alport's syndrome, nephrotic syndrome, chronic renal failure, chronic kidney disease, periglomerular fibrosis/atubular glomeruli, combined apical emphysema and basal fibrosis syndrome (emphysema/fibrosis syndrome), glomerular hypertension, nephrogenic fibrosing dermatopathy, polycystic kidney disease, Fabry's disease, and renal hypertension. In some

examples, the fibrosis is a fibrotic condition of the pancreas selected from the group consisting of stromal remodeling pancreatitis and stromal fibrosis. In some examples, the fibrosis is a fibrotic condition of the gastrointestinal tract selected from the group consisting of Crohn's disease, ulcerative colitis, collagenous colitis, colorectal fibrosis, villous atrophy, crypt hyperplasia, polyp formation, healing gastric ulcer, and microscopic colitis. In some examples, the fibrosis is a fibrotic condition of the eye selected from the group consisting of ocular fibrosis, ophthalmic fibrosis, proliferative vitreoretinopathy, vitreoretinopathy of any etiology, fibrosis associated with retinal dysfunction, fibrosis associated with wet or dry macular degeneration, scarring in the cornea and conjunctiva, fibrosis in the corneal endothelium, anterior subcapsular cataract and posterior capsule opacification, anterior segment fibrotic diseases of the eye, fibrosis of the corneal stroma (e.g., associated with corneal opacification), fibrosis of the trabecular network (e.g., associated with glaucoma), posterior segment fibrotic diseases of the eye, fibrovascular scarring (e.g., in retinal or choroidal vasculature of the eye), retinal fibrosis, epiretinal fibrosis, retinal gliosis, subretinal fibrosis (e.g., associated with age related macular degeneration), tractional retinal detachment in association with contraction of the tissue in diabetic retinopathy, congenital orbital fibrosis, lacrimal gland fibrosis, corneal subepithelial fibrosis, and Grave's ophthalmopathy. In some examples, the fibrosis is selected from fibrosis resulting from spinal cord injury/fibrosis or central nervous system fibrosis such as fibrosis after a stroke, Duchenne muscular dystrophy, fibrosis associated with neurodegenerative disorder such as Alzheimer's disease or multiple sclerosis, vascular restenosis, uterine fibrosis, endometriosis, ovarian fibroids, Peyronie's disease, polycystic ovarian syndrome, disease related pulmonary apical fibrosis in ankylosing spondylitis, scarring, and fibrosis incident to microbial infections (e.g., bacterial, viral, parasitic, fungal). In a specific example, the fibrosis is SSc. In a specific example, the fibrosis is IPF. In a specific example, the fibrosis is chronic obstructive pulmonary disease (COPD). In a specific example, the fibrosis is progressive-fibrosing interstitial lung disease (PF-ILD). In a specific example, the PF-ILD is a disease or condition selected from the group consisting of non-specific interstitial pneumonia (NSIP), cryptogenic organizing pneumonia (COP), progressive massive fibrosis, a complication of coal worker's pneumoconiosis, scleroderma/systemic sclerosis, bronchiolitis obliterans-organizing pneumonia; connective tissue disease-associated ILD (CT-ILD), and hypersensitivity pneumonitis. In a specific example, the fibrosis is liver cirrhosis or chronic hepatic fibrosis. In a specific example, the fibrosis is GI tract fibrosis, e.g., intestinal fibrosis, optionally, selected from the group consisting of fibrosis associated with Crohn's disease, ulcerative colitis,

collagenous colitis, colorectal fibrosis, villous atrophy, crypt hyperplasia, polyp formation, healing gastric ulcer, and microscopic colitis.. In a specific example, the fibrosis is a fibrotic condition of the eye, fibrosis resulting from spinal cord injury, fibrosis or central nervous system fibrosis, or fibrosis associated with a neurodegenerative disorder.

In another example, a method of diagnosing a subject as having SSc is provided. In some examples, the method includes detecting the expression levels of the genes in an 18-gene signature set consisting of PRSS23, PXDN, COL8A1, COL6A3, SERPINE2, TNC, COMP, THBS1, COL11A1, COL1A1, COL5A2, COL1A2, COL4A1, COL4A2, SFRP4, ALPK2, COL5A1, and TAGLN, and diagnosing the subject with SSc if the levels of the genes are determined to be elevated relative to the gene levels in a healthy control set or reference gene signature. In some examples, a gene level is elevated if the expression increase relative to the healthy control set or reference gene signature is statistically significant, optionally, at least two-fold increased, or at least three-fold increased, or at least four-fold increased, relative to the healthy control set or reference gene signature. In some examples, the gene expression level is detected using qPCR or microarray or RNAseq.

