CLAIMS

1. Use of an antibody in the manufacture of a medicament for the treatment of an inflammatory disease in a subject in need thereof, wherein the antibody binds to the extracellular domain of human Tissue Factor (TF), wherein the antibody binds human TF at a human TF binding site that is distinct from a human TF binding site bound by human FVIIa.

2. The use of claim 1, wherein the inflammatory disease is:

colitis, inflammatory bowel disease, arthritis, acute lung injury, acute respiratory distress syndrome (ARDS), and Respiratory Syncytial Virus (RSV);

a viral infection, optionally a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2);

a cardiovascular disease or injury, optionally myocardial infarction; or

a cardiovascular disease associated with upregulation of protease-activated receptor 2 (PAR-2).

3. The use of claim 1, wherein the inflammatory disease is a neurological disease, an inflammatory skin disease, rheumatism, vasculitis, lupus, dermatitis, or dermatosis due to acute inflammatory component.

4. The use of claim 1, wherein the inflammatory disease is an inflammatory disease that damages the skin or an inflammatory disease that damages the gastrointestinal tract.

5. The use of any one of claims 1 to 4, wherein:

(a) the antibody does not inhibit human thrombin generation as determined by thrombin generation assay (TGA); and/or

(b) the isolated human antibody does not inhibit or inhibits human thrombin generation to a lesser extent, as determined by thrombin generation assay (TGA), compared to a reference antibody comprising a V_H sequence of SEQ ID NO:821 and a V_L sequence of SEQ ID NO:822, optionally wherein binding between the isolated antibody and a variant TF extracellular domain comprising a mutation at amino acid residue 149 of the sequence shown in SEQ ID NO:810 is less than 50% of the binding between the isolated antibody and the extracellular domain of TF of the sequence shown in SEQ ID NO:810, as determined by the median fluorescence intensity value of the isolated antibody relative to an isotype control in a live cell staining assay; and/or

(c) the antibody comprises

(i) all three heavy chain Complementary Determining Regions (CDRs) and all three light chain CDRs from an antibody group in Table 35 wherein the all three heavy chain CDRs and the all three light chain CDRs are from the same antibody group, or

(ii) all three heavy chain Complementary Determining Regions (CDRs) and all three light chain CDRs from an antibody in any one of Tables 15-34, wherein the all three heavy chain CDRs and the all three light chain CDRs are from the same antibody, optionally comprising all three heavy chain CDRs and all three light chain CDRs from: the antibody designated 25A, the antibody designated 25A5, the antibody designated 25A5-T, the antibody designated 25G, the antibody designated 25G1, the antibody designated 25G9, the antibody designated 43B, the antibody designated 43B1, the antibody designated 43B7, the antibody designated 43D, the antibody designated 43D7, the antibody designated 43D8, the antibody designated 43E, or the antibody designated 43Ea; or

(iii) a VH Domain sequence and VL domain sequence from Table 14, wherein the VH and VL domain sequences are from the same group in Table 14; or

(iv) a VH Domain sequence and VL domain sequence from Table 13, wherein the VH and VL domain sequences are from the same clone in Table 13.

6. The use of claim 1 or 5(a), wherein the antibody comprises: a VH-CDR1 comprising the sequence set forth in SEQ ID NO:797; a VH-CDR2 comprising the sequence set forth in SEQ ID NO:798; a VH-CDR3 comprising the sequence set forth in SEQ ID NO:799; a VL-CDR1 comprising the sequence set forth in SEQ ID NO:800; a VL-CDR2 comprising the sequence set forth in SEQ ID NO:801; and a VL-CDR3 comprising the sequence set forth in SEQ ID NO:802, optionally wherein

the antibody comprises: a VH-CDR1 comprising the sequence set forth in SEQ ID NO:571; a VH-CDR2 comprising the sequence set forth in SEQ ID NO:572; a VH-CDR3 comprising the sequence set forth in SEQ ID NO:573; a VL-CDR1 comprising the sequence set forth in SEQ ID NO:574; a VL-CDR2 comprising the sequence set forth in SEQ ID NO:575; and a VL-CDR3 comprising the sequence set forth in SEQ ID NO:576; or

