CLAIMS

1. ~~A method~~Use of a composition in the manufacture of a medicament for ~~treating~~the treatment of a hereditary bleeding disorder in a subject ~~comprising administering to~~wherein the ~~subject a therapeutic effective amount of a pharmaceutic~~ composition ~~comprising~~comprises a VWF targeting agent.

2. The ~~method~~use of claim 1, wherein the hereditary bleeding disorder is an acquired platelet function defect, congenital platelet function defects, disseminated intravascular coagulation (DIC), prothrombin deficiency, fibrinogen deficiency, FV deficiency, FVII deficiency, FX deficiency, FXI deficiency (hemophilia C), FXIII deficiency, combined FV and FVIII deficiency (F5F8D), VKCFD, Glanzmann thrombasthenia, hemophilia A, hemophilia B, immune thrombocytopenic purpura (ITP), von Willebrand disease (VWD) Type 1, von Willebrand disease (VWD) Type 2, and Von Willebrand disease (VWD) Type 3~~.~~; optionally,

~~3. The method of claim 2, wherein the hereditary bleeding disorder is hemophilia A, VWD Type 1, VWD Type 2, or VWD Type 3.~~

~~4. The method of claim 3,~~ wherein the hereditary bleeding disorder is hemophilia A, mild hemophilia, moderate hemophilia, ~~or~~ severe hemophilia~~.~~

~~5. The method of claim 3, wherein the hereditary bleeding disorder is,~~ VWD Type 1, VWD Type 1 Vicenza subtype, VWD Type 2a, VWD Type 2b, VWD Type 2b with thrombocytopenia, VWD Type 2m, VWD Type 2n~~,~~,, or VWD Type 3.

~~6~~3. The ~~method~~use of ~~any one of claims~~claim 1~~-5~~ or 2, wherein the VWF targeting agent is a VWF binding agent selected from the group consisting of a synthetic polynucleotide, an antibody, a nanobody, a peptide, an oligonucleotide, a siRNA, a microRNA, ~~a synthetic polynucleotide,~~ and a small molecule.

~~7~~4. The ~~method~~use of claim ~~6~~3, wherein the VWF binding agent is a synthetic polynucleotide selected from the group consisting of BT200 (SEQ ID No.: 6), SEQ ID No.: 3, BT99 (SEQ

ID No.: 4), BT100 (SEQ ID No.: ~~5), BT200 (SEQ ID No.: 6~~5), ARC15105 (SEQ ID No.: 7), and ARC1779 (SEQ ID No.: 8) and variants thereof.

~~8~~5. The ~~method~~use of claim ~~7~~4, wherein the VWF binding agent is BT200 (SEQ ID No.: 6) or a variant thereof.

~~9~~6. The ~~method~~use of claim ~~8~~5, wherein BT200 increases the levels and activity of VWF, the levels and activity of FVIII, and/or the platelet counts in the blood.

~~10~~7. The ~~method~~use of claim ~~8~~5, wherein BT200 is to be administered to the subject at a dose ranging from 0.1 mg to 48.0 mg, or from 0.1mg to 20.0 mg, or from 1.0mg to 10mg~~.~~; and optionally,

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~~11. The method of claim 10,~~ wherein BT200 is to be administered to the subject at a dose ranging from 0.6 mg to 6.0 mg.

~~12. The method of claim~~ 8. The use of claim 4, wherein the VWF binding agent is to be administered to the subject via subcutaneous injection.

~~13~~9. The ~~method~~use of claim ~~12~~4, wherein the VWF binding agent is to be administered to the subject with multiple doses, and wherein each dose is to be administered once every other day, or once every three days, or once every five days, or once a week, or once every other week.

~~14~~10. The ~~method~~use of any one of claims 1-~~13~~9, wherein the treatment of the hereditary bleeding disorder is a therapy treatment or a prophylactic treatment.

~~15~~11. The ~~method~~use of claim ~~3~~2, wherein the VWF targeting agent is to be administered in combination with coagulation factor substitute treatment; the coagulation factor substitute is plasma derived FVIII/VWF concentrates, recombinant FVIII preparations, or recombinant VWF preparations.

