

CLAIMS

1. A bispecific polypeptide comprising at least 1 immunoglobulin single variable domain (ISVD) binding a serum albumin and at least 1 ISVD binding an A Disintegrin and Metalloproteinase with Thrombospondin 5 motifs (ADAMTS5), wherein said ISVD binding ADAMTS5 comprises three complementarity determining regions (CDR1, CDR2, CDR3), wherein said CDR1, CDR2, and CDR3 are selected from the group consisting of:
 - i. CDR1 is SEQ ID NO: 21, CDR2 is SEQ ID NO: 37 and CDR3 is SEQ ID NO: 55;
 - ii. CDR1 is SEQ ID NO: 35, CDR2 is SEQ ID NO: 53 and CDR3 is SEQ ID NO: 118;
 - iii. CDR1 is SEQ ID NO: 35, CDR2 is SEQ ID NO: 53 and CDR3 is SEQ ID NO: 71;
 - iv. CDR1 is SEQ ID NO: 20, CDR2 is SEQ ID NO: 36 and CDR3 is SEQ ID NO: 54;
 - v. CDR1 is SEQ ID NO: 22, CDR2 is SEQ ID NO: 36 and CDR3 is SEQ ID NO: 54;
 - vi. CDR1 is SEQ ID NO: 25, CDR2 is SEQ ID NO: 40 and CDR3 is SEQ ID NO: 58;
 - vii. CDR1 is SEQ ID NO: 33, CDR2 is SEQ ID NO: 50 and CDR3 is SEQ ID NO: 68;
 - viii. CDR1 is SEQ ID NO: 33, CDR2 is SEQ ID NO: 51 and CDR3 is SEQ ID NO: 69;
 - ix. CDR1 is SEQ ID NO: 28, CDR2 is SEQ ID NO: 44 and CDR3 is SEQ ID NO: 62;
 - x. CDR1 is SEQ ID NO: 28, CDR2 is SEQ ID NO: 45 and CDR3 is SEQ ID NO: 63;
 - xi. CDR1 is SEQ ID NO: 28, CDR2 is SEQ ID NO: 43 and CDR3 is SEQ ID NO: 61;
 - xii. CDR1 is SEQ ID NO: 24, CDR2 is SEQ ID NO: 39 and CDR3 is SEQ ID NO: 57;
 - xiii. CDR1 is SEQ ID NO: 23, CDR2 is SEQ ID NO: 38 and CDR3 is SEQ ID NO: 56;
 - xiv. CDR1 is SEQ ID NO: 26, CDR2 is SEQ ID NO: 41 and CDR3 is SEQ ID NO: 59;
 - xv. CDR1 is SEQ ID NO: 27, CDR2 is SEQ ID NO: 119 and CDR3 is SEQ ID NO: 60;
 - xvi. CDR1 is SEQ ID NO: 27, CDR2 is SEQ ID NO: 42 and CDR3 is SEQ ID NO: 60;
 - xvii. CDR1 is SEQ ID NO: 29, CDR2 is SEQ ID NO: 46 and CDR3 is SEQ ID NO: 64;
 - xviii. CDR1 is SEQ ID NO: 30, CDR2 is SEQ ID NO: 47 and CDR3 is SEQ ID NO: 65;
 - xix. CDR1 is SEQ ID NO: 31, CDR2 is SEQ ID NO: 48 and CDR3 is SEQ ID NO: 66;
 - xx. CDR1 is SEQ ID NO: 32, CDR2 is SEQ ID NO: 49 and CDR3 is SEQ ID NO: 67;
 - and
 - xxi. CDR1 is SEQ ID NO: 34, CDR2 is SEQ ID NO: 52 and CDR3 is SEQ ID NO: 70.

2. The polypeptide according to claim 1, in which said ISVD binding ADAMTS5 is chosen from the group consisting of SEQ ID NO:s 2, 116, 19, 1, 3, 6, 16, 17, 10, 11, 9, 5, 4, 7, 8, 117, 12, 13, 14, 15, 18, and amino acids 1-124 of SEQ ID NO: 129.

3. A polypeptide comprising two or more ISVDs, wherein

- a) at least a first ISVD specifically binds ADAMTS5, wherein said first ISVD specifically binding ADAMTS5 is selected from the group consisting of SEQ ID NO:s 2, 116, 19, 1, 3, 6, 16, 17, 10, 11, 9, 5, 4, 7, 8, 117, 12, 13, 14, 15, 18, and amino acids 1-124 of SEQ ID NO: 129; and wherein,
- b) at least a second ISVD specifically binds serum albumin, wherein said second ISVD specifically binding serum albumin is SEQ ID NO: 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, or 145.

