

What is claimed:

1. A binding molecule comprising one binding domain that binds to an antigen expressed on an activated hepatic stellate cell (HSC), and a functional domain that is capable of enhancing an antibody effector function toward the activated HSC, wherein the antigen expressed on the activated HSC is PDGFRb.
2. The binding molecule of claim 1, wherein the binding domain comprises a heavy chain complementarity-determining region 1 (HCDR1), a heavy chain complementarity-determining region 2 (HCDR2), and a heavy chain complementarity-determining region 3 (HCDR3) as set forth in SEQ ID NO: 67, and a light chain complementarity-determining region 1 (LCDR1), a light chain complementarity-determining region 2 (LCDR2), and a light chain complementarity-determining region 3 (LCDR3) as set forth in SEQ ID NO: 68.
3. The binding molecule of claim 2, wherein the HCDR1 comprises the amino acid sequence of SEQ ID NO: 1, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 2, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 3, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 4, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 5, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 6.
4. The binding molecule of claim 2 or claim 3, wherein the binding domain comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 67 and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 68.
5. The binding molecule of any one of claims 1 to 4, wherein the functional domain is:
 - (i) an Fc region comprising one or more mutation(s) that enhances antibody-dependent cell-mediated cytotoxicity (ADCC); or

(ii) a domain that activates an immune cell, and wherein optionally the immune cell is a NK cell.

6. The binding molecule of claim 5, wherein the functional domain is an Fc region comprising one or more mutation(s) that enhances ADCC, and wherein optionally the one or more mutation(s) of the Fc region is at the position of 233, 234, 235, 236, 237, 238, 239, 240, 241, 243, 244, 245, 246, 247, 248, 250, 253, 254, 255, 256, 258, 260, 262, 263, 264, 265, 266, 267, 268, 268, 269, 270, 272, 274, 276, 280, 282, 283, 285, 286, 288, 290, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 303, 307, 311, 312, 313, 315, 317, 318, 320, 322, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 337, 338, 339, 340, 342, 344, 345, 347, 355, 356, 358, 359, 360, 361, 362, 373, 375, 376, 378, 380, 382, 383, 384, 386, 388, 389, 390, 391, 392, 396, 398, 400, 401, 413, 414, 415, 416, 418, 419, 421, 422, 424, 428, 430, 433, 434, 435, 436, 437, 438, 439, 440, 442, 444, and/or 447 according to EU numbering.

7. The binding molecule of claim 6, wherein the Fc region comprises S239D/I332E, S239D/A330L/I332E, L235V/F243L/R292P/Y300L/P396L, or F243L/R292P/Y300L mutations.

8. The binding molecule of claim 5, wherein the functional domain is a domain that activates an immune cell, and wherein the functional domain promotes immune cell activation signaling or suppresses immune cell inhibitory signaling.

9. The binding molecule of claim 8, wherein the functional domain binds to and/or modulates a receptor on the immune cell, and wherein optionally the receptor is selected from a group consisting of NKp46, NKp30, NKp44, NKG2C, CD94, KIR2DS1, KIR2DS4, KIR2DS2, KIR2DL4, KIR3DS1, CD160, NKG2D, NKp80, DNAM1, 2B4, NTB-A, CRACC, 4-1BB, OX40, CRTAM, CD16, LFA1, NKG2A, KIR2DL1, KIR2DL2, KIR2DL3, KIR3DL1, KIR3DL2, LILRB1, KIR2DL5, KLRG1, CD161, SIGLEC7, SIGLEC9, LAIR1, TIGIT, CD96,

PD-1, PVRIG, CD122, CD132, CD218a, CD218b, IL12Rb1, IL12Rb2, IL21R, TGFBR1, TGFBR2, TGFBR3, ACVR2A, ACVR2B, ALK4, , and A2a.

10. The binding molecule of claim 9, wherein the functional domain binds to NKG2D, wherein optionally the functional domain is derived from a NKG2D ligand.

11. The binding molecule of claim 10, wherein the functional domain is the extracellular domain of MICA, MICB, ULBP1, or ULBP2 or a fragment or a variant thereof, and wherein optionally the functional domain comprises an amino acid sequence of any one of SEQ ID NOs: 90-93 or a fragment thereof.

12. The binding molecule of claim 9, wherein the functional domain binds to NKp46, and wherein the functional domain comprises an antibody that binds to NKp46.

13. The binding molecule of claim 12, wherein the antibody comprises a HCDR1, a HCDR2, and a HCDR3 as set forth in SEQ ID NO: 87, and a LCDR1, a LCDR2, and a LCDR3 as set forth in SEQ ID NO: 88.

14. The binding molecule of claim 13, wherein the HCDR1 comprises the amino acid sequence of SEQ ID NO: 61, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 62, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 63, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 64, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 65, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 66.

