

COMPOSITIONS AND METHODS FOR INHIBITING EXPRESSION OF HUNTINGTIN
(HTT)

Field of the Invention

5 The invention relates, in part, to compositions and methods that can be used to inhibit a huntingtin (HTT) gene expression.

Background

10 The Huntingtin (HTT) gene, also known as IT15 or HD (Huntington's disease) gene, encodes the huntingtin protein whose expansion of poly glutamine at its N terminus is causally linked to Huntington's disease. HTT gene spans 169 kb on chromosome 4 and gives rise to large transcripts around 14 kb and consequently HTT proteins about 350 kDa under physiological condition. HTT is widely expressed in various tissues of the body with brain at the highest level. Within the brain HTT is expressed in all neurons as well as in glia cells. Although the exact
15 functions of HTT is still elusive, previous studies have demonstrated its pivotal roles in vesicle traffic, autophagy, transcription and cell division. Consequently, HTT is essential for embryonic development, tissue maintenance and cell survival.

 Huntington's disease (HD) is a neurodegenerative disease caused by an expansion of the number of CAG repeats in exon 1 of HTT gene. Huntington's disease manifests with a variety
20 of symptoms that include motor, cognitive and psychiatric impairment. The genetic mutation involves a DNA segment of the huntingtin gene known as the CAG trinucleotide repeat. Expansion of the number of CAG repeats to above 40 copies causes adult onset of Huntington's disease whereas CAG repeats of above 60-70 copies leads to a juvenile and a more progressive form of the disease. The expansion of poly glutamine (polyQ) translated from CAG repeats in
25 protein's N terminus underlies the pathogenesis of HD caused by familial inherited mutation of HTT. Transgenic mice overexpressing mutant HTT exon1 recapitulates symptoms of Huntington's disease. Meanwhile, N terminal fragment containing PolyQ repeats generated by proteolysis facilitates the accumulation and translocation to nucleus for neurotoxic effect. All points to the key role of PolyQ itself in onset and progression of Huntington's disease. More
30 interestingly, a transcript isoform which contains mutant exon1 and part of intron1 is aberrantly generated proportional to the number of CAG repeats under pathological condition. Therefore, there are three transcripts of HTT under pathological condition including full-length wild type, full-length mutant and HTT-1A isoforms. Recently there are two more transcript isoforms uploaded to ENSEMBLE database can be translated to full-length HTT protein without PolyQ,
35 in other words, a Exon1-deleted HTT. Huntington's disease has been shown to be caused by an expanding glutamine repeat in exon 1 of a gene termed IT15 or Huntingtin (HTT) (WO2016/102664). Although this gene is widely expressed and is required for normal development, the pathology of Huntington's disease is restricted to the brain, for reasons that remain poorly understood. Huntington's disease (an autosomal dominant disease) has been

shown to be caused by the expansion of the polyglutamine repeat results in a full-length mutant transcript encoding an expanded polyglutamine repeat, as well as a truncated mutant transcript which retains intron 1 and encodes an expanded polyglutamine repeat (WO202376450). In patients having HD (an autosomal dominant disease), the expansion of the polyglutamine repeat results in a wild-type transcript, a full-length mutant transcript having the expanded polyglutamine repeat, as well as a truncated mutant transcript having the expanded polyglutamine repeat. It has been shown that, although the Huntingtin gene product is expressed at similar levels in patients and controls, it is the expansion of the polyglutamine repeat and the presence of the full-length mutant transcript and the truncated mutant transcript that induces toxicity. Furthermore, HTT-1A mRNA levels are higher in HD patient's motor cortex and hippocampus as compared to controls.

Effective treatment for Huntington's disease is currently not available. The choreic movements and agitated behaviors may be suppressed, usually only partially, by antipsychotics (e.g., chlorpromazine or haloperidol) or reserpine begun with 0.1 mg/day and increased until adverse effects of lethargy, hypotension, or parkinsonism occur.

Accordingly, despite significant advances in the field of RNAi and Huntington's disease treatment, there remains a need for an agent that can selectively and efficiently silence the HD gene using the cell's own RNAi machinery that has both high biological activity and in vivo stability, and that can effectively inhibit expression of a target Huntingtin gene.