In another example, a method of monitoring response to treatment of a subject with an anti-TGFβ2 antibody and/or an anti-TGFβ3 antibody is provided. In some examples, the method includes determining the expression level of one or more of the TGFβ-inducible genes selected from the group consisting of serpine1, col1a1, col1a2, and col3a1 in a sample from the subject, wherein the subject has received one or more administrations of the anti-TGFβ2 antibody and/or the anti-TGFβ3 antibody. In some examples, the subject is determined to be responding to treatment with the anti-TGFβ2 antibody and/or anti-TGFβ3 antibody, if the expression level of the one or more TGFβ-inducible genes is significantly reduced compared to pre-treatment levels of the one or more TGFβ-inducible genes, wherein optionally the method further comprises administering one or more additional administrations of the anti-TGFβ2 antibody and/or the anti-TGFβ3 antibody if the expression level of the one or more TGFβ-inducible genes is determined to be significantly reduced. In some examples, the subject is administered the anti-TGFβ2 antibody as a monotherapy. In some examples, the subject is administered the anti-TGFβ3 antibody as a monotherapy. In some examples, the expression level of the one or more TGFβ-inducible genes is determined by qPCR or microarray analysis. In one example of the method, the antibody is an anti-TGFβ3 antibody comprising: (a1) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 5, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising

CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a2) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 34, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a3) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (a4) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (b) a VH/VL pair, the VH of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 57, and the VL of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 56; or (c) a complete H/L chain pair, the H chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 79 and the L chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 78. In another example of the method, the antibody is an anti-TGFβ2 antibody comprising: (a) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 16, CDR-H2 has the amino acid sequence of SEQ ID NO: 17, and CDR-H3 has the amino acid sequence of SEQ ID NO: 18; and (b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21. In one example, the anti-TGFβ2 antibody selectively neutralizes TGFβ2. In some examples, the anti-TGFβ2 antibody: (a) has reduced toxicity relative to the pan-TGFβ antibody 1D11; (b) has reduced toxicity in rodents relative to the pan-TGFβ antibody 1D11; (c) has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; and/or (d) has reduced toxicity in rodents relative to the pan-TGFβ small

molecule inhibitor galunisertib. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142.

In any of the above examples for uses, medicaments, and methods of treatment and diagnosis and monitoring response to treatment, the subject can be a human, e.g., a human patient.

In another example, a kit comprising an antibody of any of the above examples is provided. In another aspect of the present disclosure, there is provided a kit comprising an antibody as disclosed herein. In one example of the kit, the antibody is an anti-TGFβ3 antibody comprising: (a1) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 5, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a2) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 34, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; (a3) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 35, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (a4) (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 4, CDR-H2 has the amino acid sequence of SEQ ID NO: 159, and CDR-H3 has the amino acid sequence of SEQ ID NO: 6; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 7; CDR-L2 has the amino acid sequence of SEQ ID NO: 8, and CDR-L3 has the amino acid sequence of SEQ ID NO: 9; or (b) a VH/VL pair, the VH of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 57, and the VL of the VH/VL pair comprising the amino acid sequence of SEQ ID NO: 56; or (c) a complete H/L

chain pair, the H chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 79 and the L chain of the H/L chain pair comprising the amino acid sequence of SEQ ID NO: 78. In another example of the kit, the antibody is an anti-TGFβ2 antibody comprising: (a) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 16, CDR-H2 has the amino acid sequence of SEQ ID NO: 17, and CDR-H3 has the amino acid sequence of SEQ ID NO: 18; and (b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21. In one example, the anti-TGFβ2 antibody selectively neutralizes TGFβ2. In some examples, the anti-TGFβ2 antibody: (a) has reduced toxicity relative to the pan-TGFβ antibody 1D11; (b) has reduced toxicity in rodents relative to the pan-TGFβ antibody 1D11; (c) has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; and/or (d) has reduced toxicity in rodents relative to the pan-TGFβ small molecule inhibitor galunisertib. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142. In one example, the anti-TGFβ2 antibody comprises a VH amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142. In another example of the kit, the antibody is an anti-TGFβ2/3 antibody comprising (i) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 10, CDR-H2 has the amino acid sequence of SEQ ID NO: 11, and CDR-H3 has the amino acid sequence of SEQ ID NO: 12; and (ii) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 13; CDR-L2 has the amino acid sequence of SEQ ID NO: 14, and CDR-L3 has the amino acid sequence of SEQ ID NO: 15.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 shows the primary amino acid sequence alignment of human TGFβ1, 2, and 3 having accession numbers as follows: huTGFβ1: XP_011525544.1, huTGFβ2: NP_003229.1, huTGFβ3: ABQ59024.1, with domains of TGFβ1 (α-sheets and β-strands, latency lasso, fastener, integrin-binding, furin cleavage, and cytokine) indicated as per Shi *et al.*, *Nature* 474:343 (2011). Residues are numbered from the predicted ATG (methionine) start site; Shi *et al.* numbering starts from L30 at the start of the α1 helix. The black arrow