4. The polypeptide according to claim 1, wherein said ISVD binding serum albumin is chosen from the group consisting of SEQ ID NOs: 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, or 145.

5. The polypeptide according to claim 25, wherein the polypeptide is selected from the group consisting of

SEQ ID NO: 129 (clone 577 2F3^{so}-Alb),

SEQ ID NO: 130 (clone 579 2F3^{so}-093-Alb),

SEQ ID NO: 120 (clone 4 2A12-Alb),

SEQ ID NO: 121 (clone 5 2D7-Alb),

SEQ ID NO: 122 (clone 6 2F3-Alb),

SEQ ID NO: 123 (clone 69 049-Alb),

SEQ ID NO: 124 (clone 70 9D3-Alb),

SEQ ID NO: 125 (clone 71 3B2-Alb)

SEQ ID NO: 126 (clone 129 2F3-093-Alb),
SEQ ID NO: 127 (clone 130 049-093-Alb), and
SEQ ID NO: 128 (clone 131 9D3-093-Alb).

6. The polypeptide according to claim 1, wherein said polypeptide has at least 90%, 95% or 100% sequence identity with any of SEQ ID NO:s 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, or 130.

7. The polypeptide according to claim 1, wherein CDR1 is SEQ ID NO: 21, CDR2 is SEQ ID NO: 37, and CDR3 is SEQ ID NO: 55.

8. The polypeptide according to claim 1, wherein CDR1 is SEQ ID NO: 20, CDR2 is SEQ ID NO: 36, and CDR3 is SEQ ID NO: 54.

9. The polypeptide according to claim 1, wherein CDR1 is SEQ ID NO: 22, CDR2 is SEQ ID NO: 36, and CDR3 is SEQ ID NO: 54.

10. The polypeptide according to claim 1, wherein CDR1 is SEQ ID NO: 27, CDR2 is SEQ ID NO: 119, and CDR3 is SEQ ID NO: 60.

11. The polypeptide according to claim 1, wherein CDR1 is SEQ ID NO: 25, CDR2 is SEQ ID NO: 40, and CDR3 is SEQ ID NO: 58.

12. The polypeptide according to claim 1, wherein CDR1 is SEQ ID NO: 33, CDR2 is SEQ ID NO: 50, and CDR3 is SEQ ID NO: 68.

13. The polypeptide according to claim 7, wherein said polypeptide is SEQ ID NO: 122, 126, 129, or 130, or a polypeptide which has at least 95% sequence identity to SEQ ID NO: 122, 126, 129, or 130.

14. The polypeptide according to claim 8, wherein said polypeptide is SEQ ID NO: 120, or a polypeptide which has at least 95% sequence identity to SEQ ID NO: 120.
15. The polypeptide according to claim 9, wherein said polypeptide is SEQ ID NO: 124 or 128, or a polypeptide which has at least 95% sequence identity to SEQ ID NO: 124 or 128.
16. The polypeptide according to claim 10, wherein said polypeptide is SEQ ID NO: 123 or 127, or a polypeptide which has at least 95% sequence identity to SEQ ID NO: 123 or 127.
17. The polypeptide according to claim 11, wherein said polypeptide is SEQ ID NO: 121, or a polypeptide which has at least 95% sequence identity to SEQ ID NO: 121.
18. The polypeptide according to claim 12, wherein said polypeptide is SEQ ID NO: 125, or a polypeptide which has at least 95% sequence identity to SEQ ID NO: 125.
19. The polypeptide according to claim 13, wherein said polypeptide is SEQ ID NO: 122.
20. The polypeptide according to claim 13, wherein said polypeptide is SEQ ID NO: 126.
21. The polypeptide according to claim 13, wherein said polypeptide is SEQ ID NO: 129.
22. The polypeptide according to claim 13, wherein said polypeptide is SEQ ID NO: 130.

23. The polypeptide according to claim 14, wherein said polypeptide is SEQ ID NO: 120.
24. The polypeptide according to claim 15, wherein said polypeptide is SEQ ID NO: 124.
25. The polypeptide according to claim 15, wherein said polypeptide is SEQ ID NO: 128.
26. The polypeptide according to claim 16, wherein said polypeptide is SEQ ID NO: 123.
27. The polypeptide according to claim 16, wherein said polypeptide is SEQ ID NO: 127.
28. The polypeptide according to claim 17, wherein said polypeptide is SEQ ID NO: 121.
29. The polypeptide according to claim 18, wherein said polypeptide is SEQ ID NO: 125.
30. The polypeptide according to claim 1, wherein said ISVD binding ADAMTS5 has at least 90%, 95% or 100% sequence identity with any of SEQ ID NO:s 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 116, 117, or amino acids 1-124 of SEQ ID NO: 129.