the antibody comprises: a VH-CDR1 comprising the sequence set forth in SEQ ID NO:609; a VH-CDR2 comprising the sequence set forth in SEQ ID NO:610; a VH-CDR3 comprising the sequence set forth in SEQ ID NO:611; a VL-CDR1 comprising the sequence set forth in SEQ ID NO:612; a VL-CDR2 comprising the sequence set forth in SEQ ID NO:613; and a VL-CDR3 comprising the sequence set forth in SEQ ID NO:614; or

the antibody comprises: a VH sequence comprising the sequence set forth in SEQ ID NO:769 and a VL sequence comprising the sequence set forth in SEQ ID NO:770, optionally wherein the antibody comprises: (i) a VH sequence comprising the sequence set forth in SEQ ID NO:569 and a VL sequence comprising the sequence set forth in SEQ ID NO:570, or (ii) a VH sequence comprising the sequence set forth in SEQ ID NO:607 and a VL sequence comprising the sequence set forth in SEQ ID NO:608; or

the antibody comprises: a heavy chain comprising the sequence set forth in SEQ ID NO:924 and a light chain comprising the sequence set forth in SEQ ID NO:925; or

the antibody comprises: a VH sequence comprising the sequence set forth in SEQ ID NO:645 and a VL sequence comprising the sequence set forth in SEQ ID NO:646; or

the antibody comprises: a heavy chain comprising the sequence set forth in SEQ ID NO:926 and a light chain comprising the sequence set forth in SEQ ID NO:927.

7. The use of any one of claims 1 to 05(b), wherein:

the antibody comprises: a VH-CDR1 comprising the sequence set forth in SEQ ID NO:779; a VH-CDR2 comprising the sequence set forth in SEQ ID NO:780; a VH-CDR3 comprising the sequence set forth in SEQ ID NO:781; a VL-CDR1 comprising the sequence set forth in SEQ ID NO:782; a VL-CDR2 comprising the sequence set forth in SEQ ID NO:783; and a VL-CDR3 comprising the sequence set forth in SEQ ID NO:784; or

the antibody comprises: a VH-CDR1 comprising the sequence set forth in SEQ ID NO:872; a VH-CDR2 comprising the sequence set forth in SEQ ID NO:873; a VH-CDR3 comprising the sequence set forth in SEQ ID NO:874; a VL-CDR1 comprising the sequence set forth in SEQ ID NO:875; a VL-CDR2 comprising the sequence set forth in SEQ ID NO:876; and a VL-CDR3 comprising the sequence set forth in SEQ ID NO:877, optionally wherein the antibody comprises: a VH-CDR1 comprising the sequence set forth in SEQ ID NO:884; a VH-CDR2 comprising the sequence set forth in SEQ ID NO:885; a VH-CDR3 comprising the sequence set forth in SEQ ID NO:886; a VL-CDR1 comprising the sequence

set forth in SEQ ID NO:887; a VL-CDR2 comprising the sequence set forth in SEQ ID NO:888; and a VL-CDR3 comprising the sequence set forth in SEQ ID NO:889; or

the antibody comprises: a VH sequence comprising the sequence set forth in SEQ ID NO:868 and a VL sequence comprising the sequence set forth in SEQ ID NO:869, optionally wherein the antibody comprises: (i) a VH sequence comprising the sequence set forth in SEQ ID NO:189 and a VL sequence comprising the sequence set forth in SEQ ID NO:190, or (ii) a VH sequence comprising the sequence set forth in SEQ ID NO:836 and a VL sequence comprising the sequence set forth in SEQ ID NO:837; or

the antibody comprises: a heavy chain comprising the sequence set forth in SEQ ID NO:920 and a light chain comprising the sequence set forth in SEQ ID NO:921.