CLAIMS

What is claimed is:

1. An isolated anti-TGFβ2 antibody, wherein the antibody comprises:

(a) heavy chain CDRs comprising CDR-H1, -H2 and -H3, wherein CDR-H1 has the amino acid sequence of SEQ ID NO: 16, CDR-H2 has the amino acid sequence of SEQ ID NO: 17, and CDR-H3 has the amino acid sequence of SEQ ID NO: 18; and

(b) light chain CDRs comprising CDR-L1, -L2 and -L3, wherein CDR-L1 has the amino acid sequence of SEQ ID NO: 19; CDR-L2 has the amino acid sequence of SEQ ID NO: 20, and CDR-L3 has the amino acid sequence of SEQ ID NO: 21.

2. The anti-TGFβ2 antibody of claim 1, wherein the antibody selectively neutralizes TGFβ2.

3. The anti-TGFβ2 antibody of claim 2, wherein the antibody:

(a) has reduced toxicity relative to the pan-TGFβ antibody 1D11;

(b) has reduced toxicity in rodents relative to the pan-TGFβ antibody 1D11;

(c) has reduced toxicity relative to the pan-TGFβ small molecule inhibitor galunisertib; and/or

(d) has reduced toxicity in rodents relative to the pan-TGFβ small molecule inhibitor galunisertib.

4. The anti-TGFβ2 antibody of claim 1 or 2, wherein the antibody comprises a VH amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142.

5. The anti-TGFβ2 antibody of claim 4, wherein the antibody comprises a VH amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 132, and 138-142.

6. The anti-TGFβ2 antibody of claim 4, wherein the antibody comprises a VH amino acid sequence comprising the amino acid sequence of SEQ ID NO: 132.

7. The anti-TGFβ2 antibody of claim 1 or 2, wherein the antibody comprises a complete H chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%,

at least 99%, or 100% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 31, 146, and 152-156.

8. The anti-TGFβ2 antibody of claim 7, wherein the antibody comprises a complete H chain amino acid sequence selected from the group consisting of SEQ ID NOs: 31, 146, and 152-156.

9. The anti-TGFβ2 antibody of claim 7, wherein the antibody comprises a complete H chain amino acid sequence comprising the amino acid sequence of SEQ ID NO: 146.

10. The anti-TGFβ2 antibody of claim 1 or 2, wherein the antibody comprises a VL amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 24, 131, 133-137, 143, and 144.

11. The anti-TGFβ2 antibody of claim 10, wherein the antibody comprises a VL amino acid sequence selected from the group consisting of SEQ ID NOs: 24, 131, 133-137, 143, and 144.

12. The anti-TGFβ2 antibody of claim 10, wherein the antibody comprises a VL amino acid sequence comprising the amino acid sequence of SEQ ID NO: 143.

13. The anti-TGFβ2 antibody of claim 1 or 2, wherein the antibody comprises a complete L chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 30, 145, 147-151, 157, and 158.

14. The anti-TGFβ2 antibody of claim 13, wherein the antibody comprises a complete L chain amino acid sequence selected from the group consisting of SEQ ID NOs: 30, 145, 147-151, 157, and 158.

15. The anti-TGFβ2 antibody of claim 13, wherein the antibody comprises a complete L chain amino acid sequence comprising the amino acid sequence of SEQ ID NO: 157.

16. The anti-TGFβ2 antibody of claim 1 or 2, wherein the antibody comprises a VH/VL pair, the VH/VL pair comprising amino acid sequences selected from the group consisting of SEQ ID NOs: 25/24 (rabbit 6F12), SEQ ID NOs: 132/131 (v1), SEQ ID NOs: 132/133 (v1.1), SEQ ID NOs: 132/134 (v1.2), SEQ ID NOs: 132/135 (v1.3), SEQ ID NOs:

132/136 (v1.4), SEQ ID NOs: 132/137 (v1.5), SEQ ID NOs: 138/131 (v1.6), SEQ ID NOs: 139/131 (v1.7), SEQ ID NOs: 140/131 (v1.8), SEQ ID NOs: 141/131 (v1.9), SEQ ID NOs: 142/131 (v2), SEQ ID NOs: 132/143 (v3), and SEQ ID NOs: 142/144 (v4).

