

We claim:

1. A use of a nuclease agent or one or more nucleic acids encoding the nuclease agent and an exogenous donor nucleic acid comprising an antigen-binding-protein coding sequence in the manufacture of a medicament for treating or effecting prophylaxis of a disease in an animal having or at risk for the disease,
wherein the nuclease agent targets a target site in a safe harbor locus,
wherein the antigen-binding protein targets an antigen associated with the disease,
wherein the nuclease agent cleaves the target site and the antigen-binding protein coding sequence is to be inserted into the safe harbor locus to produce a modified safe harbor locus, and
whereby the antigen-binding protein is expressed in the animal and binds the antigen associated with the disease.
2. The use of any claim 1, wherein the inserted antigen-binding-protein coding sequence is operably linked to an endogenous promoter in the safe harbor locus.
3. The use of any preceding claim, wherein the modified safe harbor locus encodes a chimeric protein comprising an endogenous secretion signal and the antigen-binding-protein.
4. The use of any preceding claim, wherein the safe harbor locus is an albumin locus.
5. The use of claim 4, wherein the antigen-binding-protein coding sequence is to be inserted into the first intron of the albumin locus.
6. The use of any preceding claim, wherein the antigen-binding protein coding sequence is to be inserted into the safe harbor locus in one or more liver cells in the animal.
7. The use of any preceding claim, wherein the nuclease agent is a zinc finger nuclease (ZFN), a Transcription Activator-Like Effector Nuclease (TALEN), or a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated (Cas) protein and a guide RNA (gRNA).

8. The use of claim 7, wherein the nuclease agent is the Cas protein and the gRNA, wherein the Cas protein is a Cas9 protein, and wherein the gRNA comprises:
- (a) a CRISPR RNA (crRNA) that targets the target site, wherein the target site is immediately flanked by a Protospacer Adjacent Motif (PAM) sequence; and
 - (b) a trans-activating CRISPR RNA (tracrRNA).
9. The use of claim 8, wherein the at least one gRNA comprises 2'-O-methyl analogs and 3' phosphorothioate internucleotide linkages at the first three 5' and 3' terminal RNA residues.
10. The use of any preceding claim, wherein the antigen-binding-protein coding sequence is to be inserted via non-homologous end joining.
11. The use of any one of claims 1-9, wherein the antigen-binding-protein coding sequence is to be inserted via homology-directed repair.
12. The use of any one of claims 1-10, wherein the exogenous donor nucleic acid does not comprise homology arms.
13. The use of any preceding claim, wherein the exogenous donor nucleic acid is single-stranded.
14. The use of any one of claims 1-12, wherein the exogenous donor nucleic acid is double-stranded.
15. The use of any preceding claim, wherein the antigen-binding protein coding sequence in the exogenous donor nucleic acid is flanked on each side by the target site for the nuclease agent.
16. The use of claim 15, wherein the target site in the safe harbor locus is no longer present if the antigen-binding protein coding sequence is inserted into the safe harbor locus in the correct orientation but it is reformed if the antigen-binding protein coding sequence is inserted into the safe harbor locus in the opposite orientation.

17. The use of claim 15 or 16, wherein the exogenous donor nucleic acid is in an adeno-associated virus (AAV) vector, and cleavage of the target sites flanking the antigen-binding protein coding sequence removes the inverted terminal repeats of the AAV.
18. The use of any preceding claim, wherein the antigen-binding protein is an antibody, an antigen-binding fragment of an antibody, a multispecific antibody, an scFV, a bis-scFV, a diabody, a triabody, a tetrabody, a V-NAR, a VHH, a VL, a F(ab), a F(ab)₂, a dual variable domain antigen-binding protein, a single variable domain antigen-binding protein, a bispecific T-cell engager, or a Davisbody.
19. The use of any preceding claim, wherein the antigen-binding protein is not a single-chain antigen-binding protein.
20. The use of claim 19, wherein the antigen-binding protein comprises a heavy chain and a separate light chain, optionally wherein the heavy chain coding sequence comprises V_H, D_H, and J_H segments, and the light chain coding sequence comprises V_L and J_L gene segments.
21. The use of claim 20, wherein the heavy chain coding sequence is upstream of the light chain coding sequence in the antigen-binding-protein coding sequence.
22. The use of claim 21, wherein the antigen-binding-protein coding sequence comprises an exogenous secretion signal sequence upstream of the light chain coding sequence.
23. The use of claim 20, wherein the light chain coding sequence is upstream of the heavy chain coding sequence in the antigen-binding-protein coding sequence.
24. The use of claim 23, wherein the antigen-binding-protein coding sequence comprises an exogenous secretion signal sequence upstream of the heavy chain coding sequence.
25. The use of claim 22 or 24, wherein the exogenous secretion signal sequence is a ROR1 secretion signal sequence.

