

CLAIMS

1. A method for increasing levels of SynGAP1 protein in a cell, comprising contacting the cell with an antisense oligonucleotide that enhances splicing at a splice site of a retained intron in an intron-retaining SynGAP1 mRNA or pre-mRNA, wherein the retained intron is selected from among intron 5, 8, 9, 12, 13 and 14 and wherein the antisense oligonucleotide comprises a sequence of nucleobases that is complementary to a target region in the SynGAP1 mRNA or pre-mRNA.
2. A method for increasing levels of SynGAP1 protein in a subject, comprising administering to the subject an antisense oligonucleotide that enhances splicing at a splice site of a retained intron in an intron-retaining SynGAP1 mRNA or pre-mRNA, wherein the retained intron is selected from among intron 5, 8, 9, 12, 13 and 14 and wherein the antisense oligonucleotide comprises a sequence of nucleobases that is complementary to a target region in the SynGAP1 mRNA or pre-mRNA.
3. The method of claim 2, wherein the subject has a heterozygous loss-of-function mutation in *SYNAP1*.
4. The method of claim 2 or 3, wherein the subject has a disorder associated with a heterozygous loss-of-function mutation in *SYNAP1*.
5. The method of claim 4, wherein the disorder associated with a heterozygous loss-of-function mutation in *SYNAP1* is mental retardation, autosomal dominant 5 (MRD5), autism or intellectual disability.
6. A method for treating a disorder associated with a heterozygous loss-of-function mutation in *SYNAP1*, comprising administering to the subject an antisense oligonucleotide that enhances splicing at a splice site of a retained intron in an intron-retaining SynGAP1 mRNA or pre-mRNA, wherein the retained intron is selected from among intron 5, 8, 9, 12, 13 and 14, and wherein the antisense oligonucleotide comprises a sequence of nucleobases that is complementary to a target region in the SynGAP1 mRNA or pre-mRNA.
7. The method of claim 6, wherein the disorder associated with a heterozygous loss-of-function mutation in *SYNAP1* is mental retardation, autosomal dominant 5 (MRD5), autism or intellectual disability.
8. The method of any one of claims 1-7, wherein the antisense oligonucleotide binds to, or adjacent to, an intron splicing silencer (ISS); binds to nucleotides within a G-quadruplex; or binds to nucleotides with an RNA secondary structure.
9. The method of claim 8, wherein the ISS is recognised by a heterogeneous nuclear ribonucleoproteins (hnRNP).

