

deficiency are infrequent, often mild, result from injury or trauma, and very rarely affect critical organs (Salomon *et al.* (2011)).

[0006] Antibodies that bind Factor XI and/or Factor XIa have been studied. For example, WO 2016/207858 describes one such anti-Factor XI and/or Factor XIa antibody, disclosed herein in Table 1 as Antibody 1. The present disclosure adds to these developments and provides further clinical methods, including dosage regimens, to treat patients with specific thromboembolic disorders with desired safety and efficacy. Furthermore, the present disclosure adds to the earlier developments in the field by providing pharmaceutical formulations comprising such FXI and/or FXIa antibodies that are sufficiently stable and suitable for administration to patients.

SUMMARY

[0007] The present disclosure provides dosage regimens for anti-Factor XI and/or Factor XIa antibodies or antigen-binding fragments thereof, or pharmaceutical formulations comprising the same.

[0007a] In one aspect, the present disclosure provides a use of a first dose of about 150 mg of an isolated anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or an antigen-binding fragment thereof, in the manufacture of a first medicament for intravenous administration and use of a second dose of the isolated anti-FXI and/or anti-FXIa antibody or the antigen-binding fragment thereof in the manufacture of a second medicament for subcutaneous administration, wherein the first and second medicaments are to be used in combination therapy to treat a cancer in a subject in need thereof, optionally wherein the cancer is gastrointestinal cancer or genitourinary cancer, and wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) comprising complementary determining regions HCDR1, HCDR2, and HCDR3 in SEQ ID NOs: 9 or 29; and a light chain variable region (VL) comprising complementary determining regions LCDR1, LCDR2, LCDR3 in SEQ ID NOs: 19 or 39.

[0007b] In another aspect, the present disclosure provides a use of a drug delivery formulation comprising about 150 mg of an isolated anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or antigen-binding fragment thereof in the manufacture of a medicament for

treating a subject with a cancer, wherein the drug delivery formulation is to be administered once intravenously and subsequently is to be administered subcutaneously about once a month, wherein the subject is to be treated for about six months, and wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) comprising complementary determining regions HCDR1, HCDR2, and HCDR3 in SEQ ID NOs: 9 or 29; and a light chain variable region (VL) comprising complementary determining regions LCDR1, LCDR2, LCDR3 in SEQ ID NOs: 19 or 39.

[0007c] In another aspect, the present disclosure provides a use of a single dose of a drug delivery formulation comprising: (a) a therapeutically effective amount of an isolated anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or antigen-binding fragment thereof at a concentration of about 150 mg; (b) a histidine buffer at a concentration of about 20 mM; (c) sucrose at a concentration of about 220 mM; (d) polysorbate-20 at a concentration of about 0.04% (v/v), and (e) a diluent comprising glucose at pH 5.5, in the manufacture of a medicament for treating a primate subject at risk of thrombosis, and wherein the drug delivery formulation is to be administered before or during formation of a blood clot.

[0007d] In another aspect, the present disclosure provides a use of an anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating a subject having a thrombocytopenia, wherein the thrombocytopenia is selected from the group consisting of: chemotherapy-induced thrombocytopenia, congenital thrombocytopenia, thrombocytopenia associated with infection, and idiopathic thrombocytopenia, and wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) comprising complementary determining regions HCDR1, HCDR2, and HCDR3 in SEQ ID NOs: 9 or 29; and a light chain variable region (VL) comprising complementary determining regions LCDR1, LCDR2, LCDR3 in SEQ ID NOs: 19 or 39.

[0007e] In another aspect, the present disclosure provides a use of an anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or an antigen-binding fragment thereof in the manufacture of a medicament for treating a cancer subject having a cancer and a chemotherapy-induced thrombocytopenia, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable (VH) comprising complementary determining regions HCDR1, HCDR2, and HCDR3 in SEQ ID NO: 9 or 29s; and a light chain variable region (VL) comprising

complementary determining regions LCDR1, LCDR2, LCDR3 in SEQ ID NOs: 19 or 39.

[0008] Accordingly, in one example, provided herein is a method of treating a disease or disorder in a subject in need thereof, the method comprising intravenously administering to the subject a first dose of about 150 mg of an isolated anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody, or an antigen-binding fragment thereof, and subcutaneously administering to the subject a second dose of the isolated anti-FXI and/or anti-FXIa antibody, or the antigen-binding fragment thereof.