26. The use of any preceding claim, wherein the antigen-binding-protein coding sequence encodes a heavy chain and a light chain linked by a 2A peptide or an internal ribosome entry site (IRES).
27. The use of claim 26, wherein the heavy chain and the light chain are linked by the 2A peptide.
28. The use of claim 27, wherein the 2A peptide is a T2A peptide.
29. The use of any preceding claim, wherein the disease-associated antigen is a cancer-associated antigen.
30. The use of any one of claims 1-28, wherein the disease-associated antigen is an infectious-disease-associated antigen.
31. The use of claim 30, wherein the disease-associated antigen is a viral antigen.
32. The use of claim 31, wherein the viral antigen is an influenza antigen or a Zika antigen.
33. The use of claim 32, wherein the viral antigen is an influenza hemagglutinin antigen.
34. The use of claim 33, wherein the antigen-binding protein comprises a light chain comprising three light chain CDRs and a heavy chain comprising three heavy chain CDRs, wherein:
- (I) the light chain comprises, consists essentially of, or consists of a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 18 and the heavy chain comprises, consists essentially of, or consists of a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 20,
- optionally wherein the three light chain CDRs comprise, consist essentially of, or consist of sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 76-78, respectively, and the three heavy chain CDRs comprise, consist essentially of, or

consist of sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 79-81, respectively; or

(II) the modified safe harbor locus comprises a coding sequence at least 90% identical to the sequence set forth in SEQ ID NO: 120; or

(III) the light chain comprises, consists essentially of, or consists of a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 126 and the heavy chain comprises, consists essentially of, or consists of a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 128,

optionally wherein the three light chain CDRs comprise, consist essentially of, or consist of sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 129-131, respectively, and the three heavy chain CDRs comprise, consist essentially of, or consist of sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 132-134, respectively; or

(IV) the modified safe harbor locus comprises a coding sequence at least 90% identical to the sequence set forth in SEQ ID NO: 146.

35. The use of claim 32, wherein the viral antigen is a Zika Envelope (Env) antigen.

36. The use of claim 35, wherein the antigen-binding protein comprises a light chain comprising three light chain CDRs and a heavy chain comprising three heavy chain CDRs, wherein:

(I) the light chain comprises, consists essentially of, or consists of a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 3 and the heavy chain comprises, consists essentially of, or consists of a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 5,

optionally wherein the three light chain CDRs comprise, consist essentially of, or consist of sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 64-66, respectively, and the three heavy chain CDRs comprise, consist essentially of, or consist of sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 67-69, respectively; or

(II) the modified safe harbor locus comprises a coding sequence at least 90% identical to the sequence set forth in SEQ ID NO: 115.

37. The use of claim 35, wherein the antigen-binding protein comprises a light chain comprising three light chain CDRs and a heavy chain comprising three heavy chain CDRs, wherein:

(I) the light chain comprises, consists essentially of, or consists of a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 13 and the heavy chain comprises, consists essentially of, or consists of a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 15,

optionally wherein the three light chain CDRs comprise, consist essentially of, or consist of sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 70-72, respectively, and the three heavy chain CDRs comprise, consist essentially of, or consist of sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 73-75, respectively; or

(II) the modified safe harbor locus comprises a coding sequence at least 90% identical to the sequence set forth in any one of SEQ ID NOS: 116-119.

38. The use of claim 30, wherein the disease-associated antigen is a bacterial antigen, optionally wherein the bacterial antigen is a *Pseudomonas aeruginosa* PcrV antigen.

39. The use of any preceding claim, wherein the antigen-binding protein is a neutralizing antigen-binding protein or a neutralizing antibody.

40. The use of claim 39, wherein the antigen-binding protein is a broadly neutralizing antigen-binding protein or a broadly neutralizing antibody.

41. The use of any preceding claim, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are in separate delivery vehicles.

42. The use of any one of claims 1-40, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are together in the same delivery vehicle.

43. The use of any preceding claim, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are to be introduced simultaneously.