10. The method of claim 9, wherein the hnRNP is hnRNPA1 or hnRNP I.
11. The method of claim 9 or 10, wherein the retained intron is intron 8 and the ISS is at positions +17-22, +23-28, +17-28, or +57-62 relative to the 5' splice site of intron 8.
12. The method of any one of claims 1-11, wherein the retained intron is intron 8 and the target region spans positions +4-35, +5-35, +6-35, +7-35, +8-35, +9-35, +10-35, +11-35, +12-35, +13-35, +4-34, +5-34, +6-34, +7-34, +8-34, +9-34, +10-34, +11-34, +12-34, +13-34, +4-33, +5-33, +6-33, +7-33, +8-33, +9-33, +10-33, +11-33, +12-33, +13-33, +4-32, +5-32, +6-32, +7-32, +8-32, +9-32, +10-32, +11-32, +12-32, +13-32, +4-31, +5-31, +6-31, +7-31, +8-31, +9-31, +10-31, +11-31, +12-31, +13-31, +4-30, +5-30, +6-30, +7-30, +8-30, +9-30, +10-30, +11-30, +12-30, +13-30, +4-29, +5-29, +6-29, +7-29, +8-29, +9-29, +10-29, +11-29, +12-29, +13-29, +4-28, +5-28, +6-28, +7-28, +8-28, +9-28, +10-28, +11-28, +12-28, +13-28, +4-27, +5-27, +6-27, +7-27, +8-27, +9-27, +10-27, +11-27, +12-27, +13-27, +4-26, +5-26, +6-26, +7-26, +8-26, +9-26, +10-26, +11-26, +12-26, +13-26, +4-25, +5-25, +6-25, +7-25, +8-25, +9-25, +10-25, +11-25, +12-25, +13-25, +4-24, +5-24, +6-24, +7-24, +8-24, +9-24, +10-24, +11-24, +12-24, +13-24, +4-23, +5-23, +6-23, +7-23, +8-23, +9-23, +10-23, +11-23, +12-23, +13-23, +4-22, +5-22, +6-22, +7-22, +8-22, +9-22, +10-22, +11-22, +12-22, +13-22, +4-21, +5-21, +6-21, +7-21, +8-21, +9-21, +10-21, +11-21, +12-21, +13-21, +4-20, +5-20, +6-20, +7-20, +8-20, +9-20, +10-20, +11-20, +12-20, +13-20, +4-19, +5-19, +6-19, +7-19, +8-19, +9-19, +10-19, +11-19, +12-19, +13-19, +4-18, +5-18, +6-18, +7-18, +8-18, +9-18, +10-18, or +11-18 relative to the 5' splice site of intron 8.
13. The method of any one of claims 1-11, wherein the retained intron is intron 8 and the target region spans positions +45-70, +46-70, +47-70, +48-70, +49-70, +50-70, +51-70, +52-70, +53-70, +45-69, +46-69, +47-69, +48-69, +49-69, +50-69, +51-69, +52-69, +53-69, +45-68, +46-68, +47-68, +48-68, +49-68, +50-68, +51-68, +52-68, +53-68, +45-67, +46-67, +47-67, +48-67, +49-67, +50-67, +51-67, +52-67, +53-67, +45-66, +46-66, +47-66, +48-66, +49-66, +50-66, +51-66, +52-66, +53-66, +45-65, +46-65, +47-65, +48-65, +49-65, +50-65, +51-65, +52-65, +53-65, +45-64, +46-64, +47-64, +48-64, +49-64, +50-64, +51-64, +52-64, +53-64, +45-63, +46-63, +47-63, +48-63, +49-63, +50-63, +51-63, +52-63, +53-63, +45-62, +46-62, +47-62, +48-62, +49-62, +50-62, +51-62, +52-62, or +53-62 relative to the 5' splice site of intron 8.
14. The method of any one of claims 1-13, wherein the antisense oligonucleotide comprises a sequence having at least or about 70%, 80%, or 90% sequence identity to a sequence set forth in any one of SEQ ID NOs:83-143, or a sequence having at least 8, 9, 10, 11, 12, 13, 14 or 15 contiguous nucleotides from a sequence set forth in any one of SEQ ID NOs:83-143.
15. The method of any one of claims 1-14, wherein the antisense oligonucleotide comprises the sequence set forth in any one of SEQ ID NOs:91-93, or a sequence comprising at least 8, 9, 10, 11, 12, 13, 14 or 15 contiguous nucleotides from a sequence set forth in any one of SEQ ID NOs:91-93.

16. The method of claim 9 or 10, wherein the retained intron is intron 9 and the ISS is at positions +21-29, +104-108 or +190-195 relative to the 5' splice site of intron 9.

17. The method of any one of claims 1-10 or 16, wherein the retained intron is intron 9 and the target region spans +10-40, +11-40, +12-40, +13-40, +14-40, +15-40, +16-40, +17-40, +18-40, +10-39, +11-39, +12-39, +13-39, +14-39, +15-39, +16-39, +17-39, +18-39, +10-38, +11-38, +12-38, +13-38, +14-38, +15-38, +16-38, +17-38, +18-38, +10-37, +11-37, +12-37, +13-37, +14-37, +15-37, +16-37, +17-37, +18-37, +10-36, +11-36, +12-36, +13-36, +14-36, +15-36, +16-36, +17-36, +18-36, +10-35, +11-35, +12-35, +13-35, +14-35, +15-35, +16-35, +17-35, +18-35, +10-34, +11-34, +12-34, +13-34, +14-34, +15-34, +16-34, +17-34, +18-34, +10-33, +11-33, +12-33, +13-33, +14-33, +15-33, +16-33, +17-33, +18-33, +10-32, +11-32, +12-32, +13-32, +14-32, +15-32, +16-32, +17-32, +18-32, +10-31, +11-31, +12-31, +13-31, +14-31, +15-31, +16-31, +17-31, +18-31, +10-30, +11-30, +12-30, +13-30, +14-30, +15-30, +16-30, +17-30, or +18-30 relative to the 5' splice site of intron 9.

