

CLAIMS

1. An antibody that binds Protein S, wherein the antibody is an inhibitor of the cofactor activity of Protein S for activated Protein C (APC), an inhibitor of the cofactor activity of Protein S for tissue factor pathway inhibitor (TFPI), or an inhibitor of the cofactor activity of Protein S for both APC and TFPI, and wherein the antibody is human, humanized, or chimeric.
2. An antibody that binds Protein S, wherein the antibody is capable of promoting coagulation and/or modulating a component in the coagulation cascade.
3. The antibody of any one of claims 1-2, wherein the antibody is an inhibitor for the cofactor activity of Protein S for APC.
4. The antibody of any one of claims 1-2, wherein the antibody is an inhibitor for the cofactor activity of Protein S for TFPI.
5. The antibody of any one of claims 1-2, wherein the antibody is an inhibitor for the cofactor activity of Protein S for both APC and TFPI.
6. The antibody of claim 3, wherein the capability of the antibody for inhibiting the cofactor activity of Protein S for TFPI is negligible.
7. The antibody of claim 4, wherein the capability of the antibody for inhibiting the cofactor activity of Protein S for APC is negligible.
8. The antibody of any one of claims 1-7, wherein the antibody binds to the C-terminus of Protein S.
9. The antibody of any one of claims 1-7, wherein the antibody binds to the N-terminus of Protein S.
10. The antibody of any one of claims 1-9, wherein the antibody binds to a thrombin-sensitive region of the Protein S.
11. The antibody of any one of claims 1-9, wherein the antibody binds to an EGF region of the Protein S.
12. The antibody of any one of claims 1-9, wherein the antibody binds to an SHBG region of Protein S.
13. The antibody of any one of claims 1-12, wherein the antibody is capable of promoting generation of a marker associated with coagulation activity.
14. The antibody of any one of claims 1-13, wherein the antibody is capable of promoting thrombin generation.

15. The antibody of any one of claims 1-14, wherein the antibody is capable of promoting D-dimer levels.
16. The antibody of any one of claims 1-15, wherein the antibody is capable of promoting fibrin generation.
17. The antibody of any one of claims 1-16, wherein activity of the antibody is dose-dependent.
18. The antibody of any one of claims 1-17, wherein activity of the antibody is measured *in vitro*.
19. The antibody of any one of claims 1-17, wherein activity of the antibody is measured *in vivo*.
20. The antibody of any one of claims 1-19, wherein the binding affinity of the antibody to Protein S is calcium-dependent.
21. The antibody of any one of claims 1-19, wherein the binding affinity of the antibody to Protein S is calcium-independent.
22. The antibody of any one of claims 1-21, wherein the antibody binds to free Protein S.
23. The antibody of any one of claims 1-21, wherein the antibody binds to complexed Protein S.
24. The antibody of claim 23, wherein the Protein S is complexed with C4BP.
25. The antibody of claim 23, wherein the Protein S is complexed with TFPI.
26. The antibody of any one of claims 1-25, wherein the antibody is a monoclonal antibody.
27. The antibody of any one of claims 1-26, wherein the antibody is a full-length antibody.
28. The antibody of any one of claims 1-26, wherein the antibody is an antibody fragment.
29. The antibody of any one of claims 1-28, wherein the antibody is a humanized antibody.
30. The antibody of any of claims 1-29, wherein the antibody comprises a Fc domain.
31. The antibody of claim 30, wherein the Fc domain is human.
32. The antibody of claim 31, wherein the human Fc domain is IgG1, IgG2, IgG3, or IgG4.
33. The antibody of claim 32, wherein the Fc domain of the antibody is human IgG4, optionally SEQ ID NO: 218, and comprises at least one amino acid substitution at a position selected from the group consisting of: 215, 221, 222, 228, 234, 235, 236, 239, 240, 241, 243, 244, 245, 247, 250, 252, 254, 256, 262, 263, 264, 265, 266, 267, 268, 269, 270, 292, 296, 297, 298, 299, 300, 305, 313, 324, 325, 326, 327, 328, 329, 330, 332, 333, 334, 345, 396, 428, 430, 433, 434, and 440, or comprises one or more of the substitutions

selected from the group consisting of T250Q/M428L, M252Y/S254T/T256E, M428L/N434S, S267E/L328F, N325S/L328F, and H433K/N434F, wherein the position numbers of the amino acid residues are of the EU numbering scheme.