Summary of the Invention

In general, the present disclosure features novel HTT gene-specific RNAi agents, compositions that include HTT RNAi agents target full-length of mutant HTT gene, full-length of wild-type HTT gene or a particular portion of intron 1 retained in the truncated mutant HTT gene, thereby inhibiting expression of full-length of mutant HTT gene and/or the truncated mutant HTT transcript encoding an expanded polyglutamine repeat –and methods for inhibiting expression of a HTT gene in vitro and/or in vivo using the HTT RNAi agents and compositions that include HTT RNAi agents described herein. The HTT RNAi agents described herein can selectively and efficiently decrease, inhibit, or silence expression of a HTT gene in a subject, e.g., a human or animal subject for the treatment of Huntington's disease (HD) .

According to an aspect of the invention, a double-stranded ribonucleic acid (dsRNA) agent for inhibiting expression of HTT is provided, wherein the dsRNA agent including a sense strand and an antisense strand, wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2 or 3 nucleotides from the nucleotide sequence of SEQ ID NO: 1, 3, 5, or 7 and the antisense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2 or 3 nucleotides from the nucleotide sequence of SEQ ID NO: 2, 4, 6, or 8, wherein the sense strand and the antisense strand can be partially, substantially, or fully complementary to each other.

In some embodiments, the dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein said antisense strand comprises a region of complementarity to a HTT RNA transcript which comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from any one of the antisense sequences listed in any one of Tables 1-3, Tables 1A-3A. In some embodiments, the dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein said antisense strand comprises a region of complementarity to a HTT RNA transcript which comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides from any one of the antisense sequences listed in any one of Tables 1-3, Tables 1A-3A.

In some embodiments, the dsRNA agent including a sense nucleotide and an antisense strand, nucleotide positions 2 to 18 in the antisense strand including a region of complementarity to a HTT RNA transcript at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides that differ by 0, 1, 2, or 3 nucleotides from one of the antisense sequences listed in one of Tables 1-3, Tables 1A-3A, and optionally including a targeting ligand.

In some embodiments, a double-stranded ribonucleic acid (dsRNA) agent for inhibiting expression of HTT is provided, wherein the dsRNA agent includes a sense strand and an antisense strand, wherein the sense strand comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides that differ by 0, 1, 2, or 3 nucleotides from any one of the nucleotide sequences of nucleotides 4394-4524, 6503-6633, 2327-2457, 1892-2022, 3141-3271, 7517-7647, 1503-1633, 2062-2192, 6570-6700, 393-523, 394-524, 395-525, 396-526, 397-527, 398-528, 399-529, 400-530, 401-531, 403-533, 404-534, 410-540, 426-556, 428-558, 432-562, 435-565, 436-566, 438-568, 440-570, 446-576, 448-578, 481-611, 490-620, 491-621, 522-652, 590-720, 600-730, 602-732, 605-735, 608-738, 609-739, 610-740, 614-744, 618-748, 619-749, 621-751, 833-963, 834-964, 836-966, 844-974, 854-984, 890-1020, 905-1035, 1160-1290, 1161-1291, 1200-1330, 1206-1336, 1208-1338, 1213-1343, 1214-1344, 1218-1348, 1391-1521, 1394-1524, 1457-1587, 1501-1631, 1864-1994, 1871-2001, 1872-2002, 1874-2004, 2070-2200, 2196-2326, 2200-2330, 2204-2334, 2206-2336, 2207-2337, 2320-2450, 2321-2451, 2330-2460, 2332-2462, 2334-2464, 2340-2470, 2390-2520, 2395-2525, 2397-2527, 2399-2529, 2527-2657, 2561-2691, 2592-2722, 2595-2725, 2630-2760, 2658-2788, 2706-2836, 2797-2927, 2828-2958, 2858-2988, 2864-2994, 2867-2997, 2878-3008, 2880-3010, 3006-3136, 3009-3139, 3090-3220, 3134-3264, 3157-3287, 3195-3325, 3202-3332, 3213-3343, 3214-3344, 3217-3347, 3219-3349, 3248-3378, 3249-3379, 3250-3380, 3301-3431, 3393-3523, 3766-3896, 3785-3915, 3797-3927, 3799-3929, 3816-3946, 3817-3947, 3827-3957, 3828-3958, 3835-3965, 3845-3975, 3852-3982, 4030-4160, 4058-4188, 4060-4190, 4063-4193, 4064-4194, 4075-4205, 4076-4206, 4083-4213, 4365-4495, 4371-4501, 4377-4507, 4380-4510, 4382-4512, 4389-4519, 4394-4524, 4398-4528, 4400-4530,