18. The method of claim 17, wherein the antisense oligonucleotide comprises a sequence having at least or about 70%, 80%, or 90% sequence identity to a sequence set forth in any one of SEQ ID NOs:144-167, or a sequence having at least 8, 9, 10, 11, 12, 13, 14 or 15 contiguous nucleotides from a sequence set forth in any one of SEQ ID NOs:144-167.

19. The method of any one of claims 1-10 or 16, wherein the retained intron is intron 9 and the target region spans positions +87-120, +88-120, +89-120, +90-120, +91-120, +92-120, +93-120, +94-120, +95-120, +96-120, +97-120, +98-120, +87-119, +88-119, +89-119, +90-119, +91-119, +92-119, +93-119, +94-119, +95-119, +96-119, +97-119, +98-119, +87-118, +88-118, +89-118, +90-118, +91-118, +92-118, +93-118, +94-118, +95-118, +96-118, +97-118, +98-118, +87-117, +88-117, +89-117, +90-117, +91-117, +92-117, +93-117, +94-117, +95-117, +96-117, +97-117, +98-117, +87-116, +88-116, +89-116, +90-116, +91-116, +92-116, +93-116, +94-116, +95-116, +96-116, +97-116, +98-116, +87-115, +88-115, +89-115, +90-115, +91-115, +92-115, +93-115, +94-115, +95-115, +96-115, +97-115, +98-115, +87-114, +88-114, +89-114, +90-114, +91-114, +92-114, +93-114, +94-114, +95-114, +96-114, +97-114, +98-114, +87-113, +88-113, +89-113, +90-113, +91-113, +92-113, +93-113, +94-113, +95-113, +96-113, +97-113, +98-113, +87-112, +88-112, +89-112, +90-112, +91-112, +92-112, +93-112, +94-112, +95-112, +96-112, +97-112, +98-112, +87-111, +88-111, +89-111, +90-111, +91-111, +92-111, +93-111, +94-111, +95-111, +96-111, +97-111, +98-111, +87-110, +88-110, +89-110, +90-110, +91-110, +92-110, +93-110, +94-110, +95-110, +96-110, +97-110, or +98-110 relative to the 5' splice site of intron 9.

20. The method of claim 19, wherein the antisense oligonucleotide comprises a sequence having at least or about 70%, 80%, or 90% sequence identity to a sequence set forth in any one of SEQ ID NOs: 168-189, or a sequence having at least 8, 9, 10, 11, 12, 13, 14 or 15 contiguous nucleotides from a sequence set forth in any one of SEQ ID NOs: 168-189.

21. The method of any one of claims 1-10 or 16, wherein the retained intron is intron 9 and the target region spans positions +175-205, +176-205, +177-205, +178-205, +179-205, +180-205, +181-205, +182-205, +183-205, +184-205, +185-205, +175-204, +176-204, +177-204, +178-204, +179-204, +180-204, +181-204, +182-204, +183-204, +184-204, +185-204, +175-203, +176-203, +177-203, +178-203, +179-203, +180-203, +181-203, +182-203, +183-203, +184-203, +185-203, +175-202, +176-202, +177-202, +178-202, +179-202, +180-202, +181-202, +182-202, +183-202, +184-202, +185-202, +175-201, +176-201, +177-201, +178-201, +179-201, +180-201, +181-201, +182-201, +183-201, +184-201, +185-201, +175-200, +176-200, +177-200, +178-200, +179-200, +180-200, +181-200, +182-200, +183-200, +184-200, +185-200, +175-199, +176-199, +177-199, +178-199, +179-199, +180-199, +181-199, +182-199, +183-199, +184-199, +185-199, +175-198, +176-198, +177-198, +178-198, +179-198, +180-198, +181-198, +182-198, +183-198, +184-198, +185-198, +175-197, +176-197, +177-197, +178-197, +179-197, +180-197, +181-197, +182-197, +183-197, +184-197, +185-197, +175-196, +176-196, +177-196, +178-196, +179-196, +180-196, +181-196, +182-196, +183-196, +184-196, +185-196, +175-195, +176-195, +177-195, +178-195, +179-195, +180-195, +181-195, +182-195, +183-195, +184-195, or +185-195, relative to the 5' splice site of intron 9.