[0009] In some examples, the second dose comprises about 150 mg of the isolated anti-FXI and/or anti-FXIa antibody, or the antigen-binding fragment thereof. In some examples, the first dose of the isolated anti-FXI and/or anti-FXIa antibody, or the antigen-binding fragment thereof, is formulated as an intravenous drug delivery formulation comprising about 150 mg of the antibody, or the antigen-binding fragment thereof. In some examples, the second dose of the isolated anti-FXI and/or anti-FXIa antibody, or the antigen-binding fragment thereof, is formulated as a subcutaneous drug delivery formulation comprising about 150 mg of the antibody or the antigen-binding fragment thereof.

[0010] In some examples, the antibody is a human monoclonal antibody. In some examples, the antibody is a human IgG1 isotype. In some examples, the antibody comprises D265A and P329A substitutions in the Fc domain.

[0011] In some examples, the antibody or antigen-binding fragment thereof is administered in a drug delivery formulation comprising a histidine buffer at a concentration of about 20 mM. In some examples, the antibody or antigen-binding fragment thereof is administered in a drug delivery formulation comprising sucrose at a concentration of about 220 mM. In some examples, the antibody or antigen-binding fragment thereof is administered in a drug delivery formulation comprising polysorbate 20 at a concentration of about 0.04%. In some examples, the antibody or antigen-binding fragment thereof is administered in a drug delivery formulation at pH 5.5. In some examples, the antibody or antigen-binding fragment thereof is administered in an intravenous drug delivery formulation, the intravenous drug delivery formulation further comprises about 5% glucose.

[0012] In some examples, the subject has a cancer. In certain examples, the subject has an active cancer. In certain examples, the subject has a cancer selected from the group consisting of gastrointestinal cancer and genitourinary cancer. In some examples, the subject is at high risk of venous thromboembolism. In some examples, the subject has had one or more previous venous thromboembolisms.

[0013] In some examples, the method further comprises one or more additional subcutaneous doses of the antibody or antigen-binding fragment thereof. In some examples, the method comprises administering five subcutaneous doses of the antibody or antigen-binding fragment thereof. In some examples, the antibody or antigen-binding fragment thereof is administered subcutaneously about once a month. In some examples, the antibody or antigen-binding fragment thereof is administered intravenously on day 1 and is administered subcutaneously on days 31, 61, 91, 121, and 151. In some examples, the subject is treated for about six months.

[0014] In another example, provided herein is a method of treating a subject with a cancer, wherein the method comprises administering a drug delivery formulation comprising about 150 mg of an isolated anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or antigen-binding fragment thereof to the subject in need thereof, wherein the drug delivery formulation is administered once intravenously and subsequently is administered subcutaneously about once a month, and wherein the subject is treated for about six months.

[0015] In some examples, the cancer is selected from the group consisting of gastrointestinal cancer and genitourinary cancer.

[0016] In another example, provided herein is a method of treating a primate subject at risk of thrombosis, wherein the method comprises administering to the primate subject a single dose of a drug delivery formulation comprising:

(a) a therapeutically effective amount of an isolated anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody, or antigen-binding fragment thereof at a concentration of about 150 mg;

(b) a histidine buffer at a concentration of about 20 mM;

(c) sucrose at a concentration of about 220 mM; and

(d) polysorbate-20 at a concentration of about 0.04% (v/v),

(e) a diluent comprising glucose,
at pH 5.5,

and wherein the administering is before or during formation of a blood clot.

[0017] In some examples, the primate subject is a baboon. In some examples, the primate subject is a human. In some examples, the thrombosis is an experimentally-induced thrombosis. In some examples, the primate subject is at risk of vascular graft thrombosis. In some examples, the single dose is administered to prevent thrombosis. In some examples, the single dose is administered to treat thrombosis. In some examples, the single dose is parenteral or intravenous. In certain examples, the single dose is followed by subsequent doses. In certain examples, the subsequent doses are parenteral.

[0018] In some examples, about 1 mg/kg is the therapeutically effective amount of the anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or antigen-binding fragment thereof, for administration to the primate subject. In some examples, about 150 mg is the therapeutically effective amount of the anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or antigen-binding fragment thereof, for administration to the primate subject.

