We claim:

1. A mouse comprising in its genome a humanized endogenous *F12* locus in which a segment of the endogenous *F12* locus has been deleted and replaced with a corresponding human *F12* sequence,

wherein a region of the endogenous *F12* locus comprising both coding sequence and non-coding sequence has been deleted and replaced with a corresponding human *F12* sequence comprising both coding sequence and non-coding sequence,

wherein the region of the endogenous *F12* locus from the start codon to the stop codon has been deleted and replaced with the corresponding human *F12* sequence, and

wherein the mouse expresses a short human coagulation factor XII isoform in the brain, wherein:

(i) the short human coagulation factor XII isoform is encoded by an *F12* mRNA detected by probes against exons 11-14 of human *F12* but not by probes against exons 1-6 of human *F12*; and/or

(ii) the short human coagulation factor XII isoform is $FXII_{297-596}$.

2. The mouse of claim 1, wherein the humanized endogenous *F12* locus comprises the endogenous *F12* promoter, wherein the human *F12* sequence is operably linked to the endogenous *F12* promoter.

3. The mouse of any preceding claim, wherein:

(I) the endogenous *F12* 3' untranslated region has not been deleted and replaced with the corresponding human *F12* sequence; and/or

(II) the endogenous *F12* 5' untranslated region has not been deleted and replaced with the corresponding human *F12* sequence.

4. The mouse of any preceding claim, wherein:

(I) the human *F12* sequence at the humanized endogenous *F12* locus comprises a sequence at least 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence set forth in SEQ ID NO: 31 or 32; and/or

(II) the humanized endogenous *F12* locus encodes a protein comprising a sequence at least 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence set forth in SEQ ID NO: 5 or 46; and/or

(III) the humanized endogenous *F12* locus comprises a coding sequence comprising a sequence at least 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence set forth in SEQ ID NO: 13 or 48; and/or

(IV) the humanized endogenous *F12* locus comprises a sequence at least 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the sequence set forth in SEQ ID NO: 17 or 18.

5. The mouse of any preceding claim, wherein the humanized endogenous *F12* locus comprises a selection cassette or a reporter gene within an intron of the corresponding human *F12* sequence, or wherein the humanized endogenous *F12* locus does not comprise a selection cassette or a reporter gene.

6. The mouse of any preceding claim, wherein the mouse is homozygous for the humanized endogenous *F12* locus.

7. The mouse of any preceding claim, wherein the mouse comprises the humanized endogenous *F12* locus in its germline.

8. The mouse of any preceding claim, wherein the mouse has an activated partial thromboplastin time (aPTT) that is not significantly different from an aPTT in a corresponding wild type mouse and/or wherein the mouse has a prothrombin time (PT) that is not significantly different from a PT in the corresponding wild type mouse.

9. The mouse of any preceding claim, wherein the mouse has human coagulation factor XII plasma levels of at least 5 μg/mL.

10. A method of assessing the activity of a human-coagulation-factor-XII-targeting reagent *in vivo*, comprising:

(a) administering the human-coagulation-factor-XII-targeting reagent to the mouse of any one of claims 1-9; and

(b) assessing the activity of the human-coagulation-factor-XII-targeting reagent in the mouse.

11. The method of claim 10, wherein the administering comprises adeno-associated virus (AAV)-mediated delivery, lipid nanoparticle (LNP)-mediated delivery, hydrodynamic delivery (HDD), or injection.

12. The method of claim 10 or 11, wherein:

(I) step (b) comprises isolating plasma from the mouse and assessing activity of the human-coagulation-factor-XII-targeting reagent in the plasma; and/or

(II) step (b) comprises assessing the activity of the human-coagulation-factor-XII-targeting reagent in the liver or the brain of the mouse; and/or

(III) step (b) comprises assessing coagulation or thrombin generation; and/or

(IV) step (b) comprises assessing HGF-Met signaling; and/or

(V) step (b) comprises measuring expression of an *F12* messenger RNA encoded by the humanized endogenous *F12* locus; and/or

(VI) step (b) comprises measuring expression of a coagulation factor XII protein encoded by the humanized endogenous coagulation factor XII locus; and/or

(VII) the human-coagulation-factor-XII-targeting reagent is a genome-editing agent, and step (b) comprises assessing modification of the humanized endogenous *F12* locus, optionally wherein step (b) comprises measuring the frequency of insertions or deletions within the humanized endogenous *F12* locus.

13. The method of any one of claims 10-12, wherein:

(I) the human-coagulation-factor-XII-targeting reagent comprises a nuclease agent designed to target a region of a human *F12* gene, optionally wherein the nuclease agent comprises a Cas protein and a guide RNA designed to target a guide RNA target sequence in the human *F12* gene, and optionally wherein the Cas protein is a Cas9 protein;

(II) the human-coagulation-factor-XII-targeting reagent comprises an exogenous donor nucleic acid, wherein the exogenous donor nucleic acid is designed to target the human *F12* gene, and optionally wherein the exogenous donor nucleic acid is delivered via AAV;

(III) the human-coagulation-factor-XII-targeting reagent is an RNAi agent or an antisense oligonucleotide;

(IV) the human-coagulation-factor-XII-targeting reagent is an antigen-binding protein; or

(V) the human-coagulation-factor-XII-targeting reagent is a small molecule.

14. A method of optimizing the activity of a human-coagulation-factor-XII-targeting reagent *in vivo*, comprising:

(I) performing the method of any one of claims 10-13 a first time in a first mouse comprising in its genome a humanized endogenous *F12* locus;

(II) changing a variable and performing the method of step (I) a second time with the changed variable in a second mouse comprising in its genome a humanized endogenous *F12* locus; and

(III) comparing the activity of the human-coagulation-factor-XII-targeting reagent in step (I) with the activity of the human-coagulation-factor-XII-targeting reagent in step (II), and selecting the method resulting in the higher activity.

15. The method of claim 14, wherein the changed variable in step (II) is:

(i) the delivery method of introducing the human-coagulation-factor-XII-targeting reagent into the mouse;

(ii) the route of administration of introducing the human-coagulation-factor-XII-targeting reagent into the mouse;

(iii) the concentration or amount of the human-coagulation-factor-XII-targeting reagent introduced into the mouse;

(iv) the form of the human-coagulation-factor-XII-targeting reagent introduced into the mouse; or

(v) the human-coagulation-factor-XII-targeting reagent introduced into the mouse.