WHAT IS CLAIMED IS:

1. Use of at least one dose twice-weekly of recombinant von Willebrand Factor (rVWF) in the manufacture of a medicament for prophylactically treating spontaneous bleeding episodes in a subject with severe von Willebrand Disease (VWD), wherein the recombinant von Willebrand Factor (rVWF) ranges from at least 40 IU/kg to 80 IU/kg.

2. The use of claim 1, wherein the at least one dose of rVWF ranges from at least 50 IU/kg to 80 IU/kg.

3. The use of claim 1 or 2, wherein the subject has a baseline VWF ristocetin cofactor activity (VWF:RCo) ranging from 20 IU/dL or less, or is diagnosed with Type 1 VWD.

4. The use of claim 1 or 2, wherein the subject is diagnosed with Type 2A, 2B, or 2M VWD.

5. The use of claim 1 or 2, wherein the subject has a VWF:antigen content (VWF:Ag) ranging from 3 IU/dL or greater, or is diagnosed with Type 3 VWD.

6. The use of any one of claims 1 to 5, wherein the subject has been administered prophylactic treatment of plasma-derived VWF (pdVWF) within the past 12 months before initial administration of rVWF.

7. The use of any one of claims 1 to 6, wherein the subject has experienced at least 3 spontaneous bleeding episodes within the past 12 months.

8. The use of any one of claims 1 to 7, wherein the administration occurs every 3 to 4 days.

9. The use of any one of claims 1 to 8, wherein the administration occurs on day 1 and day 5, day 2 and day 6, or day 3 and day 7 of a 7 day period.

10. The use of any one of claims 1 to 9, wherein the administration occurs at least every 24 hours, 36 hours, 48 hours, 72 hours, or 84 hours.

11. The use of any one of claims 1 to 10, wherein the administration occurs at least every 72 hours.

12. The use of any one of claims 1 to 11, further comprising that at least one dose of recombinant Factor VIII (rFVIII) is to be administered to the subject.

13. The use of claim 12, wherein the at least one dose of rFVIII is to be concomitantly or sequentially administered with the at least one dose of rVWF.

14. The use of any one of the preceding claims, wherein the subject resumes the prophylactic treatment after receiving elective surgery or oral surgery.

15. The use of claim 14, wherein if the elective surgery is minor surgery or oral surgery and the subject has FVIII activity (FVIII:C) of at least 0.4 IU/mL or greater, the subject is to be administered rVWF without rFVIII before surgery.

16. The use of claim 14, wherein if the elective surgery is major surgery and the subject has FVIII activity (FVIII:C) of at least 0.8 IU/mL or greater, the subject is to be administered rVWF without rFVIII before surgery.

17. The use of any one of claims 1 to 16, wherein prophylactic treatment efficacy is indicated by a reduction of ≥25% in annual bleeding rate (ABR) for spontaneous bleeding episodes during rVWF prophylaxis relative to the pretreatment ABR.

18. The use of any one of claims 1 to 16, wherein prophylactic treatment efficacy is indicated by a reduction of ≥25%, ≥30%, ≥35%, ≥40%, ≥45%, ≥50%, ≥55%, ≥60%, ≥65%, ≥70%, ≥75%, ≥80%, ≥85%, ≥90%, or ≥95% in annual bleeding rate (ABR) for spontaneous bleeding episodes during rVWF prophylaxis relative to the pretreatment ABR.

19. The use of any one of claims 1 to 18, wherein prophylactic treatment efficacy is measured by examining vWF:RCo and/or FVIII activities in samples obtained from the subject before and after prophylactic treatment with rVWF.

20. The use of any one of claims 1 to 19, wherein prophylactic treatment efficacy is measured by examining FVIII, FVIII:C, VWF:RCo, VWF:Ag, and/or VWF collagen-binding

capacity activities in samples obtained from the subject before and after prophylactic treatment with rVWF.