44. The use of any one of claims 1-41, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are to be introduced sequentially.

45. The use of any preceding claim, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are to be introduced in single doses.

46. The use of any one of claims 1-44, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and/or the exogenous donor nucleic acid are to be introduced in multiple doses.

47. The use of any preceding claim, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are to be delivered via intravenous injection.

48. The use of any preceding claim, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are associated with a lipid nanoparticle or in an adeno-associated virus (AAV) vector, optionally wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are both in AAV vectors, and optionally wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are in two different AAV vectors.

49. The use of claim 48, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent is associated with the lipid nanoparticle.

50. The use of claim 49, wherein the lipid nanoparticle comprises Dlin-MC3-DMA (MC3), cholesterol, DSPC, and PEG-DMG in a 50:38.5:10:1.5 molar ratio.

51. The use of claim 49 or 50, wherein the nuclease agent is a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated 9 (Cas9) protein and a guide RNA (gRNA).
52. The use of claim 51, wherein the Cas9 is in the form of mRNA, and the gRNA is in the form of RNA.
53. The use of any one of claims 48-52, wherein the exogenous donor nucleic acid is in the AAV vector.
54. The use of claim 53, wherein the AAV is a single-stranded AAV (ssAAV).
55. The use of claim 53, wherein the AAV is a self-complementary AAV (scAAV).
56. The use of any one of claims 53-55, wherein the AAV is AAV8 or AAV2/8.
57. The use of any one of claims 1-48, wherein the nuclease agent comprises a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated 9 (Cas9) and a guide RNA (gRNA), wherein the gRNA and an mRNA encoding the Cas9 are associated with a lipid nanoparticle, and the exogenous donor nucleic acid is in an AAV8 or AAV2/8 vector.
58. The use of any one of claims 1-48, wherein the nuclease agent comprises a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated 9 (Cas9) and a guide RNA (gRNA), wherein a DNA encoding the Cas9 is in a first AAV8 vector or a first AAV2/8 vector, and the exogenous donor nucleic acid and a DNA encoding the gRNA are in a second AAV8 vector or a second AAV2/8 vector.
59. The use of any preceding claim, wherein expression of the antigen-binding protein in the animal results in plasma levels of at least about 2.5 µg/mL, at least about 5 µg/mL, at least about 10 µg/mL, at least about 100 µg/mL, at least about 200 µg/mL, at least about 300 µg/mL, at least about 400 µg/mL, at least about 500 µg/mL, at least about 600 µg/mL, at least about 700 µg/mL, at least about 800 µg/mL, at least about 900 µg/mL, or at least about 1000

µg/mL about 2 weeks, about 4 weeks, about 8 weeks, about 12 weeks, or about 16 weeks after introducing the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor sequence.

60. The use of any preceding claim, wherein the animal is a non-human animal.
61. The use of claim 60, wherein the animal is a non-human mammal.
62. The use of claim 61, wherein the non-human mammal is a rat or a mouse.
63. The use of any one of claims 1-59, wherein the animal is a human.
64. The use of any preceding claim, wherein the nuclease agent is a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated 9 (Cas9) protein and a guide RNA (gRNA),
wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor sequence are associated with a lipid nanoparticle, are in AAV8 vectors, or are in AAV2/8 vectors,
wherein the antigen-binding-protein coding sequence is to be inserted into the first intron of an endogenous albumin locus via non-homologous end joining in one or more liver cells in the animal,
wherein the inserted antigen-binding-protein coding sequence is operably linked to the endogenous albumin promoter,
wherein the modified albumin locus encodes a chimeric protein comprising an endogenous albumin secretion signal and the antigen-binding-protein,
wherein the antigen-binding protein targets a viral antigen or a bacterial antigen,
wherein the antigen-binding protein is a broadly neutralizing antibody, and
wherein the antigen-binding-protein coding sequences encodes a heavy chain and a separate light chain linked by a 2A peptide.

65. The use of claim 64, wherein the heavy chain coding sequence is upstream of the light chain coding sequence in the antigen-binding-protein coding sequence, wherein the antigen-binding-protein coding sequence comprises an exogenous secretion signal sequence

upstream of the light chain coding sequence, and wherein the exogenous secretion signal sequence is an ROR1 secretion signal sequence.

