

CLAIMS

1. Use of an ADAMTS5 inhibiting polypeptide in the manufacture of a medicament for the treatment of osteoarthritis in a subject in need thereof, wherein 75 – 300 mg of the ADAMTS5 inhibiting polypeptide is to be administered to a human subject, wherein the ADAMTS5 inhibiting polypeptide comprises at least one immunoglobulin single variable domain (ISVD) comprising 3 complementarity determining regions (CDR), wherein the complementary determining regions are CDR1 to CDR3, wherein the CDRs are CDR1 to CDR3, in which:

- (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; or
- (xxi) CDR1 is SEQ ID NO: 34, CDR2 is SEQ ID NO: 52 and CDR3 is SEQ ID NO: 70.

2. The use of claim 1, wherein the ADAMTS5 inhibiting polypeptide comprises at least one ISVD comprising 3 CDRs, wherein the CDRs are CDR1 to CDR3, in which CDR1 is SEQ ID NO: 21, CDR2 is SEQ ID NO: 37 and CDR3 is SEQ ID NO: 55.

3. The use of claim 1, wherein the ISVD is chosen from the group consisting of SEQ ID NOs: 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.

4. The use of claim 3, wherein the ISVD is amino acids 1-124 of SEQ ID NO: 129.

5. The use of claim 1, wherein the ADAMTS5 inhibiting polypeptide comprises two or more ISVDS, wherein

- a) at least a first ISVD specifically binds a first antigenic determinant, epitope, part, domain, subunit or conformation of ADAMTS5; and wherein,
- b) at least a second ISVD specifically binds a second antigenic determinant, epitope, part, domain, subunit or conformation of serum albumin.

6. The use of claim 5, wherein the first ISVD is chosen from the group consisting of SEQ ID NOs: 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.
7. The use of claim 6, wherein the first ISVD is amino acids 1-124 of SEQ ID NO: 129.
8. The use of claim 5, wherein the second ISVD 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.
9. The use of claim 8, wherein the second ISVD is SEQ ID NO: 138.
10. The use of claim 5, wherein the first ISVD is amino acids 1-124 of SEQ ID NO: 129, and the second ISVD is SEQ ID NO: 138.
11. The use of claim 1, wherein the ADAMTS5 inhibiting 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).
12. The use of claim 11, wherein the ADAMTS5 inhibiting polypeptide is SEQ ID NO: 129 (clone 577 2F3^{so}-Alb).
13. The use of any of claims 1-12, wherein the osteoarthritis is knee osteoarthritis.
14. The use of any of claims 1-13, wherein the dose of the ADAMTS5 inhibiting polypeptide is 150 mg.
15. The use of any of claims 1-13, wherein the dose of the ADAMTS5 inhibiting polypeptide is 300 mg.

16. The use of any of claims 1-15, wherein the ADAMTS5 inhibiting polypeptide is to be administered once a month.

17. The use of any of claims 1-16, wherein administration of the ADAMTS5 inhibiting polypeptide decreases the formation of ARGS fragments.

18. The use of any of claims 1-17, wherein administration of the ADAMTS5 inhibiting polypeptide decreases pain in an osteoarthritis affected joint as determined by KOOS score or WOMAC score.

19. The use of any of claims 1-18, wherein administration of the ADAMTS5 inhibiting polypeptide maintains the structure of an osteoarthritis affected joint as determined by automated segmentation in MRI.