21. The use of claim 19 or 20, wherein the samples for examining FVIII, FVIII:C, VWF:RCo, VWF:Ag, and/or VWF collagen-binding capacity activities are obtained 15 minutes, 30 minutes, 60 minutes, 3 hours, 6 hours, 12 hours, 24 hours, 28 hours, 32 hours, 48 hours, 72 hours, or 96 hours, after prophylactic treatment with rVWF.

22. The use of any one of claims 19 to 21, wherein the samples for examining FVIII, FVIII:C, VWF:RCo, VWF:Ag, and/or VWF collagen-binding capacity activities are obtained 25 to 31 days after prophylactic treatment with rVWF.

23. The use of any one of claims 1 to 22, wherein prophylactic treatment efficacy is determined after or during a bleeding episode, wherein samples for examining FVIII, FVIII:C, VWF:RCo, VWF:Ag, and/or VWF collagen-binding capacity activities are obtained after the bleeding episode, and further wherein the samples are obtained prior to rVWF administration, 2 hours after rVWF administration and then every 12-24 hours until resolution of the bleeding episode.

24. The use of any one of claims 1 to 23, wherein prophylactic treatment efficacy is indicated by an improvement in FVIII, FVIII:C, VWF:RCo, VWF:Ag, and/or VWF collagen-binding capacity activity levels after the prophylactic treatment with rVWF as compared to the levels prior to the prophylactic treatment with rVWF.

25. Use of a weekly dose of recombinant von Willebrand Factor (rVWF) in the manufacture of a medicament for prophylactically treating spontaneous bleeding episodes in a subject with severe von Willebrand Disease (VWD), wherein the recombinant von Willebrand Factor (rVWF) is substantially equivalent to a corresponding weekly dose of plasma-derived VWF (pdVWF) previously administered to said subject.

26. The use of claim 25, wherein the weekly dose of rVWF is about 10% less than the corresponding weekly dose of pdVWF.

27. The use of claim 25, wherein the weekly dose of rVWF is about 10% more than the corresponding weekly dose of pdVWF.

28. The use of any one of claims 25 to 27, wherein the weekly dose of rVWF is two individual infusions to be administered on separate days.

29. The use of any one of claims 25 to 27, wherein the weekly dose of rVWF is three individual infusions to be administered on separate days.

30. The use of any one of claims 25 to 27, wherein the weekly dose of rVWF is a single infusion.

31. The use of any one of claims 28 to 30, wherein each individual infusion comprises up to 80 IU/kg rVWF.

32. The use of any one of claims 28 to 31, wherein each individual infusion comprises 80 IU/kg rVWF.

33. The use of any one of claims 28 to 31, wherein each individual infusion comprises 50 IU/kg rVWF.

34. The use of any one of claims 25 to 33, wherein the subject has a baseline VWF ristocetin cofactor activity (VWF:RCo) ranging from 20 IU/dL or less, or is diagnosed with Type 1 VWD.

35. The use of any one of claims 25 to 34, wherein the subject is diagnosed with Type 2A, 2B, or 2M VWD.

36. The use of any one of claims 25 to 35, wherein the subject has a VWF:antigen content (VWF:Ag) ranging from 3 IU/dL or greater, or is diagnosed with Type 3 VWD.

37. The use of any one of claims 25 to 36, wherein the subject has received prophylactic treatment of pdVWF for at least 12 months.

38. The use of any one of claims 28 and 31 to 37, wherein the two individual infusions are to be administered on day 1 and day 5, or day 2 and day 6, or day 3 and day 7 of a 7 day period.

39. The use of any one of claims 27 and 31 to 37, wherein the three individual infusions are to be administered on day 1, day 3, and day 6 of a 7 day period.

40. The use of any one of claims 25 to 37, wherein the administration occurs at least every 24 hours, 36 hours, 48 hours, 72 hours, or 84 hours.