[0019] In another example, provided herein is a method of treating a subject having a thrombocytopenia, wherein the thrombocytopenia is selected from the group consisting of: chemotherapy-induced thrombocytopenia, congenital thrombocytopenia, thrombocytopenia associated with infection, and idiopathic thrombocytopenia, the method comprising administering a therapeutically effective amount of a Factor XI and/or Factor XIa antibody, or an antigen-binding fragment thereof, to the subject in need thereof.

[0020] In some examples, the subject having a thrombocytopenia has a cancer.

[0021] In some examples, the subject having a thrombocytopenia has cirrhosis.

[0022] In some examples, the subject having a thrombocytopenia has idiopathic thrombocytopenic purpura (ITP).

[0023] In another example, provided herein is a method of treating a cancer subject having a chemotherapy-induced thrombocytopenia, wherein the method comprises administering a therapeutically effective amount of a Factor XI and/or Factor XIa antibody, or an antigen-binding fragment thereof, to the cancer subject in need thereof.

[0024] In some examples, the subject or the cancer subject is afflicted with or at risk of developing a thromboembolic disorder.

[0025] In some examples of the above examples, the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) comprising complementary determining regions HCDR1, HCDR2, and HCDR3 in SEQ ID NO: 9 or 29; and a light chain variable region (VL) comprising complementary determining regions LCDR1, LCDR2, LCDR3 in SEQ ID NO: 19 or 39.

[0026] In some examples of the above examples, the antibody or antigen-binding fragment thereof comprises:

- i. a heavy chain variable region CDR1 of SEQ ID NO: 23; a heavy chain variable region CDR2 of SEQ ID NO: 24; a heavy chain variable region CDR3 of SEQ ID NO: 25; a light chain variable region CDR1 of SEQ ID NO: 33; a light chain variable region CDR2 of SEQ ID NO: 34; and a light chain variable region CDR3 of SEQ ID NO: 35;
- ii. a heavy chain variable region CDR1 of SEQ ID NO: 26; a heavy chain variable region CDR2 of SEQ ID NO: 27; a heavy chain variable region CDR3 of SEQ ID NO: 28; a light chain variable region CDR1 of SEQ ID NO: 36; a light chain variable region CDR2 of KNY; and a light chain variable region CDR3 of SEQ ID NO: 38;
- iii. a heavy chain variable region CDR1 of SEQ ID NO: 43; a heavy chain variable region CDR2 of SEQ ID NO: 44; a heavy chain variable region CDR3 of SEQ ID NO: 45; a light chain variable region CDR1 of SEQ ID NO: 47; a light chain variable region CDR2 of KNY; and a light chain variable region CDR3 of SEQ ID NO: 15; or
- iv. a heavy chain variable region CDR1 of SEQ ID NO: 46; a heavy chain variable region CDR2 of SEQ ID NO: 4; a heavy chain variable region CDR3 of SEQ ID NO: 5; a light chain variable region

CDR1 of SEQ ID NO: 33; a light chain variable region CDR2 of SEQ ID NO: 14; and a light chain variable region CDR3 of SEQ ID NO: 15.

[0027] In some examples, the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) selected from the group consisting of SEQ ID NO: 9, 29, and a VH with 90% identity thereto; and a light chain variable region (VL) selected from the group consisting of SEQ ID NO: 19, 39, and a VL with 90% identity thereto.

[0028] In some examples, the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) selected from the group consisting of SEQ ID NO: 9 and 29; and a light chain variable region (VL) selected from the group consisting of SEQ ID NO: 19 and 39. In some examples, the antibody comprises a heavy chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 31, 11, and a heavy chain with 90% identity thereto; and a light chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 41, 21, and a light chain with 90% identity thereto. In some examples, the antibody comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 31 and a light chain comprising an amino acid sequence of SEQ ID NO: 41.

[0029] In some examples, the antibody is a human monoclonal antibody. In some examples, the antibody is a human IgG1 isotype. In certain examples, the antibody comprises D265A and P329A substitutions in the Fc domain.

[0030] In some examples, the administering of the antibody or antigen-binding fragment thereof does not affect platelet aggregation in the subject as compared to platelet aggregation prior to the administering. In certain examples, the platelet aggregation is measured by impedance platelet aggregometry. In certain examples, the platelet aggregation is induced by collagen, adenosine 5'-diphosphate (ADP), or thrombin receptor activating peptide-6 (TRAP-6). In certain examples, the platelet aggregation is determined *ex vivo* or *in vitro*.