22. The method of any one of claims 1-21, wherein the antisense oligonucleotide consists of from 8 to 50, 8 to 40, 8 to 35, 8 to 30, 8 to 25, 8 to 20, 8 to 15, 9 to 50, 9 to 40, 9 to 35, 9 to 30, 9 to 25, 9 to 20, 9 to 15, 10 to 50, 10 to 40, 10 to 35, 10 to 30, 10 to 25, 10 to 20, 10 to 15, 11 to 50, 11 to 40, 11 to 35, 11 to 30, 11 to 25, 11 to 20, 11 to 15, 12 to 50, 12 to 40, 12 to 35, 12 to 30, 12 to 25, 12 to 20, or 12 to 15 nucleobases.

23. The method of any one of claims 1-22, wherein the antisense oligonucleotide is at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% complementary to the target region.

24. The method of any one of claims 1-23, wherein the antisense oligonucleotide comprises least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 contiguous nucleobases that are 100% complementary to the target region.

25. The method of any one of claims 1-24, wherein the antisense oligonucleotide comprises at least one modification.

26. The method of claim 25, wherein the modification is a nucleobase modification, a modification of the oligonucleotide backbone or a modification of a ribose sugar.

27. The method of any one of claims 1-26, wherein the antisense oligonucleotide comprises a modified sugar selected from among a 2'-O-methyl (2OMe), 2'-O-methoxy-ethyl (MOE), locked nucleic acids (LNA), 2'-fluoro or S-constrained-ethyl (cEt).

28. The method of any one of claims 1-27, wherein antisense oligonucleotide comprises backbone that comprises phosphorothioates.

29. The method of any one of claims 1-28, wherein the antisense oligonucleotide activates RNase H.
30. The method of any one of claims 2-29, wherein the subject is determined to have a heterozygous loss-of-function mutation in *SYNAP1*.
31. The method of any one of claims 2-30, wherein the subject has been genotyped to identify a heterozygous loss-of-function mutation in *SYNAP1*.
32. The method of any one of claims 2-31, wherein the antisense oligonucleotide is administered to the subject by parenteral administration or intranasal administration.
33. The method of claim 32, wherein the parenteral administration is selected from among subcutaneous administration, intravenous administration, intramuscular administration, intraarterial administration, intraperitoneal administration, or intracranial administration.
34. The method of claim 33, wherein intracranial administration is intrathecal or intracerebroventricular administration.
35. The method of any one of claims 2-34, wherein the antisense oligonucleotide or composition is administered to the subject about every 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more months.
36. The method of any one of claims 2-35, wherein the antisense oligonucleotide or composition is administered to the subject about every 3 months.
37. An antisense oligonucleotide comprising a sequence of nucleobases that is complementary to a target region in an intron-retaining SynGAP1 mRNA or pre-mRNA, wherein the target region is in a retained intron and wherein the retained intron is selected from among intron 5, 8, 9, 12, 13 or 14.
38. The antisense oligonucleotide of claim 37, wherein the antisense oligonucleotide binds to, or adjacent to, an intron splicing silencer (ISS); binds to nucleotides within a G-quadruplex; or binds to nucleotides with an RNA secondary structure.
39. The antisense oligonucleotide of claim 38, wherein the ISS is recognised by a heterogeneous nuclear ribonucleoproteins (hnRNP).
40. The antisense oligonucleotide of claim 39, wherein the hnRNP is hnRNP A1 or hnRNP I.
41. The antisense oligonucleotide of claim 39 or 40, wherein the retained intron is intron 8 and the ISS is at positions +17-22, +23-28, +17-28, or +57-62 relative to the 5' splice site of intron 8.
42. The antisense oligonucleotide of any one of claims 37-41, wherein the retained intron is intron 8 and the target region spans positions +4-35, +5-35, +6-35, +7-35, +8-35, +9-35,