8. The use of any one of claims 1 to 5(c)(i), wherein:

the antibody comprises: a VH-CDR1 comprising the sequence set forth in SEQ ID NO:878; a VH-CDR2 comprising the sequence set forth in SEQ ID NO:879; a VH-CDR3 comprising the sequence set forth in SEQ ID NO:880; a VL-CDR1 comprising the sequence set forth in SEQ ID NO:881; a VL-CDR2 comprising the sequence set forth in SEQ ID NO:882; and a VL-CDR3 comprising the sequence set forth in SEQ ID NO:883, optionally wherein the antibody comprises: a VH-CDR1 comprising the sequence set forth in SEQ ID NO:267; a VH-CDR2 comprising the sequence set forth in SEQ ID NO:268; a VH-CDR3 comprising the sequence set forth in SEQ ID NO:269; a VL-CDR1 comprising the sequence set forth in SEQ ID NO:270; a VL-CDR2 comprising the sequence set forth in SEQ ID NO:271; and a VL-CDR3 comprising the sequence set forth in SEQ ID NO:272; or

the antibody comprises: a VH sequence comprising the sequence set forth in SEQ ID NO:870 and a VL sequence comprising the sequence set forth in SEQ ID NO:871, optionally wherein the antibody comprises: a VH sequence comprising the sequence set forth in SEQ ID NO:303 and a VL sequence comprising the sequence set forth in SEQ ID NO:304; or

the antibody comprises: a heavy chain comprising the sequence set forth in SEQ ID NO:922 and a light chain comprising the sequence set forth in SEQ ID NO:923.

9. The use of any one of claims 1 to 8, wherein:

the antibody competes for binding to human TF with the antibody designated 25A, the antibody designated 25A5, the antibody designated 25A5-T, the antibody designated 25G, the antibody designated 25G1, the antibody designated 25G9, the antibody designated 43B, the

antibody designated 43B1, the antibody designated 43B7, the antibody designated 43D, the antibody designated 43D7, the antibody designated 43D8, the antibody designated 43E, or the antibody designated 43Ea; and/or

the antibody binds to the same human TF epitope bound by the antibody designated 25A, the antibody designated 25A5, the antibody designated 25A5-T, the antibody designated 25G, the antibody designated 25G1, the antibody designated 25G9, the antibody designated 43B, the antibody designated 43B1, the antibody designated 43B7, the antibody designated 43D, the antibody designated 43D7, the antibody designated 43D8, the antibody designated 43E, or the antibody designated 43Ea.

10. The use of any one of claims 1 to 9, wherein the antibody does not inhibit human thrombin generation as determined by thrombin generation assay (TGA), does not reduce the thrombin peak on a thrombin generation curve (Peak IIa) compared to an isotype control, does not increase the time from the assay start to the thrombin peak on a thrombin generation curve (ttPeak) compared to an isotype control, does not decrease the endogenous thrombin potential (ETP) as determined by the area under a thrombin generation curve compared to an isotype control, allows human thrombin generation as determined by thrombin generation assay (TGA), maintains the thrombin peak on a thrombin generation curve (Peak IIa) compared to an isotype control, maintains the time from the assay start to the thrombin peak on a thrombin generation curve (ttPeak) compared to an isotype control, preserves the endogenous thrombin potential (ETP) as determined by the area under a thrombin generation curve compared to an isotype control, binds human TF at a human TF binding site that is distinct from a human TF binding site bound by human FX, does not interfere with the ability of TF:FVIIa to convert FX into FXa, and does not compete for binding to human TF with FVIIa.

11. The use of any one of claims 1 to 10, wherein:

the three heavy chain CDRs and the three light chain CDRs are determined using exemplary, Kabat, Chothia, AbM, Contact, or IMGT numbering; and/or

the antibody specifically binds to cynomolgus TF; and/or

the antibody binds to specifically mouse TF; and/or

the antibody binds to specifically rabbit TF; and/or

the antibody binds to specifically pig TF; and/or

the disease involves vascular inflammation; and/or

the disease involves local inflammation; and/or

the disease involves systemic inflammation; and/or

the disease involves infiltration of mononuclear cells and/or granulocytes, optionally wherein the mononuclear cells comprise macrophages and/or lymphocytes, and/or wherein the granulocytes comprise neutrophils and/or eosinophils.