[0031] In some examples, the antibody or antigen-binding fragment thereof is administered intravenously.

[0032] In some examples, the antibody or antigen-binding fragment thereof is administered subcutaneously.

[0033] In some examples, a first dose of the antibody or antigen-binding fragment thereof is administered intravenously and a second dose of the antibody or antigen-binding fragment is administered subcutaneously. In certain examples, the method further

comprises one or more additional doses of the antibody or antigen-binding fragment thereof administered subcutaneously following the administering of the second dose.

[0034] In some examples, the antibody or antigen-binding fragment thereof is administered once a month.

[0035] Other examples and details of the disclosure are presented herein below.

BRIEF DESCRIPTION OF THE DRAWINGS

[0036] **FIG. 1** depicts line graphs showing a time course of activated partial thromboplastin time (aPTT) following 1 mg/kg intravenous administration of Antibody 1 in four baboons.

[0037] **FIGs. 2A-2B** depict bleeding time (**FIG. 2A**) and bleeding volume (**FIG. 2B**) before and during each arteriovenous (AV) shunt experiment.

[0038] **FIGs. 3A-3B** depict platelet deposition in the tail segment of the AV shunt for collagen-coating (**FIG. 3A**) or collagen + tissue factor (TF) coating (**FIG. 3B**). Vertical dotted line depicts time of Antibody 1 administration and the arrow shows the inflection point where platelet deposition was halted. Time between the dotted vertical line and arrow measures time between drug administration and the point where platelet deposition rate turns negative.

[0039] **FIGs. 4A-4F** depict platelet deposition in the tail segment of the AV shunt for the three treated baboons. **FIG. 4A**, **FIG. 4B**, and **FIG. 4C** showing collagen-coating and **FIG. 4D**, **FIG. 4E**, and **FIG. 4F** show collagen + TF coating.

[0040] **FIGs. 5A-5B** show platelet deposition in the collagen-coated (**FIG. 5A**) or collagen + TF coated (**FIG. 5B**) segments of the AV shunt. Data are an average of the three baboons.

[0041] **FIGs. 6A-6D** depict fibrin content of the thrombi in the collagen-coated graft (**FIG. 6A**), collagen + TF-coated graft (**FIG. 6B**), tail segment downstream to a collagen-coated graft (**FIG. 6C**), and tail segment downstream to a collagen + TF-coated graft (**FIG. 6D**).

[0042] **FIGs. 7A-7B** depict *in vitro* platelet aggregation in donor whole blood supplemented with vehicle, Antibody 1, or abciximab following induction with collagen (**FIG. 7A**) or TRAP-6 (**FIG. 7B**).

WHAT IS CLAIMED IS:

1. Use of a first dose of about 150 mg of an isolated anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or an antigen-binding fragment thereof, in the manufacture of a first medicament for intravenous administration and use of a second dose of the isolated anti-FXI and/or anti-FXIa antibody or the antigen-binding fragment thereof in the manufacture of a second medicament for subcutaneous administration, wherein the first and second medicaments are to be used in combination therapy to treat a cancer in a subject in need thereof, optionally wherein the cancer is gastrointestinal cancer or genitourinary cancer, and wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) comprising complementary determining regions HCDR1, HCDR2, and HCDR3 in SEQ ID NOs: 9 or 29; and a light chain variable region (VL) comprising complementary determining regions LCDR1, LCDR2, LCDR3 in SEQ ID NOs: 19 or 39.
2. The use of claim 1, wherein the second dose comprises about 150 mg of the isolated anti-FXI and/or anti-FXIa antibody or the antigen-binding fragment thereof.
3. The use of claim 1 or 2, wherein the first dose of the isolated anti-FXI and/or anti-FXIa antibody or the antigen-binding fragment thereof is formulated as an intravenous drug delivery formulation comprising about 150 mg of the antibody or the antigen-binding fragment thereof.
4. The use of any one of claims 1-3, wherein the second dose of the isolated anti-FXI and/or anti-FXIa antibody or the antigen-binding fragment thereof is formulated as a subcutaneous drug delivery formulation comprising about 150 mg of the antibody or the antigen-binding fragment thereof.
5. The use of any one of claims 1-4, wherein the antibody is a human monoclonal antibody, optionally wherein the antibody is a human IgG1 isotype, further optionally wherein the antibody comprises an Fc domain, and wherein the Fc domain comprises D265A and P329A substitutions.

