

CLAIMS:

1. An antisense oligonucleotide that binds within a targeted portion of the:
 - (i) 3' UTR of a *SHANK3* mRNA;
 - (ii) 5' untranslated region (UTR) of a *SHANK3* mRNA;
 - (iii) 5'-proximal non-coding region (PNCr) of a *SHANK3* pre-mRNA; orwhereby binding of the antisense oligonucleotide within the targeted portion in a mammalian cell results in an increased level of SHANK3 protein in the mammalian cell.
2. A vector for expression, in a mammalian neuron, of an antisense RNA (AR) that binds within a targeted portion of the:
 - (i) 3' UTR of a *SHANK3* mRNA;
 - (ii) 5' untranslated region (UTR) of a *SHANK3* mRNA;
 - (iii) 5'-proximal non-coding region (PNCr) of a *SHANK3* pre-mRNA; orwhereby binding of the AR within the targeted portion in a mammalian cell results in an increased level of SHANK3 protein in the mammalian cell.
3. The vector according to claim 0, wherein the mammalian cell is a neuron.
4. The vector according to claim 0, wherein the vector comprises a neuron-selective promoter for driving expression of the antisense RNA in the mammalian neuron and/or the vector comprises an inducible promoter.
5. The vector according to any one of claims 0 to 4, wherein the vector is a viral vector.
6. The antisense oligonucleotide according to claim 1, wherein the antisense oligonucleotide comprises a backbone modification.
7. The antisense oligonucleotide according to claim 0 wherein the antisense oligonucleotide comprises a backbone modification comprising a phosphorothioate linkage or a phosphorodiamidate linkage.

8. The antisense oligonucleotide according to claim 0 or claim 0, wherein the antisense oligonucleotide comprises a phosphorodiamidate morpholino, a locked nucleic acid, a peptide nucleic acid, a 2'-*O*-methyl, a 2'-fluoro, or a 2'-*O*-methoxyethyl moiety.
9. The antisense oligonucleotide according to any one of claims 0 to 0, wherein the antisense oligonucleotide comprises at least one modified sugar moiety.
10. The antisense oligonucleotide according to claim 0, wherein each sugar moiety in the antisense oligonucleotide is a modified sugar moiety.
11. The antisense oligonucleotide according to any one of claims 0 to 0, wherein the antisense oligonucleotide comprises a 2'-*O*-methoxyethyl moiety.
12. The antisense oligonucleotide according to claim 0, wherein each nucleotide of the antisense oligonucleotide comprises a 2'-*O*-methoxyethyl moiety.
13. The antisense oligonucleotide according to any one of claims 0 or 0 to 0, or the vector according to claim 0, wherein the nucleotide sequence of the antisense oligonucleotide or the AR consists of 10 to 50 nucleotides, 15 to 40 nucleotides, 18 to 40 nucleotides, 17 to 25 nucleotides, 20 to 35 nucleotides, 20 to 30 nucleotides, 22 to 30 nucleotides, 24 to 30 nucleotides, 25 to 30 nucleotides, or 26 to 30 nucleotides.
14. The antisense oligonucleotide according to claim 0, wherein the nucleotide sequence of the antisense oligonucleotide or the AR consists of 17 to 30 nucleotides.
15. The antisense oligonucleotide according to claim 0, wherein the antisense oligonucleotide comprises one or more phosphorodiamidate morpholino moieties.
16. The antisense oligonucleotide according to any one of claims 0 or 0 to 0, wherein the antisense oligonucleotide is linked to a functional moiety.

17. The antisense oligonucleotide according to claim 0, wherein the functional moiety comprises a delivery moiety.
18. The antisense oligonucleotide according to claim 0, wherein the delivery moiety is selected from the group consisting of lipids, polyethers, peptides, carbohydrates, receptor binding domains (RBDs), and antibodies.
19. The antisense oligonucleotide according to claim 0 or claim 0, wherein the delivery moiety comprises a cell-penetrating peptide (CPP).
20. The antisense oligonucleotide, or vector according to any one of claims 1 to 26, wherein the nucleotide sequence of the antisense oligonucleotide or the AR is at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% complementary to the nucleotide sequence of the targeted portion over the length of the antisense oligonucleotide or the AR.
21. The antisense oligonucleotide according to any one of claims 0 or 0 to 0, the vector according to any one of claim 0, wherein the nucleotide sequence of the ASO or AR corresponds to any one of **SEQ ID NOs:1847, 1193, 293, 299, 301, 302, 304-309, 311, 313, 315, 318, 606, 797, 1193, 1195, 1934-1937, 2858, 2874, 3510, 12644, 12666, 12669, 12671, 12688, or 12690.**
22. The antisense oligonucleotide according to any one of claims 0 or 0 to 0, the vector according to claim 0, wherein the binding is within a targeted portion of the 3' UTR corresponding to **SEQ ID NO:2.**
23. The antisense oligonucleotide, or vector according to claim 0, wherein the nucleotide sequence of the antisense oligonucleotide or the antisense RNA corresponds to any one of **SEQ ID NOs:623-1934, 4169-4174, 12645, 12655-12663, or 12688.**

24. The antisense oligonucleotide, or vector according to claim 0, wherein the nucleotide sequence of the antisense oligonucleotide or the antisense RNA corresponds to any one of **SEQ ID NOs:1847, 1193, 1852, 1934, 12661-12663, or 12688**.
25. The antisense oligonucleotide according to any one of claims 1 or 3 to 0, further comprising a delivery nanocarrier, wherein the nanocarrier is complexed with the antisense oligonucleotide.
26. The antisense oligonucleotide according to claim 0, wherein the delivery nanocarrier is selected from the group consisting of: lipoplexes, liposomes, exosomes, inorganic nanoparticles, and DNA nanostructures or wherein the delivery nanocarrier comprises a lipid nanoparticle (LNP) encapsulating the antisense oligonucleotide.
27. A pharmaceutical composition comprising the antisense oligonucleotide or vector, or composition according to any one of claims 0 to 0, and a pharmaceutically acceptable excipient.
28. Use of the pharmaceutical composition according to claim 27 for preventing or treating a condition associated with SHANK3 haploinsufficiency.
29. The use according to claim 0, wherein the condition is Phelan-McDermid syndrome, an autism spectrum disorder, schizophrenia, or an intellectual disability.
30. Use of the antisense oligonucleotide, vector, or composition according to any one of claims 0 to 0 in the manufacture of a medicament for prevention or treatment of a condition associated with SHANK3 haploinsufficiency.
31. The use according to any one of claims 0 to 30, wherein the level of SHANK3 protein in at least a plurality of cells in the subject is increased about 1.1 to about 5 fold in cells, *e.g.*, 1.2 fold, 1.3 fold, 1.5 fold, 1.7 fold, 2 fold, 2.2 fold, 2.5 fold, 2.7 fold, 3 fold, 3.3 fold, 3.5 fold, 4 fold, 4.3 fold, 4.5 fold, 4.7 fold, or another increase in SHANK3

protein levels from about 1.1 fold to about 5 fold compared to the level in the absence of the pharmaceutical composition.