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In some embodiments, a double-stranded ribonucleic acid (dsRNA) agent for inhibiting 25 expression of HTT is provided, wherein the sense strand comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides that differ by 0, 1, 2, or 3 nucleotides from any one of the nucleotide sequences of nucleotides 4399-4419, 6508-6528, 2332-2352, 1897-1917, 3146-3166, 7522-7542, 1508-1528, 2067-2087, 6575-6595, 398-418, 399-419, 400-420, 401-421, 402-422, 403-423, 404-424, 405-425, 406-426, 408-428, 409-429, 402-429, 415-435, 431-451, 30 433-453, 437-457, 431-457, 440-460, 441-461, 443-463, 445-465, 451-471, 453-473, 440-473, 486-506, 495-515, 496-516, 527-547, 595-615, 605-625, 607-627, 610-630, 613-633, 614-634, 615-635, 619-639, 623-643, 624-644, 626-646, 838-858, 839-859, 841-861, 849-869, 859-879, 895-915, 910-930, 1165-1185, 1166-1186, 1205-1225, 1211-1231, 1213-1233, 1218-1238, 1219-1239, 1223-1243, 1396-1416, 1399-1419, 1462-1482, 1506-1526, 1869-1889, 1876-

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 5 comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the corresponding nucleotide sequence of SEQ ID NO:2, wherein the sense strand and the antisense strand can be partially, substantially, or fully complementary to each other.

In some embodiments, the antisense strand comprises at least 14, 15, 16, 17, 18, 19, 20
 10 or 21 contiguous nucleotides which differ by 0, 1, 2, or 3 nucleotides from the complement of nucleotides 4399-4419, 6508-6528, 2332-2352, 1897-1917, 3146-3166, 7522-7542, 1508-1528, 2067-2087, 6575-6595, 398-418, 399-419, 400-420, 401-421, 402-422, 403-423, 404-424, 405-425, 406-426, 408-428, 409-429, 402-429, 415-435, 431-451, 433-453, 437-457, 431-457, 440-460, 441-461, 443-463, 445-465, 451-471, 453-473, 440-473, 486-506, 495-
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In some embodiments, a double-stranded ribonucleic acid (dsRNA) agent for inhibiting
 expression of HTT is provided, wherein the sense strand comprises at least 15, 16, 17, 18, 19,
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In some embodiments, a double-stranded ribonucleic acid (dsRNA) agent for inhibiting expression of HTT is provided, wherein the sense strand comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides that differ by 0, 1, 2, or 3 nucleotides from any one of the nucleotide sequences of nucleotides 28-48, 23-43, 36-56, 4-24, 11-31, 22-42, 28-48, 30-50, 31-51, 32-52, 33-53, 34-54, 35-55, 36-56, 40-60, 57-77, 61-81, 62-82, 73-93, 79-99, 89-109, 91-111, 101-121, 102-122, 106-126, 111-131, 113-133, 120-140, 131-151, 133-153, 136-156, 139-159, 145-165, 150-170, 151-171, 152-172, 153-173, 154-174, 155-175, 157-177, 158-178, 160-180, 161-181, 163-183, 165-185, 169-189, 175-195, 179-199, 180-200, 181-201, 182-202, 183-203, 184-204, 188-208, 286-306, 287-307, 308-328, 312-332, 314-334, 316-336, 373-393, 377-397, 383-403, 388-408, 150-170, 7-27, 147-167, 125-145, 777-797, 923-943, 925-945, 926-946, 999-1019, 1015-1035, 1045-1065, 1052-1072, 1071-1091, 1083-1103, 1089-1109, 1097-1117, 1121-1141, 1123-1143, 1134-1154, 1169-1189, 1194-1214, 1197-1217, 1200-1220, 1231-1251, 1247-1267, 1256-1276, 1317-1337, 1324-1344, 1326-1346, 1406-1426, 1407-1427, 1439-1459, 1440-1460, 1466-1486, 1467-1487, 1485-1505, 1512-1532, 1602-1622, 1613-1633, 1615-1635, 1656-1676, 1701-1721, 1726-1746, 1732-1752, 1737-1757, 1739-1759, 1740-1760, 1784-1804, 1785-1805, 1786-1806, 1824-1844, 1870-1890, 1875-1895, 1879-1899, 1882-1902, 1896-1916, 1906-1926, 1933-1953, 1951-1971, 1953-1973, 1957-1977, 1963-1983, 1964-1984, 1966-1986, 1968-1988, 2030-2050, 2031-2051, 2051-2071, 2052-2072, 2056-2076, 2057-2077, 2066-2086, 2071-2091, 2079-2099,