6. The use of any one of claims 1-5, wherein the antibody or antigen-binding fragment thereof is to be administered in a drug delivery formulation comprising:
 - (a) a histidine buffer at a concentration of about 20 mM;
 - (b) sucrose at a concentration of about 220 mM;
 - (c) polysorbate 20 at a concentration of about 0.04%; and/or
 - (d) about 5% glucose,optionally wherein the antibody or antigen-binding fragment thereof is to be administered in a drug delivery formulation at pH 5.5.
7. The use of any one of claims 1-6, wherein the subject is at high risk of venous thromboembolism and/or wherein the subject has had one or more previous venous thromboembolisms.
8. The use of any one of claims 1-7, wherein the use further comprises one or more additional subcutaneous doses of the antibody or antigen-binding fragment thereof, optionally wherein the use comprises five subcutaneous doses of the antibody or antigen-binding fragment thereof to be administered.
9. The use of any one of claims 1-8, wherein the antibody or antigen-binding fragment thereof is to be administered subcutaneously about once a month, optionally wherein the antibody or antigen-binding fragment thereof is to be administered intravenously on day 1 and is to be administered subcutaneously on days 31, 61, 91, 121, and 151, optionally wherein the subject is to be treated for about six months.
10. Use of a drug delivery formulation comprising about 150 mg of an isolated anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating a subject with a cancer, wherein the drug delivery formulation is to be administered once intravenously and subsequently is to be administered subcutaneously about once a month, wherein the subject is to be treated for about six months, and wherein the antibody or antigen-binding fragment

thereof comprises a heavy chain variable region (VH) comprising complementary determining regions HCDR1, HCDR2, and HCDR3 in SEQ ID NOs: 9 or 29; and a light chain variable region (VL) comprising complementary determining regions LCDR1, LCDR2, LCDR3 in SEQ ID NOs: 19 or 39.

11. The use of claim 10, wherein the cancer is selected from the group consisting of gastrointestinal cancer and genitourinary cancer.
12. Use of a single dose of a drug delivery formulation comprising:
 - (a) a therapeutically effective amount of an isolated anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or antigen-binding fragment thereof at a concentration of about 150 mg;
 - (b) a histidine buffer at a concentration of about 20 mM;
 - (c) sucrose at a concentration of about 220 mM;
 - (d) polysorbate-20 at a concentration of about 0.04% (v/v), and
 - (e) a diluent comprising glucose at pH 5.5,in the manufacture of a medicament for treating a primate subject at risk of thrombosis, and wherein the drug delivery formulation is to be administered before or during formation of a blood clot.
13. The use of claim 12, wherein the primate subject is a baboon or a human, optionally wherein the primate subject is a baboon and the thrombosis is an experimentally-induced thrombosis.
14. The use of claim 12 or 13, wherein the primate subject is at risk of vascular graft thrombosis.
15. The use of any one of claims 12-14, wherein the single dose is to be administered to prevent or treat thrombosis.
16. The use of any one of claims 12-15, wherein the single dose is parenteral or intravenous.

17. The use of any one of claims 12-16, wherein the primate subject is a baboon and the therapeutically effective amount of the anti-FXI and/or anti-FXIa antibody or antigen-binding fragment thereof is about 1 mg/kg.
18. The use of any one of claims 12-17, wherein the primate subject is a human and the therapeutically effective amount of the anti-FXI and/or anti-FXIa antibody or antigen-binding fragment thereof is about 150 mg.
19. Use of an anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating a subject having a thrombocytopenia,
wherein the thrombocytopenia is selected from the group consisting of: chemotherapy-induced thrombocytopenia, congenital thrombocytopenia, thrombocytopenia associated with infection, and idiopathic thrombocytopenia, and
wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) comprising complementary determining regions HCDR1, HCDR2, and HCDR3 in SEQ ID NOs: 9 or 29; and a light chain variable region (VL) comprising complementary determining regions LCDR1, LCDR2, LCDR3 in SEQ ID NOs: 19 or 39.
20. The use of claim 19, wherein the subject having a thrombocytopenia has one or more of a cancer, cirrhosis, or idiopathic thrombocytopenic purpura (ITP).
21. Use of an anti-Factor XI (FXI) and/or anti-activated Factor XI (FXIa) antibody or an antigen-binding fragment thereof in the manufacture of a medicament for treating a cancer subject having a cancer and a chemotherapy-induced thrombocytopenia,
wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH) comprising complementary determining regions HCDR1, HCDR2, and HCDR3 in SEQ ID NO: 9 or 29s; and a light chain variable region (VL) comprising complementary determining regions LCDR1, LCDR2, LCDR3 in SEQ ID NOs: 19 or 39.
22. The use of any one of claims 19-21, wherein the subject is afflicted with or at risk of developing a thromboembolic disorder.