66. A pharmaceutical composition for use in treating or preventing a disease in a subject, comprising a nuclease agent or one or more nucleic acids encoding the nuclease agent and an exogenous donor nucleic acid comprising an antigen-binding-protein coding sequence, wherein the nuclease agent targets and cleaves a target site in a safe harbor locus of the subject, wherein the exogenous donor nucleic acid is to be inserted into the safe harbor locus, and wherein the antigen-binding protein is expressed in the subject and targets an antigen associated with the disease.

67. The composition for use of claim 66, wherein the inserted antigen-binding-protein coding sequence is operably linked to an endogenous promoter in the safe harbor locus.

68. The composition for use of claim 66 or 67, wherein the modified safe harbor locus encodes a chimeric protein comprising an endogenous secretion signal and the antigen-binding-protein.

69. The composition for use of any one of claims 66-68, wherein the safe harbor locus is an albumin locus.

70. The composition for use of claim 69, wherein the antigen-binding-protein coding sequence is to be inserted into the first intron of the albumin locus.

71. The composition for use of any one of claims 66-70, wherein the antigen-binding protein coding sequence is to be inserted into the safe harbor locus in one or more liver cells in the subject.

72. The composition for use of any one of claims 66-71, wherein the nuclease agent is a zinc finger nuclease (ZFN), a Transcription Activator-Like Effector Nuclease (TALEN), or a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated (Cas) protein and a guide RNA (gRNA).

73. The composition for use of claim 72, wherein the nuclease agent is the Cas protein and the gRNA, wherein the Cas protein is a Cas9 protein, and wherein the gRNA comprises:

- (a) a CRISPR RNA (crRNA) that targets the target site, wherein the target site is immediately flanked by a Protospacer Adjacent Motif (PAM) sequence; and
- (b) a trans-activating CRISPR RNA (tracrRNA).

74. The composition for use of claim 73, wherein the gRNA comprises 2'-O-methyl analogs and 3' phosphorothioate internucleotide linkages at the first three 5' and 3' terminal RNA residues.

75. The composition for use of any one of claims 66-74, wherein the antigen-binding-protein coding sequence is to be inserted via non-homologous end joining.

76. The composition for use of any one of claims 66-74, wherein the antigen-binding-protein coding sequence is to be inserted via homology-directed repair.

77. The composition for use of any one of claims 66-75, wherein the exogenous donor nucleic acid does not comprise homology arms.

78. The composition for use of any one of claims 66-77, wherein the exogenous donor nucleic acid is single-stranded.

79. The composition for use of any one of claims 66-77, wherein the exogenous donor nucleic acid is double-stranded.

80. The composition for use of any one of claims 66-79, wherein the antigen-binding protein coding sequence in the exogenous donor nucleic acid is flanked on each side by the target site for the nuclease agent.

81. The composition for use of claim 80, wherein the target site in the safe harbor locus is no longer present if the antigen-binding protein coding sequence is inserted into the safe harbor locus in the correct orientation but it is reformed if the antigen-binding protein coding sequence is inserted into the safe harbor locus in the opposite orientation.

82. The composition for use of claim 80 or 81, wherein the exogenous donor nucleic acid is in an adeno-associated virus (AAV) vector, and cleavage of the target sites flanking the antigen-binding protein coding sequence removes the inverted terminal repeats of the AAV.

83. The composition for use of any one of claims 66-82, wherein the antigen-binding protein is an antibody, an antigen-binding fragment of an antibody, a multispecific antibody, an scFV, a bis-scFV, a diabody, a triabody, a tetrabody, a V-NAR, a VHH, a VL, a F(ab), a F(ab)₂, a dual variable domain antigen-binding protein, a single variable domain antigen-binding protein, a bispecific T-cell engager, or a Davisbody.

84. The composition for use of any one of claims 66-83, wherein the antigen-binding protein is not a single-chain antigen-binding protein.

85. The composition for use of claim 84, wherein the antigen-binding protein comprises a heavy chain and a separate light chain, optionally wherein the heavy chain coding sequence comprises V_H, D_H, and J_H segments, and the light chain coding sequence comprises V_L and J_L gene segments.

86. The composition for use of claim 85, wherein the heavy chain coding sequence is upstream of the light chain coding sequence in the antigen-binding-protein coding sequence.

87. The composition for use of claim 86, wherein the antigen-binding-protein coding sequence comprises an exogenous secretion signal sequence upstream of the light chain coding sequence.

