What is claimed is:

1. An isolated human antibody or antigen-binding fragment thereof that specifically binds to, or blocks the biological activity of wild-type mature human GDF8 comprising SEQ ID NO:340, but does not bind to, or block the biological activity of a chimeric GDF8/TGFβ1 construct having amino acids 48-72 of mature human GDF8 replaced with the corresponding amino acid sequence of TGFβ1.

2. The isolated antibody or antigen-binding fragment of claim 1, wherein the chimeric GDF8/TGFβ1 construct comprises the amino acid sequence of SEQ ID NO:352.

3. The isolated antibody or antigen-binding fragment of claims 1 or 2, wherein the antibody or antigen-binding fragment comprises: (a) heavy chain CDRs (HCDR1, HCDR2 and HCDR3) from a heavy chain variable region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 114, 360 and 376; and (b) light chain CDRs (LCDR1, LCDR2 and LCDR3) from a light chain variable region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 122, 368 and 384.

4. An isolated human antibody or antigen-binding fragment thereof that specifically binds to wild-type mature human GDF8 comprising SEQ ID NO:340, wherein the antibody or antigen-binding fragment comprises: (a) heavy chain CDRs (HCDR1, HCDR2 and HCDR3) from a heavy chain variable region having an amino acid sequence selected from the group consisting of SEQ ID NOs:114, 360 and 376; and (b) light chain CDRs (LCDR1, LCDR2 and LCDR3) from a light chain variable region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 122, 368 and 384.

5. The isolated antibody or antigen-binding fragment of any one of the preceding claims, wherein the antibody or antigen-binding fragment comprises: (a) HCDR1/HCDR2/HCDR3 amino acid sequences selected from the group consisting of SEQ ID NOs: 116/118/120; 362/364/366; and 376/380/382; and (b) LCDR1/LCDR2/LCDR3 amino acid sequences selected from the group consisting of SEQ ID NOs: 124/126/128; 370/372/374; and 386/388/390.

6. The isolated antibody or antigen-binding fragment of any one of the preceding claims, wherein the antibody or antigen-binding fragment comprises heavy and light chain CDR amino acid sequences selected from the group consisting of: SEQ ID NOs: 116/118/120/124/126/128; 362/364/366/370/372/374; and 376/380/382/386/388/390.

7. The isolated antibody or antigen-binding fragment of any one of the preceding claims, wherein the antibody or antigen-binding fragment comprises a heavy and light chain

variable domain amino acid sequence pair (HCVR/LCVR) selected from the group consisting of SEQ ID NOs: 114/122; 360/368; and 376/384.

8. An isolated human antibody or antigen-binding fragment of any one of the preceding claims, wherein the antibody or antigen-binding fragment comprises SEQ ID NO:340, wherein the antibody or antigen-binding fragment comprises HDCR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 amino acid sequences, wherein:

(a) the HCDR1 comprises an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8$ (SEQ ID NO:329), wherein $X^1$ is Gly; $X^2$ is Phe; $X^3$ is Thr; $X^4$ is Phe; $X^5$ is Ser; $X^6$ is Ala or Ser; $X^7$ is Phe or Tyr; $X^8$ is Gly or Ala;

(b) the HCDR2 comprises an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8$ (SEQ ID NO:330), wherein $X^1$ is Ile; $X^2$ Gly or Ser; $X^3$ is Tyr or Gly; $X^4$ Ser or Asp; $X^5$ is Gly; $X^6$ is Gly; $X^7$ is Ser or Asn; and $X^8$ is Ala or Glu;

(c) the HCDR3 comprises an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 - X^9 - X^{10} - X^{11} - X^{12} - X^{13} - X^{14}$ (SEQ ID NO:331), wherein $X^1$ is Ser or Ala; $X^2$ is Thr or Lys; $X^3$ is Asp or Ile; $X^4$ is Gly or Ser; $X^5$ is Ala or His; $X^6$ is Trp or Tyr; $X^7$ is Lys or Asp; $X^8$ is Met or Ile; $X^9$ is Ser or Leu; $X^{10}$ is Gly or Ser; $X^{11}$ is Leu or Gly; $X^{12}$ is Asp or Met; $X^{13}$ is Val or Asp; $X^{14}$ is Val or absent;

(d) the LCDR1 comprises an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6$ (SEQ ID NO:332), wherein $X^1$ is Gln; $X^2$ is Asp or Gly; $X^3$ is Ile; $X^4$ is Ser; $X^5$ is Asp or Asn; and $X^6$ is Tyr or Trp;

(e) the LCDR2 comprises an amino acid sequence of the formula $X^1 - X^2 - X^3$ (SEQ ID NO:333), wherein $X^1$ is Thr or Ala; $X^2$ is Thr or Ala; and $X^3$ is Ser; and

(f) the LCDR3 comprises an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 - X^9$ (SEQ ID NO:334), wherein $X^1$ is Gln; $X^2$ is Lys or Gln; $X^3$ is Ala or Tyr; $X^4$ is Asp or Asn; $X^5$ is Ser; $X^6$ is Ala or Phe; $X^7$ is Pro; $X^8$ is Leu; and $X^9$ is Thr.