- 34.** The antibody of claim 27, wherein the antibody is a human antibody.
- 35.** The antibody of claim 27, wherein the antibody is a chimeric antibody.
- 36.** The antibody of any one of claims 1-35, wherein the antibody is conjugated.
- 37.** The antibody of claim 36, wherein the antibody is conjugated to a label.
- 38.** The antibody of any one of claims 1-37, wherein the antibody comprises any one or more of the amino acid sequences of the complementarity determining region (CDR) sequences provided in Tables 1A, 1B, 1C, 2A, 2B, and 2C.
- 39.** The Protein S antibody of any one of claims 1-38, wherein the antibody comprises:
- (a)** any one of the CDR-L1 amino acid sequences of Table 1A;
 - (b)** any one of the CDR-L2 amino acid sequences of Table 1B;
 - (c)** any one of the CDR-L3 amino acid sequences of Table 1C;
 - (d)** any one of the CDR-H1 amino acid sequences of Table 2A;
 - (e)** any one of the CDR-H2 amino acid sequences of Table 2B; and
 - (f)** any one of the CDR-H3 amino acid sequences of Table 2C.
- 40.** The Protein S antibody of any one of claims 1-39, wherein the light chain variable domain of the antibody comprises:
- (a)** a CDR-L1 comprising the amino acid sequence of any one of SEQ ID NOs: 1-6, 9-11, 117, 127, 136, 141, 174, 184, 194, and 204;
 - (b)** a CDR-L2 comprising the amino acid sequence of any one of SEQ ID NOs: 12-20, 118, 128, 142, 175, 185, 195, and 205; and

- (c) a CDR-L3 comprising the amino acid sequence of any one of SEQ ID NOs: 21-27, 30-32, 119, 123, 129, 137, 143, 176, 186, 196, and 206.

41. The Protein S antibody of any one of claims 1-40, wherein the heavy chain variable domain of antibody comprises:

- (a) a CDR-H1 comprising the amino acid sequence of any one of SEQ ID NOs: 33-39, 42-44, 120, 124, 130, 138, 144, 179, 189, 199, and 209;
- (b) a CDR-H2 comprising the amino acid sequence of any one of SEQ ID NOs: 45-51, 54-56, 121, 125, 139, 145, 180, 190, 200, and 210; and
- (c) a CDR-H3 comprising the amino acid sequence of any one of SEQ ID NOs: 57-63, 66-68, 122, 126, 131, 140, 146, 181, 191, 201, and 211.

42. The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:

- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 1;
- (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 12; and
- (c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 21.

43. The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:

- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 2;
- (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 13; and
- (c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 22.

44. The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:

- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 3;
- (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 14; and

- (c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 23.
- 45.** The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 1;
 - (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 15; and
 - (c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 24.
- 46.** The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4;
 - (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 16; and
 - (c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 25.
- 47.** The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 5;
 - (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 17; and
 - (c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 26.
- 48.** The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 6;
 - (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 18; and
 - (c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 27.

- 49.** The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a)** a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 9;
 - (b)** a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 19; and
 - (c)** a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 30.
- 50.** The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a)** a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 10;
 - (b)** a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 16; and
 - (c)** a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 31.
- 51.** The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a)** a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 11;
 - (b)** a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 20; and
 - (c)** a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 32.
- 52.** The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a)** a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 117;
 - (b)** a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 118; and
 - (c)** a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 119.
- 53.** The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:

- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 117;
 - (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 118; and
 - (c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 123.
54. The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 127;
 - (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 128; and
 - (c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 129.
55. The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 136;
 - (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 17; and
 - (c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 137.
56. The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 141;
 - (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 142; and
 - (c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 143.
57. The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:
- (a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 174;
 - (b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 175; and

(c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 176.