88. The composition for use of claim 85, wherein the light chain coding sequence is upstream of the heavy chain coding sequence in the antigen-binding-protein coding sequence.

89. The composition for use of claim 88, wherein the antigen-binding-protein coding sequence comprises an exogenous secretion signal sequence upstream of the heavy chain coding sequence.

90. The composition for use of claim 87 or 89, wherein the exogenous secretion signal sequence is a ROR1 secretion signal sequence.

91. The composition for use of any one of claims 66-90, wherein the antigen-binding-protein coding sequence encodes a heavy chain and a light chain linked by a 2A peptide or an internal ribosome entry site (IRES).

92. The composition for use of claim 91, wherein the heavy chain and the light chain are linked by the 2A peptide.

93. The composition for use of claim 92, wherein the 2A peptide is a T2A peptide.

94. The composition for use of any one of claims 66-93, wherein the disease-associated antigen is a cancer-associated antigen.

95. The composition for use of any one of claims 66-93, wherein the disease-associated antigen is an infectious-disease-associated antigen.

96. The composition for use of claim 95, wherein the disease-associated antigen is a viral antigen.

97. The composition for use of claim 96, wherein the viral antigen is an influenza antigen or a Zika antigen.

98. The composition for use of claim 97, wherein the viral antigen is an influenza hemagglutinin antigen.

99. The composition for use of claim 98, wherein the antigen-binding protein comprises a light chain comprising three light chain CDRs and a heavy chain comprising three heavy chain CDRs, wherein:

(I) the light chain comprises a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 18 and the heavy chain comprises a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 20,

optionally wherein the three light chain CDRs comprise sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 76-78, respectively, and the three heavy chain CDRs comprise of sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 79-81, respectively; or

(II) the modified safe harbor locus comprises a coding sequence at least 90% identical to the sequence set forth in SEQ ID NO: 120; or

(III) the light chain comprises a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 126 and the heavy chain comprises a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 128,

optionally wherein the three light chain CDRs comprise sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 129-131, respectively, and the three heavy chain CDRs comprise sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 132-134, respectively; or

(IV) the modified safe harbor locus comprises a coding sequence at least 90% identical to the sequence set forth in SEQ ID NO: 146.

100. The composition for use of claim 97, wherein the viral antigen is a Zika Envelope (Env) antigen.

101. The composition for use of claim 100, wherein the antigen-binding protein comprises a light chain comprising three light chain CDRs and a heavy chain comprising three heavy chain CDRs, wherein:

(I) the light chain comprises a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 3 and the heavy chain comprises a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 5,

optionally wherein the three light chain CDRs comprise sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 64-66, respectively, and the three heavy chain CDRs comprise sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 67-69, respectively; or

(II) the modified safe harbor locus comprises a coding sequence at least 90% identical to the sequence set forth in SEQ ID NO: 115.

102. The composition for use of claim 100, wherein the antigen-binding protein comprises a light chain comprising three light chain CDRs and a heavy chain comprising three heavy chain CDRs, wherein:

(I) the light chain comprises a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 13 and the heavy chain comprises a sequence at least 90% identical to the sequence set forth in SEQ ID NO: 15,

optionally wherein the three light chain CDRs comprise sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 70-72, respectively, and the three heavy chain CDRs comprise sequences at least 90% identical to the sequences set forth in SEQ ID NOS: 73-75, respectively; or

(II) the modified safe harbor locus comprises a coding sequence at least 90% identical to the sequence set forth in any one of SEQ ID NOS: 116-119.

103. The composition for use of claim 95, wherein the disease-associated antigen is a bacterial antigen, optionally wherein the bacterial antigen is a *Pseudomonas aeruginosa* PcrV antigen.

104. The composition for use of any one of claims 66-103, wherein the antigen-binding protein is a neutralizing antigen-binding protein or a neutralizing antibody.

105. The composition for use of claim 104, wherein the antigen-binding protein is a broadly neutralizing antigen-binding protein or a broadly neutralizing antibody.

106. The composition for use of any one of claims 66-105, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are in separate delivery vehicles.

107. The composition for use of any one of claims 66-105, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are together in the same delivery vehicle.

108. The composition for use of any one of claims 66-107, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are to be introduced simultaneously.

109. The composition for use of any one of claims 66-106, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are to be introduced sequentially.

110. The composition for use of any one of claims 66-109, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are to be introduced in single doses.

