CLAIMS

What is claimed is:

1. A composition comprising an oligonucleotide that inhibits the expression of FGG, wherein the oligonucleotide comprises an siRNA comprising a sense strand and an antisense strand, each strand is independently about 12-30 nucleosides in length, and at least one of the sense strand and the antisense strand comprises a nucleoside sequence comprising about 12-30 contiguous nucleosides of SEQ ID NO: 3621.

2. A composition comprising an oligonucleotide that inhibits the expression of FGG, wherein the oligonucleotide comprises an ASO about 12-30 nucleosides in length and a nucleoside sequence complementary to about 12-30 contiguous nucleosides of SEQ ID NO: 3621.

3. Use of a composition comprising an oligonucleotide that targets FGG in the manufacture of a medicament for improving a mental disorder measurement in a subject, relative to a baseline mental disorder measurement, wherein the composition is to be administered to the subject in an effective amount.

4. The use of claim 3, wherein the mental disorder comprises a psychiatric disorder.

5. The use of claim 4, wherein the psychiatric disorder comprises a depressive disorder, post-traumatic stress disorder, mood disorder, anxiety disorder, eating disorder, substance-use disorder, bipolar disorder, personality disorder, schizophrenia, or schizoaffective disorder.

6. The use of claim 3, wherein the mental disorder measurement comprises a Montgomery-Asberg Depression Rating Scale score, a Hamilton Depression Rating Scale score, or a measurement of an anxiety disorder, depressive disorder, eating disorder, substance-use disorder, post-traumatic stress disorder, bipolar disorder, schizophrenia, or psychosis sign or symptom.

7. The use of claim 3, wherein the mental disorder comprises a neurological disorder.

8. The use of claim 7, wherein the neurological disorder comprises Alzheimer's disease, dementia, delirium, cognitive decline, vascular dementia, headache, chronic pain, chronic fatigue syndrome, or motor neuron disease.

9. The use of claim 8, wherein the mental disorder measurement comprises a measurement of cognitive function, CNS amyloid plaques, CNS tau accumulation, CSF beta-amyloid 42, CSF tau, CSF phospho-tau, Lewy bodies, CSF alpha-synuclein, or a sign or symptom of headache, migraine, chronic pain, fibromyalgia, chronic fatigue syndrome, or motor neuron disease.

10. Use of a composition comprising an oligonucleotide that targets FGG in the manufacture of a medicament for decreasing fibrinogen, wherein the composition is to be administered to a subject in an effective amount.

11. The use of claim 10, wherein the composition decreases circulating fibrinogen.

12. The use of claim 10, wherein the subject has a clotting or coagulation disorder.

13. The use of claim 10, wherein the subject has a thrombophilia.

14. The use of claim 10, wherein the subject has a venous thromboembolism.

15. The use of any one of claims 3 to 14, wherein the oligonucleotide comprises a modified internucleoside linkage.

16. The use of claim 15, wherein the modified internucleoside linkage comprises alkylphosphonate, phosphorothioate, methylphosphonate, phosphorodithioate, alkylphosphonothioate, phosphoramidate, carbamate, carbonate, phosphate triester, acetamidate, or carboxymethyl ester, or a combination thereof.

17. The use of claim 15, wherein the modified internucleoside linkage comprises one or more phosphorothioate linkages.

18. The use of any one of claims 3 to 17, wherein the oligonucleotide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 modified internucleoside linkages.

19. The use of any one of claims 3 to 18, wherein the oligonucleotide comprises a modified nucleoside.

20. The use of claim 19, wherein the modified nucleoside comprises a locked nucleic acid (LNA), hexitol nucleic acid (HNA), cyclohexene nucleic acid (CeNA), 2'-methoxyethyl, 2'-O-alkyl, 2'-O-allyl, 2'-fluoro, 2'-deoxy, or a combination thereof.

21. The use of claim 19, wherein the modified nucleoside comprises a LNA.

22. The use of claim 19, wherein the modified nucleoside comprises a 2',4' constrained ethyl nucleic acid.

23. The use of claim 19, wherein the modified nucleoside comprises 2'-O-methyl nucleoside, 2'-deoxyfluoro nucleoside, 2'-O-N-methylacetamido (2'-O-NMA) nucleoside, 2'-O-dimethylaminoethoxyethyl (2'-O-DMAEOE) nucleoside, 2'-O-aminopropyl (2'-O-AP) nucleoside, 2'-ara-F, or a combination thereof.