+10-35, +11-35, +12-35, +13-35, +4-34, +5-34, +6-34, +7-34, +8-34, +9-34, +10-34, +11-34, +12-34, +13-34, +4-33, +5-33, +6-33, +7-33, +8-33, +9-33, +10-33, +11-33, +12-33, +13-33, +4-32, +5-32, +6-32, +7-32, +8-32, +9-32, +10-32, +11-32, +12-32, +13-32, +4-31, +5-31, +6-31, +7-31, +8-31, +9-31, +10-31, +11-31, +12-31, +13-31, +4-30, +5-30, +6-30, +7-30, +8-30, +9-30, +10-30, +11-30, +12-30, +13-30, +4-29, +5-29, +6-29, +7-29, +8-29, +9-29, +10-29, +11-29, +12-29, +13-29, +4-28, +5-28, +6-28, +7-28, +8-28, +9-28, +10-28, +11-28, +12-28, +13-28, +4-27, +5-27, +6-27, +7-27, +8-27, +9-27, +10-27, +11-27, +12-27, +13-27, +4-26, +5-26, +6-26, +7-26, +8-26, +9-26, +10-26, +11-26, +12-26, +13-26, +4-25, +5-25, +6-25, +7-25, +8-25, +9-25, +10-25, +11-25, +12-25, +13-25, +4-24, +5-24, +6-24, +7-24, +8-24, +9-24, +10-24, +11-24, +12-24, +13-24, +4-23, +5-23, +6-23, +7-23, +8-23, +9-23, +10-23, +11-23, +12-23, +13-23, +4-22, +5-22, +6-22, +7-22, +8-22, +9-22, +10-22, +11-22, +12-22, +13-22, +4-21, +5-21, +6-21, +7-21, +8-21, +9-21, +10-21, +11-21, +12-21, +13-21, +4-20, +5-20, +6-20, +7-20, +8-20, +9-20, +10-20, +11-20, +12-20, +13-20, +4-19, +5-19, +6-19, +7-19, +8-19, +9-19, +10-19, +11-19, +12-19, +13-19, +4-18, +5-18, +6-18, +7-18, +8-18, +9-18, +10-18, or +11-18 relative to the 5' splice site of intron 8.

43. The antisense oligonucleotide of any one of claims 37-41, wherein the retained intron is intron 8 and the target region spans positions +45-70, +46-70, +47-70, +48-70, +49-70, +50-70, +51-70, +52-70, +53-70, +45-69, +46-69, +47-69, +48-69, +49-69, +50-69, +51-69, +52-69, +53-69, +45-68, +46-68, +47-68, +48-68, +49-68, +50-68, +51-68, +52-68, +53-68, +45-67, +46-67, +47-67, +48-67, +49-67, +50-67, +51-67, +52-67, +53-67, +45-66, +46-66, +47-66, +48-66, +49-66, +50-66, +51-66, +52-66, +53-66, +45-65, +46-65, +47-65, +48-65, +49-65, +50-65, +51-65, +52-65, +53-65, +45-64, +46-64, +47-64, +48-64, +49-64, +50-64, +51-64, +52-64, +53-64, +45-63, +46-63, +47-63, +48-63, +49-63, +50-63, +51-63, +52-63, +53-63, +45-62, +46-62, +47-62, +48-62, +49-62, +50-62, +51-62, +52-62, or +53-62 relative to the 5' splice site of intron 8.

44. The antisense oligonucleotide of any one of claims 37-43, wherein the antisense oligonucleotide comprises a sequence having at least or about 70%, 80%, or 90% sequence identity to a sequence set forth in any one of SEQ ID NOs:83-143, or a sequence having at least 8, 9, 10, 11, 12, 13, 14 or 15 contiguous nucleotides from a sequence set forth in any one of SEQ ID NOs:83-143.

45. The antisense oligonucleotide of any one of claims 37-44, wherein the antisense oligonucleotide comprises the sequence set forth in any one of SEQ ID NOs:91-93, or a sequence comprising at least 8, 9, 10, 11, 12, 13, 14 or 15 contiguous nucleotides from a sequence set forth in any one of SEQ ID NOs:91-93.

46. The antisense oligonucleotide of any one of claims 37-40, wherein the retained intron is intron 9 and the ISS is at positions +21-29, +104-108 or +190-195 relative to the 5' splice site of intron 9.