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15 In some embodiments, the antisense strand comprises at least 14, 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides which differ by 0, 1, 2, or 3 nucleotides from the complement of nucleotides 28-48, 23-43, 36-56, 4-24, 11-31, 22-42, 28-48, 30-50, 31-51, 32-52, 33-53, 34-54, 35-55, 36-56, 40-60, 57-77, 61-81, 62-82, 73-93, 79-99, 89-109, 91-111, 101-121, 102-122, 106-126, 111-131, 113-133, 120-140, 131-20 151, 133-153, 136-156, 139-159, 145-165, 150-170, 151-171, 152-172, 153-173, 154-174, 155-175, 157-177, 158-178, 160-180, 161-181, 163-183, 165-185, 169-189, 175-195, 179-199, 180-200, 181-201, 182-202, 183-203, 184-204, 188-208, 286-306, 287-307, 308-328, 312-332, 314-334, 316-336, 373-393, 377-397, 383-403, 388-408, 150-170, 7-27, 147-167, 125-145, 777-797, 923-25 943, 925-945, 926-946, 999-1019, 1015-1035, 1045-1065, 1052-1072, 1071-1091, 1083-1103, 1089-1109, 1097-1117, 1121-1141, 1123-1143, 1134-1154, 1169-1189, 1194-1214, 1197-1217, 1200-1220, 1231-1251, 1247-1267, 1256-1276, 1317-1337, 1324-1344, 1326-1346, 1406-1426, 1407-1427, 1439-1459, 1440-1460, 1466-1486, 1467-1487, 1485-1505, 1512-1532, 1602-1622, 1613-1633, 1615-1635, 1656-1676, 30 1701-1721, 1726-1746, 1732-1752, 1737-1757, 1739-1759, 1740-1760, 1784-1804, 1785-1805, 1786-1806, 1824-1844, 1870-1890, 1875-1895, 1879-1899, 1882-1902, 1896-1916, 1906-1926, 1933-1953, 1951-1971, 1953-1973, 1957-1977, 1963-1983, 1964-1984, 1966-1986, 1968-1988, 2030-2050, 2031-2051, 2051-2071, 2052-2072, 2056-2076, 2057-2077, 2066-2086, 2071-2091, 2079-2099, 2085-2105, 2086-2106,