12. The use of any one of claims 1 to 11, wherein:

(a) the antibody is to be administered to a subject and the antibody reduces the total leukocyte count, optionally wherein the total leukocyte count is determined by light microscopy; and/or

(b) the antibody is to be administered to a subject and the antibody reduces the total number of granulocytes, optionally wherein the granulocytes comprise neutrophils and/or eosinophils, optionally wherein the total number of granulocytes is determined by immunohistochemical (IHC) analysis or bronco-alveolar lavage (BAL) fluid differential cell count, optionally wherein the granulocytes are in the alveoli and/or in the interstitial fluid; and/or

(c) the antibody is to be administered to a subject and the antibody reduces the total number of mononuclear cells, optionally wherein the mononuclear cells comprise macrophages optionally M1 macrophages and/or wherein the mononuclear cells comprise lymphocytes and/or wherein the mononuclear cells comprise monocytes, optionally wherein the total number of mononuclear cells is determined by immunohistochemical (IHC) analysis or bronco-alveolar lavage (BAL) fluid differential cell count, optionally wherein the mononuclear cells are in the alveoli or in the interstitial fluid; and/or

(d) the antibody is to be administered to a subject and the subject maintains or increases body weight relative to baseline levels; and/or

(e) the antibody is to be administered to a subject and the antibody maintains or increases body weight relative to a different anti-inflammatory therapeutic; and/or

(f) the antibody is to be administered to a subject and the antibody reduces the spleen size or reverses spleen enlargement relative to baseline levels, and/or wherein the antibody reduces the spleen size or reverses splenomegaly relative to a different anti-inflammatory

therapeutic, optionally wherein the spleen size or splenomegaly is determined using palpation, percussion, ultrasound, computerized tomography (CT) scan or magnetic resonance imagining (MRI); and/or

(g) the inflammatory disease is acute lung injury or acute respiratory distress syndrome (ARDS); and/or

(h) the antibody is to be administered to a subject and the antibody increases net alveolar fluid clearance relative to baseline levels or relative to a different anti-inflammatory therapeutic, optionally wherein net alveolar fluid clearance is determined by measuring sequential edema fluid protein concentrations, optionally wherein the sequential edema fluid protein concentrations are measured with ELISA; and/or

(i) the inflammatory disease is SARS-Cov-2 and wherein the antibody is to be administered to a subject and the subject maintains or increases body weight relative to baseline levels, optionally wherein the antibody maintains or increases body weight relative to a different anti-inflammatory therapeutic; and/or

(j) the antibody is to be administered to a subject and the antibody reduces the concentration of inflammatory cytokines and chemokines relative to baseline levels and/or reduces the concentration of inflammatory cytokines and chemokines relative to a different anti-inflammatory therapeutic, optionally wherein the inflammatory cytokines and chemokines are in bronco-alveolar lavage (BAL) samples and/or in lung homogenate samples, optionally wherein the inflammatory cytokines and chemokines comprise one or more of: IL-1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IFNγ, GM-CSF, TNFα, CCL2, CCL3, CCL4, CCL5, CCL19, CCL20, CCL25, CXCL1, CXCL2, and CXCL10, or wherein the inflammatory cytokines and chemokines comprise VEGF, or wherein the inflammatory cytokines and chemokines comprise one or more of: GMCSF, VEGF, IL17F, IL-1 beta, IL-6, IFNγ, IL-8, and KC, optionally wherein the inflammatory cytokines and chemokines are measured using ELISA or using Luminex Multiplex Assay.

13. The use of any one of claims 1 to 12(f), wherein:

the inflammatory disease is a viral infection, optionally wherein

the antibody is to be administered to a subject and the antibody increases anti-inflammatory cytokines and chemokines relative to baseline levels; and/or

the antibody is to be administered to a subject and the antibody increases anti-inflammatory cytokines and chemokines relative to a different anti-inflammatory therapeutic; and/or

the anti-inflammatory cytokines and chemokines comprise one or more of: IL-10 and IL27p28; and/or

the anti-inflammatory cytokines and chemokines are in bronco-alveolar lavage (BAL) samples; and/or

the inflammatory cytokines and chemokines are measured using multiplex electrochemiluminescence MSD assay or using Luminex Multiplex Assay;

or

the inflammatory disease is RSV.