58. The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:

(a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 184;

(b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 185; and

(c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 186.

59. The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:

(a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 194;

(b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 195; and

(c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 196.

60. The Protein S antibody of any one of claims 1-41, wherein the light chain variable domain of the antibody comprises:

(a) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 204;

(b) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 205; and

(c) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 206.

61. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:

(a) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 33;

(b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 45; and

(c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 57.

- 62.** The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:
- (a)** a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 34;
 - (b)** a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 46; and
 - (c)** a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 58.
- 63.** The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:
- (a)** a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 35;
 - (b)** a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 47; and
 - (c)** a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 59.
- 64.** The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:
- (a)** a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 36;
 - (b)** a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 48; and
 - (c)** a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 60.
- 65.** The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:
- (a)** a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 37;
 - (b)** a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 49; and
 - (c)** a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 61.
- 66.** The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:

- (a) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 38;
 - (b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 50; and
 - (c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 62.
67. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:
- (a) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 39;
 - (b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 51; and
 - (c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 63.
68. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:
- (a) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 42;
 - (b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 54; and
 - (c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 66.
69. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:
- (a) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 43;
 - (b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 55; and
 - (c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 67.
70. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:
- (a) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 44;
 - (b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 56; and

(c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 68.

71. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:

(a) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 120;

(b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 121; and

(c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 122.

72. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:

(a) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 124;

(b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 125; and

(c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 126.

73. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:

(a) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 130;

(b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 50; and

(c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 131.

74. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:

(a) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 138;

(b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 139; and

(c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 140.

75. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:

- (a)** a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 144;
- (b)** a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 145; and
- (c)** a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 146.

76. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:

- (a)** a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 179;
- (b)** a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 180; and
- (c)** a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 181.

77. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:

- (a)** a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 189;
- (b)** a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 190; and
- (c)** a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 191.

78. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:

- (a)** a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 199;
- (b)** a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 200; and
- (c)** a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 201.

79. The Protein S antibody of any one of claims 1-60, wherein the heavy chain variable domain of the antibody comprises:

- (a) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 209;
- (b) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 210; and
- (c) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 211.

- 80.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 1, SEQ ID NO: 12, SEQ ID NO: 21, SEQ ID NO: 33, SEQ ID NO: 45, and SEQ ID NO: 57.
- 81.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 2, SEQ ID NO: 13, SEQ ID NO: 22, SEQ ID NO: 34, SEQ ID NO: 46, and SEQ ID NO: 58.
- 82.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 3, SEQ ID NO: 14, SEQ ID NO: 23, SEQ ID NO: 35, SEQ ID NO: 47, and SEQ ID NO: 59.
- 83.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 1, SEQ ID NO: 15, SEQ ID NO: 24, SEQ ID NO: 36, SEQ ID NO: 48, and SEQ ID NO: 60.
- 84.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy amino acid sequences of SEQ ID NO: 4, SEQ ID NO: 16, SEQ ID NO: 25, SEQ ID NO: 37, SEQ ID NO: 49, and SEQ ID NO: 61.
- 85.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 5, SEQ ID NO: 17, SEQ ID NO: 26, SEQ ID NO: 38, SEQ ID NO: 50, and SEQ ID NO: 62.
- 86.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 6, SEQ ID NO: 18, SEQ ID NO: 27, SEQ ID NO: 39, SEQ ID NO: 51, and SEQ ID NO: 63.