24. The use of claim 19, wherein the modified nucleoside comprises one or more 2'-fluoro modified nucleosides.

25. The use of claim 19, wherein the modified nucleoside comprises 2'-O-alkyl modified nucleoside.

26. The use of any one of claims 3 to 25, wherein the oligonucleotide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21 modified nucleosides.

27. The use of any one of claims 3 to 26, wherein the oligonucleotide comprises a sugar moiety attached at a 3' or 5' terminus of the oligonucleotide.

28. The use of claim 27, wherein the sugar moiety comprises N-acetylgalactosamine (GalNAc), N-acetylglucosamine (GlcNAc), or mannose.

29. The use of claim 27, wherein the sugar moiety comprises GalNAc.

30. The use of claim 29, wherein the sugar moiety comprises ETL17.

31. The use of any one of claims 3 to 30, wherein the oligonucleotide comprises a small interfering RNA (siRNA) comprising a sense strand and an antisense strand.

32. The use of claim 31, wherein the sense strand is 12-30 nucleosides in length.

33. The use of claim 31, wherein the antisense strand is 12-30 nucleosides in length.

34. The use of claim 31, wherein any one of the following is true with regard to the sense strand:

all purines comprise 2’ fluoro modified purines, and all pyrimidines comprise a mixture of 2’ fluoro and 2’-O-methyl modified pyrimidines;

all purines comprise 2’-O-methyl modified purines, and all pyrimidines comprise a mixture of 2’ fluoro and 2’-O-methyl modified pyrimidines;

all purines comprise 2’ fluoro modified purines, and all pyrimidines comprise 2’-O-methyl modified pyrimidines;

all pyrimidines comprise 2’ fluoro modified pyrimidines, and all purines comprise a mixture of 2’ fluoro and 2’-O-methyl modified purines;

all pyrimidines comprise 2’-O-methyl modified pyrimidines, and all purines comprise a mixture of 2’ fluoro and 2’-O-methyl modified purines; or

all pyrimidines comprise 2’ fluoro modified pyrimidines, and all purines comprise 2’-O-methyl modified purines.

35. The use of claim 31, wherein the antisense strand comprises a mixture of 2’ fluoro and 2’-O-methyl modified nucleosides.

36. The use of claim 3 or 10, wherein the oligonucleotide comprises an antisense oligonucleotide (ASO).

37. The use of claim 36, wherein the ASO is 12-30 nucleosides in length.

38. The composition of claim 1 or 2, further comprising a pharmaceutically acceptable carrier.

39. Use of a composition comprising an oligonucleotide that targets FGG or the composition of claim 38 in the manufacture of a medicament for treating a subject having a psychiatric disorder or a neurological disorder, wherein the composition comprising the oligonucleotide that targets FGG or the composition of claim 38 is to be administered to the subject an effective amount.

40. The use of claim 39, wherein the psychiatric disorder comprises a depressive disorder, persistent depressive disorder, treatment resistant depression, a sign or symptom of depression, post-traumatic stress disorder, mood disorder, anxiety disorders, eating disorder, substance-use disorder, bipolar disorder, personality disorder, schizophrenia, or a schizoaffective disorder.

41. The use of claim 39, wherein the neurological disorder comprises Alzheimer’s disease, dementia, delirium, cognitive decline, vascular dementia, headache, chronic pain, chronic fatigue syndrome, and motor neuron disease.

42. Use of a composition comprising an oligonucleotide that targets FGG or the composition of claim 38 in the manufacture of a medicament for treating a subject having a clotting or coagulation disorder or a thrombophilia, wherein the composition comprising the oligonucleotide that targets FGG or the composition of claim 38 is to be administered to the subject an effective amount.

43. The use of claim 42, wherein the prothrombin time, International Normalized Ratio, or the activated partial thromboplastin time is increased compared to a baseline.

44. The composition of any one of claims 1, 2 and 38 for use in therapy.