23. The use of any one of claims 1-22, wherein the antibody or antigen-binding fragment thereof comprises:
- (a) a heavy chain variable region CDR1 of SEQ ID NO: 23; a heavy chain variable region CDR2 of SEQ ID NO: 24; a heavy chain variable region CDR3 of SEQ ID NO: 25; a light chain variable region CDR1 of SEQ ID NO: 33; a light chain variable region CDR2 of SEQ ID NO: 34; and a light chain variable region CDR3 of SEQ ID NO: 35;
 - (b) a heavy chain variable region CDR1 of SEQ ID NO: 26; a heavy chain variable region CDR2 of SEQ ID NO: 27; a heavy chain variable region CDR3 of SEQ ID NO: 28; a light chain variable region CDR1 of SEQ ID NO: 36; a light chain variable region CDR2 of KNY; and a light chain variable region CDR3 of SEQ ID NO: 38;
 - (c) a heavy chain variable region CDR1 of SEQ ID NO: 43; a heavy chain variable region CDR2 of SEQ ID NO: 44; a heavy chain variable region CDR3 of SEQ ID NO: 45; a light chain variable region CDR1 of SEQ ID NO: 47; a light chain variable region CDR2 of KNY; and a light chain variable region CDR3 of SEQ ID NO: 15; or
 - (d) a heavy chain variable region CDR1 of SEQ ID NO: 46; a heavy chain variable region CDR2 of SEQ ID NO: 4; a heavy chain variable region CDR3 of SEQ ID NO: 5; a light chain variable region CDR1 of SEQ ID NO: 33; a light chain variable region CDR2 of SEQ ID NO: 14; and a light chain variable region CDR3 of SEQ ID NO: 15.
24. The use of any one of claims 1-23, wherein the antibody or antigen-binding fragment thereof comprises a VH selected from the group consisting of SEQ ID NOs: 9, 29, and a VH with 90% identity thereto; and a VL selected from the group consisting of SEQ ID NOs: 19, 39, and a VL with 90% identity thereto.
25. The use of any one of claims 1-24, wherein the antibody comprises a heavy chain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 31, 11, and a heavy chain with 90% identity thereto; and a light chain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 41, 21, and a light chain with 90% identity thereto.

26. The use of any one of claims 1-25, wherein the antibody comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 31 and a light chain comprising an amino acid sequence of SEQ ID NO: 41.
27. The use of any one of claims 1-26, wherein the antibody is a human monoclonal antibody, optionally wherein the antibody is a human IgG1 isotype.
28. The use of claim 27, wherein the antibody comprises an Fc domain, and wherein the Fc domain comprises D265A and P329A substitutions.
29. The use of any one of claims 1-28, wherein the administration of the antibody or antigen-binding fragment thereof does not affect platelet aggregation in the subject as compared to platelet aggregation prior to the administration, optionally wherein the platelet aggregation is measured by impedance platelet aggregometry, optionally wherein the platelet aggregation is induced by collagen, adenosine 5'-diphosphate (ADP), or thrombin receptor activating peptide-6 (TRAP-6), optionally wherein the platelet aggregation is determined *ex vivo* or *in vitro*.
30. The use of any one of claims 19-29, wherein the antibody or antigen-binding fragment thereof is to be administered intravenously or subcutaneously.
31. The use of any one of claims 19-30, wherein a first dose of the antibody or antigen-binding fragment thereof is to be administered intravenously and a second dose of the antibody or antigen-binding fragment is to be administered subcutaneously, optionally wherein the use further comprises one or more additional doses of the antibody or antigen-binding fragment thereof to be administered subcutaneously following the administration of the second dose.
32. The use of any one of claims 19-31, wherein the antibody or antigen-binding fragment thereof is to be administered once a month.