14. The use of any one of claims 1 to 13, wherein the antibody is to be administered to a subject and the antibody reduces fibrosis in the lungs relative to baseline levels and/or relative to a different anti-inflammatory therapeutic, optionally wherein the fibrosis is determined by IHC analysis or by Quantitative High Resolution Computed Tomography (qHRCT).

15. The use of any one of claims 1 to 12(f), wherein:

the inflammatory disease is arthritis, optionally wherein the antibody is to be administered to a subject and the antibody reduces the concentration of inflammatory cytokines and chemokines relative to baseline levels and/or relative to a different anti-inflammatory therapeutic, optionally wherein the inflammatory cytokines and chemokines comprise one or more of: IL-1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IFNγ, GM-CSF, TNFα, CCL2, CCL3, CCL4, CCL5 CCL19, CCL20, CCL25, CXCL1, CXCL2, and CXCL10;

or

the inflammatory disease is colitis or inflammatory bowel disease, optionally wherein the antibody is to be administered to a subject and the antibody results in a normal stool consistency or hardens the subject's stool consistency relative to baseline levels and/or relative to a different anti-inflammatory therapeutic optionally wherein the stool consistency is determined using the Bristol Stool Scale; and/or wherein the antibody is to be administered

to a subject and the antibody reduces blood or results in the absence of blood in the subject's stool relative to baseline levels or relative to a different anti-inflammatory therapeutic, optionally wherein the blood in the subject's stool is measured using a hemoccult test; and/or wherein the antibody is to be administered to a subject and the antibody reduces the concentration of inflammatory cytokines and chemokines relative to baseline levels or relative to a different anti-inflammatory therapeutic, optionally wherein the inflammatory cytokines and chemokines comprise one or more of: IL-1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IFNγ, GM-CSF, TNFα, CCL2, CCL3, CCL4, CCL5,CCL19, CCL20, CCL25, CXCL1, CXCL2, and CXCL10;

or

the inflammatory disease is myocardial infarction, optionally wherein the antibody reduces infarct size relative to baseline levels and/or relative to a different anti-inflammatory therapeutic and/or wherein the antibody is to be administered to a subject and the antibody increases left ventricular ejection fraction relative to baseline levels and/or relative to a different anti-inflammatory therapeutic, and/or wherein the antibody is to be administered to a subject and the antibody decreases left ventricular end diastolic volume relative to baseline levels or relative to a different anti-inflammatory therapeutic, and/or wherein the antibody is to be administered to a subject and the antibody decreases inflammatory cell recruitment in the infarcted myocardium relative to baseline levels or relative to a different anti-inflammatory therapeutic, optionally wherein the inflammatory cells are selected from CD45+, $CD11b^{+}$, $Ly6C^{hi}$, $CD45^{+}/CD90.2^{-}/NK1.1^{-}/CD11b^{+}$, $CD45^{+}/CD90.2^{-}/NK1.1^{-}/CD11b^{+}/Ly6C^{hi}$, and $CD45^{+}/CD90.2^{-}/NK1.1^{-}/CD11b^{+}/Ly6C^{lo}$, optionally wherein the inflammatory cell recruitment is measured using flow cytometry.

16. The use of any one of claims 1 to 15, wherein:

the antibody is to be administered to a subject and the antibody results in a reduced need for systemic steroids; and/or

wherein the different anti-inflammatory therapeutic comprises one or more of: a non-steroidal anti-inflammatory drug (NSAID), a steroidal anti-inflammatory drug, a beta-agonist, an anticholinergic agent, an antihistamine, and a methyl xanthine; and/or

the different anti-inflammatory therapeutic comprises any one of: an IL-6 inhibitor, anti-GM-CSF, anti-TNFa, anti-IL-1a, dexamethasone, a chemokine and chemokine receptor antagonist, and a JAK inhibitor.

17. The use of any one of claims 1 to 16, wherein the antibody is to be administered biweekly or weekly.