41. The use of any one of claims 25 to 37, wherein the administration occurs at least every 72 hours.

42. The use of any one of claims 25 to 41, further comprising that at least one dose of recombinant Factor VIII (rFVIII) is to be administered to the subject.

43. The use of claim 42, wherein the at least one dose of rFVIII is to be concomitantly or sequentially administered with the weekly dose of rVWF.

44. The use of any one of claims 25 to 43, wherein the subject resumes the prophylactic treatment after receiving elective surgery or oral surgery.

45. The use of claim 44, wherein if the elective surgery is minor surgery or oral surgery and the subject has a FVIII activity (FVIII:C) of at least 0.4 IU/mL or greater, the subject is to be administered rVWF without rFVIII prior to surgery.

46. The use of claim 44, wherein if the elective surgery is major surgery and the subject has a FVIII activity (FVIII:C) of at least 0.8 IU/mL or greater, the subject is to be administered rVWF without rFVIII prior to surgery.

47. The use of any one of claims 25 to 43, wherein prophylactic treatment efficacy is indicated by a reduction of ≥25% in annual bleeding rate (ABR) for spontaneous bleeding episodes during rVWF prophylaxis relative to the pretreatment ABR.

48. The use of any one of claims 25 to 47, wherein prophylactic treatment efficacy is indicated by a reduction of ≥25%, ≥30%, ≥35%, ≥40%, ≥45%, ≥50%, ≥55%, ≥60%, ≥65%, ≥70%, ≥75%, ≥80%, ≥85%, ≥90%, or ≥95% in annual bleeding rate (ABR) for spontaneous bleeding episodes during rVWF prophylaxis relative to the pretreatment ABR.

49. The use of any one of claims 25 to 48, wherein prophylactic treatment efficacy is measured by examining vWF:RCo and/or FVIII activities in samples obtained from the subject before and after prophylactic treatment with rVWF.

50. The use of any one of claims 25 to 49, wherein prophylactic treatment efficacy is measured by examining FVIII, FVIII:C, VWF:RCo, VWF:Ag, and/or VWF collagen-binding capacity activities in samples obtained from the subject before and after prophylactic treatment with rVWF.

51. The use of claim 49 or 50, wherein the samples for examining FVIII, FVIII:C, VWF:RCo, VWF:Ag, and/or VWF collagen-binding capacity activities are obtained 15 minutes, 30 minutes, 60 minutes, 3 hours, 6 hours, 12 hours, 24 hours, 28 hours, 32 hours, 48 hours, 72 hours, or 96 hours, after prophylactic treatment with rVWF.

52. The use of any one of claims 49 to 51, wherein the samples for examining FVIII, FVIII:C, VWF:RCo, VWF:Ag, and/or VWF collagen-binding capacity activities are obtained 25 to 31 days after prophylactic treatment with rVWF.

53. The use of any one of claims 25 to 52, wherein prophylactic treatment efficacy is determined after or during a bleeding episode, wherein samples for examining FVIII, FVIII:C, VWF:RCo, VWF:Ag, and/or VWF collagen-binding capacity activities are obtained after the bleeding episode, and further wherein the samples are obtained prior to rVWF administration, 2 hours after rVWF administration and then every 12-24 hours until resolution of the bleeding episode.

54. The use of any one of claims 25 to 53, wherein prophylactic treatment efficacy is indicated by an improvement in FVIII, FVIII:C, VWF:RCo, VWF:Ag, and/or VWF collagen-binding capacity activity levels after the prophylactic treatment with rVWF as compared to the levels prior to the prophylactic treatment with rVWF.

55. The use of any one of the preceding claims, wherein spontaneous bleeding comprises any one selected from the group consisting of hemarthrosis, epistaxis, muscle bleeding, oral bleeding, and gastrointestinal bleeding.

56. The use of any one of the preceding claims, wherein the subject is not diagnosed with type 2N VWD or pseudo VWD.