12. Use of a composition in the manufacture of a medicament for use in a ~~16. A~~ method for

i) preventing a chronic bleeding condition, and/or spontaneous bleeding in a subject ~~comprising administering to the~~ ;

ii) blocking VWF clearance in the blood of a subject ~~a therapeutic effective amount~~;

iii) elevating the FVIII levels in the blood of a subject; or

iv) increasing platelet counts in the blood of a ~~pharmaceutic~~patient having a low platelet count (thrombocytopenia);

wherein the composition ~~comprising~~comprises a VWF targeting agent~~.~~

~~17. The method of claim 16, wherein the VWF targeting agent~~ that is a VWF binding agent ~~selected from the group consisting of an antibody, a nanobody, a peptide, an oligonucleotide, a siRNA, a microRNA, a synthetic polynucleotide, and a small molecule.~~

that~~18. The method of claim 17, wherein the VWF binding agent~~ is a synthetic polynucleotide comprising PEGylated nucleic acids.

~~19~~13. The ~~method~~use of claim ~~18~~12, wherein the VWF binding agent is BT200 (SEQ ID No.: 6), or a variant thereof.

~~20~~14. The ~~method~~use of claim ~~19~~13, wherein

i) when used in preventing a chronic bleeding condition, and/or spontaneous bleeding in a subject, BT200 is to be administered at a dose ranging from 1.0mg to 10.0mg, or alternatively at a dose ranging from 1.0mg to 6.0mg~~.~~; or

~~21. A method for~~ ii) when used in blocking VWF clearance in the blood ~~comprising providing an effective amount~~ of a ~~VWF targeting agent that is a synthetic polynucleotide comprising a PEGylation moiety.~~

subject,

~~22. The method of claim 21, wherein the VWF targeting agent is~~ BT200 ~~(SEQ ID No.: 6), or a variant thereof.~~

~~23. The method of claim 22, wherein BT200 is~~is to be provided at an amount ranging from 0.6mg to 6.0mg, or from 1.0mg to 6.0mg, or from 1.0mg to 10.0mg.

~~24~~15. The ~~method~~use of claim ~~23~~13, wherein when used for blocking VWF clearance in the blood of a subject, BT 200 increases VWF levels in the blood.

16. ~~25. A method for~~The use of claim 13, wherein when used in elevating the FVIII levels in the blood of a subject ~~comprising administering to the subject an efficient amount of a composition comprising a VWF targeting agent that is a synthetic polynucleotide comprising a PEGylation moiety.~~

~~26. The method of claim 25, wherein~~ , the subject is diagnosed with hemophilia A, VWD Type 1, VWD Type 2, or VWD Type 3.

~~27~~17. The ~~method~~use of claim ~~26, wherein the VWF targeting agent is BT200 (SEQ ID No.: 6).~~

~~28. The method of claim 27~~16, wherein BT200 increases FVIII clotting activity.

18. ~~29. A method for~~ The use of claim 13, wherein when used in increasing platelet counts in the blood of a patient ~~comprising administering to the patient an efficient amount of a composition comprising BT200 (SEQ ID No.: 6), wherein the patient has~~having a low platelet count ~~(thrombocytopenia).~~

~~30. The method of claim 29, wherein,~~ the thrombocytopenia is associated with a genetic disorder that causes a low platelet count, an enlarged spleen that holds abnormal platelets, a side reaction to a medicine, an autoimmune disease, or a viral infection~~.~~; optionally

~~31. The method of claim 30,~~ wherein the disorder is VWD Type 2a, VWD Type 2b with thrombocytopenia, VWD Type 2b, VWD Type 2m, or VWD Type 2n.

~~32. A~~19. Use of a pharmaceutical composition in the manufacture of a medicament for use in method for treating a hereditary bleeding disorder in a patient ~~with a~~, wherein the pharmaceutical composition ~~comprising~~comprises a VWF binding agent~~,~~ and BT200, ~~comprising~~and wherein the method comprises:

a) assessing the hereditary bleeding disorder of said patient and the baseline coagulation function in said patient;

b) determining the optimal dose of BT200 with the assessment of step a) for initial treatment; and

c) providing a weekly dose of BT200 after one-week treatment with the initial dose of BT200 in said patient~~.~~;

optionally

wherein the assessment includes FVIII activity, VWF antigen levels and/or platelet counts in the blood.

~~33~~20. The ~~method~~use of claim ~~32~~19, wherein the hereditary bleeding disorder ~~may be~~is hemophilia A, severe hemophilia, VWD Type 1, VWD Type 2a, VWD Type 2b, VWD Type 2m, VWD Type 2n, or VWD Type 3.

~~34~~21. The ~~method~~use of claim ~~33, wherein the assessment includes FVIII activity, VWF antigen levels and/or platelet counts in the blood.~~

~~35. The method of claim 33~~20, wherein the patient is treated with a coagulation factor substitute.

22. A composition for use in therapy, wherein the composition comprises a VWF targeting agent wherien the VWF targeting agent is BT200 that comprises the sequence of SEQ ID NO. 6, or variant thereof.