15. The binding molecule of claim 13 or claim 14, wherein the antibody comprises a VH comprising the amino acid sequence of SEQ ID NO: 87 and a VL comprising the amino acid sequence of SEQ ID NO: 88.
16. The binding molecule of claim 9, wherein the functional domain binds to TGFb.
17. The binding molecule of claim 16, wherein the functional domain comprises TGFb receptor II extracellular domain (TRII) or a fragment or a variant thereof, and wherein optionally the functional domain comprises the amino acid sequence of SEQ ID NO: 94 or a fragment thereof.
18. The binding molecule of claim 9, wherein the functional domain binds to TIGIT, and wherein the functional domain comprises an antibody that binds to TIGIT.
19. The binding molecule of claim 18, wherein the antibody comprises a HCDR1, a HCDR2, and a HCDR3 as set forth in SEQ ID NO: 265, and a LCDR1, a LCDR2, and a LCDR3 as set forth in SEQ ID NO: 266.
20. The binding molecule of claim 19, wherein the HCDR1 comprises the amino acid sequence of SEQ ID NO: 267, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 268, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 269, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 270, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 271, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 272.

21. The binding molecule of claim 19 or claim 20, wherein the antibody comprises a VH comprising the amino acid sequence of SEQ ID NO: 265 and a VL comprising the amino acid sequence of SEQ ID NO: 266.
22. The binding molecule of claim 9, wherein the functional domain binds to PVRIG, and wherein the functional domain comprises an antibody that binds to PVRIG.
23. The binding molecule of claim 22, wherein the antibody comprises a HCDR1, a HCDR2, and a HCDR3 as set forth in SEQ ID NO: 273, and a LCDR1, a LCDR2, and a LCDR3 as set forth in SEQ ID NO: 274.
24. The binding molecule of claim 23, wherein the HCDR1 comprises the amino acid sequence of SEQ ID NO: 275, the HCDR2 comprises the amino acid sequence of SEQ ID NO: 276, the HCDR3 comprises the amino acid sequence of SEQ ID NO: 277, the LCDR1 comprises the amino acid sequence of SEQ ID NO: 278, the LCDR2 comprises the amino acid sequence of SEQ ID NO: 279, and the LCDR3 comprises the amino acid sequence of SEQ ID NO: 280.
25. The binding molecule of claim 23 or claim 24, wherein the antibody comprises a VH comprising the amino acid sequence of SEQ ID NO: 273 and a VL comprising the amino acid sequence of SEQ ID NO: 274.
26. The binding molecule of any one of claims 8 to 25, wherein the binding molecule further comprises an Fc region comprising one or more mutation(s) that enhances ADCC.
27. The binding molecule of claim 26, wherein the Fc region comprising one or more mutation(s) at the position of 233, 234, 235, 236, 237, 238, 239, 240, 241, 243, 244, 245, 246,

247, 248, 250, 253, 254, 255, 256, 258, 260, 262, 263, 264, 265, 266, 267, 268, 268, 269, 270, 272, 274, 276, 280, 282, 283, 285, 286, 288, 290, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 303, 307, 311, 312, 313, 315, 317, 318, 320, 322, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 337, 338, 339, 340, 342, 344, 345, 347, 355, 356, 358, 359, 360, 361, 362, 373, 375, 376, 378, 380, 382, 383, 384, 386, 388, 389, 390, 391, 392, 396, 398, 400, 401, 413, 414, 415, 416, 418, 419, 421, 422, 424, 428, 430, 433, 434, 435, 436, 437, 438, 439, 440, 442, 444, and/or 447 according to EU numbering.

28. The binding molecule of claim 27, wherein the Fc region comprises S239D/I332E, S239D/A330L/I332E, L235V/F243L/R292P/Y300L/P396L, or F243L/R292P/Y300L mutations.

29. The binding molecule of any one of claims 1 to 28, wherein the binding molecule is an IgG antibody or a fusion protein comprising the IgG antibody.

30. The binding molecule of claim 29, wherein the antibody is a humanized antibody.

31. A nucleic acid molecule encoding the binding molecule of any one of claims 1 to 30 or a fragment thereof.

32. A vector comprising the nucleic acid molecule of claim 31.

33. A host cell transformed with the vector of claim 32.

34. A composition comprising a therapeutically effective amount of the binding molecule of any one of claims 1 to 30, the nucleic acid molecule of claim 31, or the vector of claim 32, and a pharmaceutically acceptable excipient.

35. Use of the composition of claim 34 in the manufacture of a medicament for the treatment of a disease or disorder in a subject.
36. The use of claim 35, wherein the disease or disorder is associated with activated HSCs.
37. The use of claim 36, wherein the disease or disorder is liver fibrosis.
38. Use of the composition of claim 34 in the manufacture of a medicament for depleting activated HSCs in a subject.
39. The use of claim 38, wherein the subject has a disease or disorder associated with activated HSCs.
40. The use of claim 38, wherein the disease or disorder is liver fibrosis.
41. The composition of claim 34 for use in therapy.