- 87.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 9, SEQ ID NO: 19, SEQ ID NO: 30, SEQ ID NO: 42, SEQ ID NO: 54, and SEQ ID NO: 66.
- 88.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 10, SEQ ID NO: 16, SEQ ID NO: 31, SEQ ID NO: 43, SEQ ID NO: 55, and SEQ ID NO: 67.
- 89.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 11, SEQ ID NO: 20, SEQ ID NO: 32, SEQ ID NO: 44, SEQ ID NO: 56, and SEQ ID NO: 68.
- 90.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 117, SEQ ID NO: 118, SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, and SEQ ID NO: 122.
- 91.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 117, SEQ ID NO: 118, SEQ ID NO: 123, SEQ ID NO: 124, SEQ ID NO: 125, and SEQ ID NO: 126.
- 92.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130, SEQ ID NO: 50, and SEQ ID NO: 131.
- 93.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 136, SEQ ID NO: 17, SEQ ID NO: 137, SEQ ID NO: 138, SEQ ID NO: 139, and SEQ ID NO: 140.
- 94.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, and SEQ ID NO: 146.
- 95.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 174, SEQ ID NO: 175, SEQ ID NO: 176, SEQ ID NO: 179, SEQ ID NO: 180, and SEQ ID NO: 181.

- 96.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 184, SEQ ID NO: 185, SEQ ID NO: 186, SEQ ID NO: 189, SEQ ID NO: 190, and SEQ ID NO: 191.
- 97.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 194, SEQ ID NO: 195, SEQ ID NO: 196, SEQ ID NO: 199, SEQ ID NO: 200, and SEQ ID NO: 201.
- 98.** The Protein S antibody of any one of claims 1-41, wherein the antibody comprises the light and heavy CDR amino acid sequences of SEQ ID NO: 204, SEQ ID NO: 205, SEQ ID NO: 206, SEQ ID NO: 209, SEQ ID NO: 210, and SEQ ID NO: 211.
- 99.** The Protein S antibody of any one of claims 1-98, wherein the antibody comprises the variable chain amino acid sequence of any one of the amino acid sequences provided in Table 4A, and/or the variable chain amino acid sequence of any one of the amino acid sequences provided in Table 4B.
- 100.** The Protein S antibody of any one of claims 1-99, wherein the antibody comprises the light and heavy variable chain amino acid sequence of any one of the amino acid sequence combinations provided in Table 4C.
- 101.** The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 69 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 70, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.
- 102.** The Protein S antibody of one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 71 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid

sequence of SEQ ID NO: 72, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

103. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 73 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 74, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

104. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 75 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 76, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

105. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 77 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 78, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

106. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 79 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%,

89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 80, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

107. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 81 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 82, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

108. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 87 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 88, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

109. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises In some embodiments, provided herein are Protein S antibodies, wherein the light chain variable domain of the antibodies comprise the amino acid sequence of SEQ ID NO: 89 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 90, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

- 110.** The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 91 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 92, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.
- 111.** The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 148 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 149, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.
- 112.** The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 150 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 151, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.
- 113.** The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 152 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 153, or an amino acid sequence with at least 80%,

81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

114. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 156 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 157, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

115. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 158 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 159, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

116. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 177 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 182, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

117. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 187 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity

thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 192, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

118. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 197 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 202, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

119. The Protein S antibody of any one of claims 1-100, wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 207 or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 212, or an amino acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

120. The Protein S antibody of any one of claims 1-119, wherein a light chain of the antibody comprises the amino acid sequence of SEQ ID NO: 214.

121. The Protein S antibody of any one of claims 1-119, wherein a light chain of the antibody comprises the amino acid sequence of SEQ ID NO: 215.

122. A pharmaceutical composition comprising any one of the antibodies of claims 1-121, and optionally a pharmaceutically acceptable excipient.

123. A complex comprising Protein S and the antibody of any one of claims 1-119, wherein the antibody is bound to the Protein S, and the Protein S is free.

124. A complex comprising Protein S and the antibody of any one of claims 1-119, wherein the antibody is bound to the Protein S, and the Protein S is complexed.