9. The isolated antibody or antigen-binding fragment of any one of the preceding claims, wherein the antibody or antigen-binding fragment does not bind a linear epitope within wild-type mature GDF8 (SEQ ID NO:340).

10. The isolated antibody or antigen-binding fragment of any one of the preceding claims, wherein the antibody or antigen-binding fragment does not bind isolated GDF8 peptides having amino acid sequences of amino acids 1-14, 1-18, 17-42, 48-65, 48-69, 48-72, 52-65, 52-72, 56-65, 56-72, 65-72, 73-90, 75-105 and 91-105, of SEQ ID NO:340.

11. An isolated human antibody or antigen-binding fragment thereof that binds to the same epitope on wild-type mature human GDF8 (SEQ ID NO:340) as the isolated antibody or antigen-binding fragment of any one of claims 1 to 10.

12. An isolated human antibody or antigen-binding fragment thereof that competes for binding to wild-type mature human GDF8 (SEQ ID NO:340) with the isolated antibody or antigen-binding fragment of any one of claims 1 to 10.

13. A pharmaceutical composition comprising the antibody or antigen-binding fragment of any one of claims 1 to 12 and a pharmaceutically acceptable carrier or diluent.

14. The isolated antibody or antigen-binding fragment of any one of claims 1 to 12, or the pharmaceutical composition of claim 13, for use in medicine.

15. The isolated antibody or antigen-binding fragment of any one of claims 1 to 12, or the pharmaceutical composition of claim 13, for use in treating a patient afflicted with, diagnosed with, or at risk of being afflicted with a disease or disorder that is treatable by inhibiting GDF8 activity.

16. The isolated antibody or antigen-binding fragment, or pharmaceutical composition of claim 15, wherein the disease or disorder that is treatable by inhibiting GDF8 activity is a disease or disorder selected from the group consisting of sarcopenia, cachexia, and muscle atrophy due to disuse or immobilization.

17. Use of the isolated antibody or antigen-binding fragment of any one of claims 1 to 12, or the pharmaceutical composition of claim 13, in the manufacture of a medicament for use in treating a patient afflicted with, diagnosed with, or at risk of being afflicted with a disease or disorder that is treatable by inhibiting GDF8 activity.

18. The use as defined in claim 17, wherein the disease or disorder that is treatable by inhibiting GDF8 activity is a disease or disorder selected from the group consisting of sarcopenia, cachexia, and muscle atrophy due to disuse or immobilization.

19. A therapeutic method for inhibiting GDF8 activity in a patient, said method comprising administering to a patient in need thereof the isolated antibody or antigen-binding fragment of any one of claims 1 to 12, or the pharmaceutical composition of claim 13.

20. The method of claim 19, wherein the patient is afflicted with, diagnosed with, or at risk of being afflicted with a disease or disorder selected from the group consisting of sarcopenia, cachexia, and muscle atrophy due to disuse or immobilization.

## CLAIMS

What is claimed is:

1. An isolated human antibody or antigen-binding fragment thereof that specifically binds to, or blocks the biological activity of wild-type mature human GDF8 comprising SEQ ID NO: 340, but (a) does not bind to, or block the biological activity of a chimeric GDF8/TGFβ1 construct having amino acids 48-72 of mature human GDF8 replaced with the corresponding amino acid sequence of TGFβ1, and (b) does not bind to an isolated polypeptide consisting of amino acids 48-72 of SEQ ID NO: 340; and wherein the antibody or antigen-binding fragment comprises a heavy and light chain variable domain amino acid sequence pair (HCVR/LCVR) selected from the group consisting of SEQ ID NOs: 114/122; 360/368; and 376/384.

2. The isolated antibody or antigen-binding fragment of claim 1, wherein the chimeric GDF8/TGFβ1 construct comprises the amino acid sequence of SEQ ID NO: 352.

3. The isolated antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment further does not bind isolated GDF8 peptides having amino acid sequences of amino acids 1-14, 1-18, 17-42, 48-65, 48-69, 52-65, 52-72, 56-65, 56-72, 65-72, 73-90, 75-105 and 91-105, of SEQ ID NO: 340.

4. An isolated human antibody or antigen-binding fragment thereof that binds to the same epitope on wild-type mature human GDF8 (SEQ ID NO: 340) as a reference antibody selected from the group consisting of:

(a) an antibody comprising a heavy chain variable region (HCVR) having the amino acid sequence of SEQ ID NO:114, and a light chain variable region (LCVR) having the amino acid sequence of SEQ. ID NO:122;

(b) an antibody comprising a HCVR having the amino acid sequence of SEQ ID NO:360, and a LCVR having the amino acid sequence of SEQ ID NO:368; and

(c) an antibody comprising a HCVR having the amino acid sequence of SEQ ID NO:376,

and a LCVR having the amino acid sequence of SEQ ID NO:384,

but (a) does not bind to, or block the biological activity of a chimeric GDF8/TGFβ1 construct having amino acids 48-72 of mature human GDF8 replaced with the corresponding amino acid sequence of TGFβ1, and (b) does not bind to an isolated polypeptide consisting of amino acids 48-72 of SEQ ID NO: 340.

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