17. The anti-TGFβ2 antibody of claim 1 or 2, wherein the antibody comprises a VH/VL pair, the VH/VL pair comprising the amino acid sequences of SEQ ID NOs: 132/143.

18. The anti-TGFβ2 antibody of claim 1 or 2, wherein the antibody comprises a complete H/L chain pair, the complete H/L chain pair comprising amino acid sequences selected from the group consisting of SEQ ID NOs: 31/30 (rabbit 6F12), SEQ ID NOs: 146/145 (v1), SEQ ID NOs: 146/147 (v1.1), SEQ ID NOs: 146/148 (v1.2), SEQ ID NOs: 146/149 (v1.3), SEQ ID NOs: 146/150 (v1.4), SEQ ID NOs: 146/151 (v1.5), SEQ ID NOs: 152/145 (v1.6), SEQ ID NOs: 153/145 (v1.7), SEQ ID NOs: 154/145 (v1.8), SEQ ID NOs: 155/145 (v1.9), SEQ ID NOs: 156/145 (v2), SEQ ID NOs: 146/157 (v3), and SEQ ID NOs: 156/158 (v4).

19. The anti-TGFβ2 antibody of claim 1 or 2, wherein the antibody comprises a complete H/L chain pair, the complete H/L chain pair comprising the amino acid sequences of SEQ ID NOs: 146/157.

20. The anti-TGFβ2 antibody of claim 1 or 2, wherein the antibody comprises a VL comprising the amino acid sequence of SEQ ID NO: 24 comprising one or more framework mutations selected from the group consisting of 43S or 43A, 66G, 69T, 71F, and 87Y.

21. The anti-TGFβ2 antibody of claim 20, wherein the VL comprises a set of framework mutations selected from the group consisting of:

(i) 43S in FR2 and 66E, 69P, 71Y and 87F in FR3 (h6F12.v1 and h6F12.v2);

(ii) 43S in FR2 and 58V, 66E, 69P, 71Y and 87F in FR3 (h6F12.v3 and h6F12.v4);

(iii) 43A in FR2 (h6F12.v1.1);

(iv) 66G in FR3 (h6F12.v1.2);

(v) 69T in FR3 (h6F12.v1.3);

(vi) 71F in FR3 (h6F12.v1.4); and

(vii) 87Y in FR3 (h6F12.v1.5).

22. The anti-TGFβ2 antibody of claim 1 or 2, wherein the antibody comprises a VH comprising the amino acid sequence of SEQ ID NO: 25 comprising one or more framework mutations selected from the group consisting of 37V or 37I, 48M or 48L, 49G or 49A, 67L, 71K and 78V, and 105P or 105R.

23. The anti-TGFβ2 antibody of claim 22, wherein the VH comprises a set of framework mutations selected from the group consisting of:

(i) 37V, 48M and 49G in FR2 and 105P in FR4 (h6F12.v1 and h6F12.v3);

(ii) 37V and 48M in FR2, 67L, 71K and 78V in FR3 and 105P in FR4 (h6F12.v2 and h6F12.v4);

(iii) 37I in FR2 (h6F12.v1.6);

(iv) 48L in FR2 (h6F12.v1.7);

(v) 49A in FR2 (h6F12.v1.8);

(vi) 105R in FR4 (h6F12.v1.9);

(vii) 37V, 48M and 49G in FR2 and 105P in FR4 (h6F12.v1 and h6F12.v3);

(viii) 37V and 48M in FR2, 67L, 71K and 78V in FR3 and 105P in FR4 (6F12.v2 and h6F12.v4);

(ix) 37I in FR2 (h6F12.v1.6);

(x) 48L in FR2 (h6F12.v1.7);

(xi) : 49A in FR2 (h6F12.v1.8); and

(xii) 105R in FR4 (h6F12.v1.9).

24. The anti-TGFβ2 antibody of any one of claims 1-23, wherein the antibody specifically binds to human TGFβ2.

25. An antibody of any one of claims 1-24, which is a monoclonal antibody.

26. An antibody of any one of claims 1-24, which is a human, humanized, or chimeric antibody.

27. An antibody of any one of claims 1-24, which is an antibody fragment.

28. The antibody of claim 27, wherein the antibody fragment binds to TGFβ2 selected from the group consisting of Fab, Fab′, Fab′-SH, Fv, single-chain Fv (scFv), diabody, and F(ab′)2 fragments.