125. The complex of claim 124, wherein the Protein S is bound to C4BP.

- 126.** The complex of claim 124, wherein the Protein S is bound to TFPI.
- 127.** A nucleic acid encoding for any one of the antibodies of claims 1-121.
- 128.** The nucleic acid of claim 127, comprising any one of the nucleic acid sequences selected from Table 5A.
- 129.** The nucleic acid of any one of claims 127-128, comprising any one of the nucleic acid sequences selected from Table 5B.
- 130.** The nucleic acid of any one of claims 127-129, wherein the nucleic acid comprises the nucleic acid sequence of any one of the nucleic acid sequence combinations provided in Table 5C.
- 131.** The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 93 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 94, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.
- 132.** The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 95 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 96, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.
- 133.** The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 97 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by

the nucleic acid sequence of SEQ ID NO: 98, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

134. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 99 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 100, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

135. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 101 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 102, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

136. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 103 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 104, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

137. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 105 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%,

89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 106, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

138. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 111 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 112, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

139. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 113 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 114, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

140. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 115 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 116, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

- 141.** The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 162 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 163, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.
- 142.** The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 164 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 165, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.
- 143.** The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 166 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 167, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.
- 144.** The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 170 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 171, or a nucleic acid sequence with at least

80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

145. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 172 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 173, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

146. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 178 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 183, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

147. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 188 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 193, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

148. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 198 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity

thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 203, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

149. The nucleic acid of any one of claims 127-130, wherein the light chain variable domain of the Protein S antibody is encoded by the nucleic acid sequence of SEQ ID NO: 208 or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto; and/or wherein the heavy chain variable domain of the antibody is encoded by the nucleic acid sequence of SEQ ID NO: 213, or a nucleic acid sequence with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

150. A vector comprising the nucleic acid of any one of claims 127-149.

151. An *in vitro* method of promoting the coagulation of blood, comprising contacting the antibody of any one of claims 1-121 with a blood sample.

152. The method of claim 151, wherein the blood sample comprises plasma.

153. The method of any one of claims 151-152, wherein a marker associated with coagulation activity is increased.

154. The method of any one of claims 151-153, wherein thrombin generation is promoted.

155. The method of any one of claims 151-154, wherein fibrin generation is promoted.

156. The method of any one of claims 151-155, wherein D-dimer levels are promoted.

157. The method of any one of claims 151-156, wherein the blood sample is obtained from a subject having a coagulation factor deficiency, von Willebrand disease, or a platelet disorder.

158. A method of promoting the coagulation of blood in a subject in need thereof, comprising administering to the subject the antibody of any one of claims 1-121 or the pharmaceutical composition of claim 122.

159. The method of claim 158, wherein a marker associated with coagulation activity is increased.

- 160.** The method of any of claims 158-159, wherein thrombin generation is promoted in the subject.
- 161.** The method of any of claims 158-160, wherein fibrin generation is promoted in the subject.
- 162.** The method of any of claims 153-161, wherein D-dimer levels are increased in the subject.
- 163.** The method of any of claims 153-162, wherein the antibody remains active in the subject for a period of time.
- 164.** The method of any of claims 151-163, wherein activity of the antibody is dose-dependent.
- 165.** A method of promoting the generation of thrombin in a subject in need thereof, comprising administering to the subject the antibody of any one of claims 1-121 or the pharmaceutical composition of claim 122.
- 166.** The method of claim 165, wherein the subject has a coagulation factor deficiency, von Willebrand disease, or a platelet disorder, and the antibody restores or promotes the generation of thrombin.
- 167.** A method of treating a condition in a subject in need thereof, comprising administering to the subject the antibody of 1-121 or the pharmaceutical composition of claim 122, wherein the condition is selected from the group consisting of: bleeding disorders, platelet disorders, trauma, and bleeding resulting from a surgery or a medical procedure.
- 168.** The method of claim 167, wherein the method of treating is prophylactic.
- 169.** The method of claim 167, wherein the method of treating is on-demand.
- 170.** The method of any one of claims 167-169, wherein the method is prophylactic and on-demand.
- 171.** The method of any one of claims 168 or 170, wherein the prophylactic method of treating is a routine prophylaxis.
- 172.** The method of any one of claims 167-171, wherein the administration of the antibody of any one of claims 1-119 is a subcutaneous administration.
- 173.** The method of any one of claims 158-172, wherein the method of treating is acute.