111. The composition for use of any one of claims 66-109, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and/or the exogenous donor nucleic acid are to be introduced in multiple doses.

112. The composition for use of any one of claims 66-111, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are to be delivered via intravenous injection.

113. The composition for use of any one of claims 66-112, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are associated with a lipid nanoparticle or are in an adeno-associated virus (AAV) vector, optionally wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are both in AAV vectors, and optionally wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor nucleic acid are in two different AAV vectors.

114. The composition for use of claim 113, wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent is associated with the lipid nanoparticle.

115. The composition for use of claim 114, wherein the lipid nanoparticle comprises Dlin-MC3-DMA (MC3), cholesterol, DSPC, and PEG-DMG in a 50:38.5:10:1.5 molar ratio.

116. The composition for use of claim 114 or 115, wherein the nuclease agent is a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated 9 (Cas9) protein and a guide RNA (gRNA).

117. The composition for use of claim 116, wherein the Cas9 is in the form of mRNA, and the gRNA is in the form of RNA.

118. The composition for use of any one of claims 113-117, wherein the exogenous donor nucleic acid is in the AAV vector.

119. The composition for use of claim 118, wherein the AAV is a single-stranded AAV (ssAAV).

120. The composition for use of claim 118, wherein the AAV is a self-complementary AAV (scAAV).

121. The composition for use of any one of claims 118-120, wherein the AAV is AAV8 or AAV2/8.

122. The composition for use of any one of claims 66-113, wherein the nuclease agent comprises a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated 9 (Cas9) and a guide RNA (gRNA), wherein the gRNA and an mRNA encoding the Cas9 are associated with a lipid nanoparticle, and the exogenous donor nucleic acid is in an AAV8 vector or an AAV2/8 vector.

123. The composition for use of any one of claims 166-113, wherein the nuclease agent comprises a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated 9 (Cas9) and a guide RNA (gRNA), wherein a DNA encoding the Cas9 is in a first AAV8 vector or a first AAV2/8 vector, and the exogenous donor nucleic acid and a DNA encoding the gRNA are in a second AAV8 vector or a second AAV2/8 vector.

124. The composition for use of any one of claims 66-123, wherein expression of the antigen-binding protein in the subject results in plasma levels of at least about 2.5 µg/mL, at least about 5 µg/mL, at least about 10 µg/mL, at least about 100 µg/mL, at least about 200 µg/mL, at least about 300 µg/mL, at least about 400 µg/mL, at least about 500 µg/mL, at least about 600 µg/mL, at least about 700 µg/mL, at least about 800 µg/mL, at least about 900 µg/mL, or at least about 1000 µg/mL about 2 weeks, about 4 weeks, about 8 weeks, about 12 weeks, or

about 16 weeks after introducing the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor sequence.

125. The composition for use of any one of claims 66-124, wherein the subject is a non-human animal.

126. The composition for use of claim 125, wherein the subject is a non-human mammal.

127. The composition for use of claim 126, wherein the non-human mammal is a rat or a mouse.

128. The composition for use of any one of claims 66-124, wherein the subject is a human.

129. The composition for use of any one of claims 66-128, wherein the nuclease agent is a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated 9 (Cas9) protein and a guide RNA (gRNA),

wherein the nuclease agent or the one or more nucleic acids encoding the nuclease agent and the exogenous donor sequence are associated with a lipid nanoparticle, are in AAV8 vectors, or are in AAV2/8 vectors,

wherein the antigen-binding-protein coding sequence is to be inserted into the first intron of an endogenous albumin locus via non-homologous end joining in one or more liver cells in the subject,

wherein the inserted antigen-binding-protein coding sequence is operably linked to the endogenous albumin promoter,

wherein the modified albumin locus encodes a chimeric protein comprising an endogenous albumin secretion signal and the antigen-binding-protein,

wherein the antigen-binding protein targets a viral antigen or a bacterial antigen,

wherein the antigen-binding protein is a broadly neutralizing antibody, and

wherein the antigen-binding-protein coding sequences encodes a heavy chain and a separate light chain linked by a 2A peptide.

130. The composition for use of claim 129, wherein the heavy chain coding sequence is upstream of the light chain coding sequence in the antigen-binding-protein coding sequence, wherein the antigen-binding-protein coding sequence comprises an exogenous secretion signal sequence upstream of the light chain coding sequence, and wherein the exogenous secretion signal sequence is an ROR1 secretion signal sequence.