29. An antibody of any one of claims 1-24, comprising a human Fc region that is an IgG1 or IgG4 isotype.

30. The antibody of claim 29, comprising a human Fc region that is an IgG1 isotype.

31. The antibody of claim 29 or 30, wherein the Fc region comprises a modification to remove the glycosylation site at amino acid residue position N297 (EU numbering as in Kabat).

32. The antibody of claim 31, wherein the modification is a mutation selected from N297G or N297A.

33. The antibody of claim 32, wherein the modification is the mutation N297G.

34. The antibody of any one of claims 29-33, wherein the Fc region is modified to remove effector function.

35. An antibody of any one of claims 1-34, wherein the antibody has a Cmax of about 230-260 μg/ml and/or a half life ($t_{½}$) of about 15 to 16 days.

36. A pharmaceutical formulation comprising the antibody of any one of claims 1-35 and a pharmaceutically acceptable carrier.

37. Isolated nucleic acid encoding the antibody of any one of claims 1-35.

38. A host cell comprising the nucleic acid of claim 37.

39. A method of producing an antibody comprising culturing the host cell of claim 38, so that the antibody is produced.

40. The method of claim 39, further comprising recovering the antibody from the host cell.

41. An antibody produced by the method of claim 39 or 40.

42. An isolated anti-TGFβ2 antibody, wherein the antibody comprises a VH/VL pair, the VH/VL pair comprising the amino acid sequences of SEQ ID NOs: 132/143.

43. The isolated anti-TGFβ2 antibody of claim 42, wherein the antibody comprises a complete H chain amino acid sequence having at least 95%, at least 96%, at least 97%, at

least 98%, at least 99%, or 100% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs: 31, 146, and 152-156.

44. The isolated anti-TGFβ2 antibody of claim 42, wherein the antibody comprises a complete L chain amino acid sequence having at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 30, 145, 147-151, 157, and 158.

45. The isolated anti-TGFβ2 antibody of claim 42, wherein the antibody is a monoclonal antibody.

46. The isolated anti-TGFβ2 antibody of claim 42, wherein the antibody is an IgG1 isotype.

47. The isolated anti-TGFβ2 antibody of claim 42, wherein the antibody is a full length antibody.

48. The isolated anti-TGFβ2 antibody of claim 42, wherein the antibody is a humanized monoclonal IgG1 antibody.

49. The isolated anti-TGFβ2 antibody of claim 42, wherein the antibody is an antibody fragment that binds to TGFβ2 selected from the group consisting of Fab, Fab′, Fab′-SH, Fv, single-chain Fv (scFv), diabody, and F(ab′)2 fragments.

50. The isolated anti-TGFβ2 antibody of claim 42, wherein the antibody comprises a human Fc region that comprises a modification to remove a glycosylation site at amino acid residue position N297 (EU numbering as in Kabat) and wherein the modification is a mutation N297G.

51. A pharmaceutical formulation comprising the antibody of claim 42, and a pharmaceutically acceptable carrier.

52. An isolated anti-TGFβ2 antibody, wherein the antibody comprises a complete H/L chain pair, the complete H/L chain pair comprising the amino acid sequences of SEQ ID NOs: 146/157.

53. A pharmaceutical formulation comprising the antibody of claim 52, and a pharmaceutically acceptable carrier.

54. An immunoconjugate comprising the antibody of any one of claims 1-35, 41-50, or 52, and a cytotoxic agent.

55. A pharmaceutical formulation comprising the antibody of any one of claims 1-35, 41-50, or 52, or the immunoconjugate of claim 54 and a pharmaceutically acceptable carrier.

56. The pharmaceutical formulation of claim 55, further comprising an additional therapeutic agent.

57. The antibody of any one of claims 1-35, 41-50, or 52, for use as a medicament.

58. Use of an antibody according to any one of claims 1-35, 41-50, or 52 in the manufacture of a medicament for treating a TGFβ-related disorder in a subject.

59. Use of an antibody of any one of claims 1-35, 41-50, or 52 in the manufacture of a medicament for inhibiting TGFBR-dependent SMAD signaling, for inhibiting the assembly of TGFβ-TGFBR signaling complexes, for inhibiting TGFβ signaling through the TGFBR1/R2 complex, for inhibiting TGFβ signaling through the TGFBR2/ALK1 complex facilitated by endoglin, and/or for inhibiting new collagen synthesis.

60. A kit comprising an antibody of any one of claims 1-35, 41-50, or 52.