174. The method of any one of claims 158-172, wherein the method of treating is chronic.
175. The method of any one of claims 158-172, wherein the method of treating is perioperative.
176. The method of any one of claims 158-172, wherein the method of treating is intermittent.
177. The method of any one of claims 158-176, wherein the antibody exhibits graded inhibition.
178. The method of any one of claims 158-176, wherein the antibody exhibits switch-like inhibition.
179. The method of any one of claims 167-178, wherein the subject suffers from two or more conditions selected from the group consisting of: bleeding disorders, platelet disorders, trauma, and bleeding resulting from a surgery or a medical procedure.
180. The method of any one of claims 165-179, wherein the subject suffers from a bleeding disorder selected from the group consisting of: hemophilia A, hemophilia B, von Willebrand disease (vWD) disease, menorrhagia, Factor I deficiency, Factor II deficiency, Factor V deficiency, Factor VII deficiency, Factor X deficiency, Factor XI deficiency, Factor VIII deficiency (hemophilia A), Factor IX deficiency (hemophilia B), trauma, and hereditary hemorrhagic telangiectasia.
181. The method of any one of claims 158-180, wherein the subject is a hemophilia carrier.
182. The method of any one of claims 165-181, wherein the subject suffers from menorrhagia.
183. The method of any one of claims 158-182, wherein the subject suffers from menorrhagia associated with one or more of the bleeding disorders or the platelet disorders.
184. The method of claim 180, wherein the bleeding disorder is vWD, and wherein the subject is undergoing a prophylactic treatment.
185. The method of claim 180, wherein the bleeding disorder is vWD, and the vWD is a subtype selected from: vWD Type 1, vWD Type 2A, vWD Type 2B, vWD Type 2N, vWD Type 2M, vWD Type 3, and acquired vWD.

- 186.** The method of any one of claims 167-185, wherein the condition is a platelet disorder selected from the group consisting of: Bernard-Soulier syndrome, Glanzmann's thrombasthenia, and platelet storage pool deficiency.
- 187.** The method of claim 186, wherein the platelet disorder is a platelet storage pool deficiency selected from the group consisting of: Gray platelet syndrome, Quebec platelet disorder, and MYH9-related thrombocytopenia (MYH9RD).
- 188.** The method of claim 180, wherein the bleeding disorder is selected from Factor I deficiency, Factor II deficiency, Factor V deficiency, Factor VII deficiency, Factor X deficiency, Factor XI deficiency, Factor VIII deficiency (hemophilia A), Factor IX deficiency (hemophilia B), and vWD disease, and wherein the subject has inhibitors.
- 189.** The method of any one of claims 167-188, wherein the antibody or the pharmaceutical composition is capable of promoting thrombin generation in the subject.
- 190.** The method of any one of claims 165-166, wherein the thrombin generation does not exceed a predetermined threshold level.
- 191.** The method of any one of claims 165-166 and 190, wherein the thrombin generation is antibody concentration-dependent.
- 192.** A kit or article of manufacture comprising an antibody of any one of claims 1-121 or the pharmaceutical composition of claim 122.
- 193.** Use of the antibody of any one of claims 1-121 or the pharmaceutical composition of claim 122 for the treatment of a condition in a subject in need thereof.
- 194.** Use of the antibody of any one of claims 1-121 or the pharmaceutical composition of claim 122 for the manufacture of a medicament for the treatment of a condition in a subject in need thereof.