47. The antisense oligonucleotide of any one of claims 37-41 or 46, wherein the retained intron is intron 9 and the target region spans +10-41, +11-41, +12-41, +13-41, +14-41, +15-41, +16-41, +17-41, +18-41, +10-40, +11-40, +12-40, +13-40, +14-40, +15-40, +16-40, +17-40, +18-40, +10-39, +11-39, +12-39, +13-39, +14-39, +15-39, +16-39, +17-39, +18-39, +10-38, +11-38, +12-38, +13-38, +14-38, +15-38, +16-38, +17-38, +18-38, +10-37, +11-37, +12-37, +13-37, +14-37, +15-37, +16-37, +17-37, +18-37, +10-36, +11-36, +12-36, +13-36, +14-36, +15-36, +16-36, +17-36, +18-36, +10-35, +11-35, +12-35, +13-35, +14-35, +15-35, +16-35, +17-35, +18-35, +10-34, +11-34, +12-34, +13-34, +14-34, +15-34, +16-34, +17-34, +18-34, +10-33, +11-33, +12-33, +13-33, +14-33, +15-33, +16-33, +17-33, +18-33, +10-32, +11-32, +12-32, +13-32, +14-32, +15-32, +16-32, +17-32, +18-32, +10-31, +11-31, +12-31, +13-31, +14-31, +15-31, +16-31, +17-31, +18-31, +10-30, +11-30, +12-30, +13-30, +14-30, +15-30, +16-30, +17-30, or +18-30 relative to the 5' splice site of intron 9.

48. The antisense oligonucleotide of claim 47, wherein the antisense oligonucleotide comprises a sequence having at least or about 70%, 80%, or 90% sequence identity to a sequence set forth in any one of SEQ ID NOs:144-167, or a sequence having at least 8, 9, 10, 11, 12, 13, 14 or 15 contiguous nucleotides from a sequence set forth in any one of SEQ ID NOs:144-167.

49. The antisense oligonucleotide of any one of claims 37-41 or 46, wherein the retained intron is intron 9 and the target region spans positions +87-120, +88-120, +89-120, +90-120, +91-120, +92-120, +93-120, +94-120, +95-120, +96-120, +97-120, +98-120, +87-119, +88-119, +89-119, +90-119, +91-119, +92-119, +93-119, +94-119, +95-119, +96-119, +97-119, +98-119, +87-118, +88-118, +89-118, +90-118, +91-118, +92-118, +93-118, +94-118, +95-118, +96-118, +97-118, +98-118, +87-117, +88-117, +89-117, +90-117, +91-117, +92-117, +93-117, +94-117, +95-117, +96-117, +97-117, +98-117, +87-116, +88-116, +89-116, +90-116, +91-116, +92-116, +93-116, +94-116, +95-116, +96-116, +97-116, +98-116, +87-115, +88-115, +89-115, +90-115, +91-115, +92-115, +93-115, +94-115, +95-115, +96-115, +97-115, +98-115, +87-114, +88-114, +89-114, +90-114, +91-114, +92-114, +93-114, +94-114, +95-114, +96-114, +97-114, +98-114, +87-113, +88-113, +89-113, +90-113, +91-113, +92-113, +93-113, +94-113, +95-113, +96-113, +97-113, +98-113, +87-112, +88-112, +89-112, +90-112, +91-112, +92-112, +93-112, +94-112, +95-112, +96-112, +97-112, +98-112, +87-111, +88-111, +89-111, +90-111, +91-111, +92-111, +93-111, +94-111, +95-111, +96-111, +97-111, +98-111, +87-110, +88-110, +89-110, +90-110, +91-110, +92-110, +93-110, +94-110, +95-110, +96-110, +97-110, or +98-110 relative to the 5' splice site of intron 9.

50. The antisense oligonucleotide of claim 49, wherein the antisense oligonucleotide comprises a sequence having at least or about 70%, 80%, or 90% sequence identity to a sequence set forth in any one of SEQ ID NOs: 168-189, or a sequence having at least 8, 9, 10, 11, 12, 13, 14 or 15 contiguous nucleotides from a sequence set forth in any one of SEQ ID NOs: 168-189.

51. The antisense oligonucleotide of any one of claims 37-41 or 46, wherein the retained intron is intron 9 and the target region spans positions +175-205, +176-205, +177-205, +178-205, +179-205, +180-205, +181-205, +182-205, +183-205, +184-205, +185-205, +175-204, +176-204, +177-204, +178-204, +179-204, +180-204, +181-204, +182-204, +183-204, +184-204, +185-204, +175-203, +176-203, +177-203, +178-203, +179-203, +180-203, +181-203, +182-203, +183-203, +184-203, +185-203, +175-202, +176-202, +177-202, +178-202, +179-202, +180-202, +181-202, +182-202, +183-202, +184-202, +185-202, +175-201, +176-201, +177-201, +178-201, +179-201, +180-201, +181-201, +182-201, +183-201, +184-201, +185-201, +175-200, +176-200, +177-200, +178-200, +179-200, +180-200, +181-200, +182-200, +183-200, +184-200, +185-200, +175-199, +176-199, +177-199, +178-199, +179-199, +180-199, +181-199, +182-199, +183-199, +184-199, +185-199, +175-198, +176-198, +177-198, +178-198, +179-198, +180-198, +181-198, +182-198, +183-198, +184-198, +185-198, +175-197, +176-197, +177-197, +178-197, +179-197, +180-197, +181-197, +182-197, +183-197, +184-197, +185-197, +175-196, +176-196, +177-196, +178-196, +179-196, +180-196, +181-196, +182-196, +183-196, +184-196, +185-196, +175-195, +176-195, +177-195, +178-195, +179-195, +180-195, +181-195, +182-195, +183-195, +184-195, or +185-195, relative to the 5' splice site of intron 9.

52. The antisense oligonucleotide of any one of claims 37-51, wherein the antisense oligonucleotide consists of from 8 to 50, 8 to 40, 8 to 35, 8 to 30, 8 to 25, 8 to 20, 8 to 15, 9 to 50, 9 to 40, 9 to 35, 9 to 30, 9 to 25, 9 to 20, 9 to 15, 10 to 50, 10 to 40, 10 to 35, 10 to 30, 10 to 25, 10 to 20, 10 to 15, 11 to 50, 11 to 40, 11 to 35, 11 to 30, 11 to 25, 11 to 20, 11 to 15, 12 to 50, 12 to 40, 12 to 35, 12 to 30, 12 to 25, 12 to 20, or 12 to 15 nucleobases.

53. The antisense oligonucleotide of any one of claims 37-52, wherein the antisense oligonucleotide is at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% complementary to the target region.

54. The antisense oligonucleotide of any one of claims 37-53, wherein the antisense oligonucleotide comprises least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 contiguous nucleobases that are 100% complementary to the target region.

55. The antisense oligonucleotide of any one of claims 37-54, wherein the antisense oligonucleotide comprises at least one modification.

56. The antisense oligonucleotide of claim 55, wherein the modification is a nucleobase modification, a modification of the oligonucleotide backbone or a modification of a ribose sugar.

57. The antisense oligonucleotide of any one of claims 37-55, wherein the antisense oligonucleotide comprises a modified sugar selected from among a 2'-O-methyl (2OMe), 2'-O-methoxy-ethyl (MOE), locked nucleic acids (LNA), 2'-fluoro or S-constrained-ethyl (cEt).

58. The antisense oligonucleotide of any one of claims 37-58, wherein the antisense oligonucleotide comprises a backbone that comprises phosphorothioates.

59. The antisense oligonucleotide of any one of claims 37-59, wherein the antisense oligonucleotide activates RNase H.

60. A composition comprising the antisense oligonucleotide of any one of claims 37-59.

61. Use of an antisense oligonucleotide for the treatment of a disorder associated with a heterozygous loss-of-function mutation in *SYNAP1*, wherein the antisense oligonucleotide enhances splicing at a splice site of a retained intron in an intron-retaining SynGAP1 mRNA or pre-mRNA, wherein the retained intron is selected from among intron 5, 8, 9, 12, 13 and 14 and wherein the antisense oligonucleotide comprises a sequence of nucleobases that is complementary to a target region in the SynGAP1 mRNA or pre-mRNA.