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 3075-3095, 3076-3096, 1650-1670, 1661-1681, 1067-1087, 596-616, 1045-1065,
- 5 633-653, 823-843, 1195-1215, 1196-1216, 1198-1218, 1199-1219, 1204-1224,
 1221-1241, 1227-1247, 1230-1250, 1233-1253, 1234-1254, 1235-1255, 1242-1262,
 1328-1348, 1329-1349, 1393-1413, 1394-1414, 1404-1424, 1405-1425, 1408-1428,
 1411-1431, 1416-1436, 1427-1447, 1428-1448, 1429-1449, 1432-1452, 1437-1457,
 1438-1458, 1444-1464, 1741-1761, 1759-1779, 1771-1791, 1774-1794, 1776-1796,
- 10 1777-1797, 1779-1799, 1780-1800, 1783-1803, 1788-1808, 1797-1817, 1799-1819,
 1821-1841, 1822-1842, 1831-1851, 1834-1854, 1839-1859, 1845-1865, 1864-1884,
 1865-1885, 1866-1886, 1868-1888, 2073-2093, 2078-2098, 2081-2101, 2082-2102,
 2084-2104, 2087-2107, 2088-2108, 2089-2109, 2090-2110, 2092-2112, 2095-2115,
 2096-2116, 2097-2117, 6-24, 13-31, 24-42, 30-48, 32-50, 33-51, 34-52, 35-53,
- 15 36-54, 37-55, 38-56, 42-60, 59-77, 63-81, 64-82, 75-93, 81-99, 91-109, 93-
 111, 103-121, 104-122, 108-126, 113-131, 115-133, 122-140, 133-151, 135-153,
 138-156, 141-159, 147-165, 152-170, 153-171, 154-172, 155-173, 156-174,
 157-175, 159-177, 160-178, 162-180, 163-181, 165-183, 167-185, 171-189,
 177-195, 181-199, 182-200, 183-201, 184-202, 185-203, 186-204, 190-208,
- 20 288-306, 289-307, 310-328, 314-332, 316-334, 318-336, 375-393, 379-397,
 385-403, 390-408, 779-797, 925-943, 927-945, 928-946, 1001-1019, 1017-1035,
 1047-1065, 1054-1072, 1073-1091, 1085-1103, 1091-1109, 1099-1117, 1123-1141,
 1125-1143, 1136-1154, 1171-1189, 1196-1214, 1199-1217, 1202-1220, 1233-1251,
 1249-1267, 1258-1276, 1319-1337, 1326-1344, 1328-1346, 1408-1426, 1409-1427,
- 25 1441-1459, 1442-1460, 1468-1486, 1469-1487, 1487-1505, 1514-1532, 1604-1622,
 1615-1633, 1617-1635, 1658-1676, 1703-1721, 1728-1746, 1734-1752, 1739-1757,
 1741-1759, 1742-1760, 1786-1804, 1787-1805, 1788-1806, 1826-1844, 1872-1890,
 1877-1895, 1881-1899, 1884-1902, 1898-1916, 1908-1926, 1935-1953, 1953-1971,
 1955-1973, 1959-1977, 1965-1983, 1966-1984, 1968-1986, 1970-1988, 2032-2050,
- 30 2033-2051, 2053-2071, 2054-2072, 2058-2076, 2059-2077, 2068-2086, 2073-2091,
 2081-2099, 2087-2105, 2088-2106, 2093-2111, 2104-2122, 2106-2124, 2157-2175,
 2172-2190, 2177-2195, 2179-2197, 2529-2547, 2542-2560, 2551-2569, 2557-2575,
 2607-2625, 2611-2629, 2658-2676, 2681-2699, 2683-2701, 2693-2711, 2760-2778,
 3061-3079, 3063-3081, 3073-3091, 3077-3095, 3078-3096, 1652-1670, 1663-1681,

1069-1087, 598-616, 1047-1065, 635-653, 825-843, 1197-1215, 1198-1216,
 1200-1218, 1201-1219, 1206-1224, 1223-1241, 1229-1247, 1232-1250, 1235-1253,
 1236-1254, 1237-1255, 1244-1262, 1330-1348, 1331-1349, 1395-1413, 1396-1414,
 1406-1424, 1407-1425, 1410-1428, 1413-1431, 1418-1436, 1429-1447, 1430-1448,
 5 1431-1449, 1434-1452, 1439-1457, 1440-1458, 1446-1464, 1743-1761, 1761-1779,
 1773-1791, 1776-1794, 1778-1796, 1779-1797, 1781-1799, 1782-1800, 1785-1803,
 1790-1808, 1799-1817, 1801-1819, 1823-1841, 1824-1842, 1833-1851, 1836-1854,
 1841-1859, 1847-1865, 1866-1884, 1867-1885, 1868-1886, 1870-1888, 2075-2093,
 2080-2098, 2083-2101, 2084-2102, 2086-2104, 2089-2107, 2090-2108, 2091-2109,
 10 2092-2110, 2094-2112, 2097-2115, 2098-2116, 2099-2117, 144-162, 149-167, of
 SEQ ID NO: 7.

In some embodiments, the HTT RNA transcript is SEQ ID NO: 1 and /or NO: 7.

In some embodiments, the antisense strand of the dsRNA agent is at least substantially
 complementary to any one of a target region of SEQ ID NO: 1 and is provided in any one of
 15 Tables 1,2, 3. In some embodiments, the antisense strand of the dsRNA agent is fully
 complementary to any one of a target region of SEQ ID NO: 1 and is provided in any one of
 Tables 1,2, 3. In some embodiments, the dsRNA agent includes a sense strand sequence set forth
 in any one of Tables 1,2, 3, wherein the sense strand sequence is at least substantially
 complementary to the antisense strand sequence in the dsRNA agent. In certain embodiments,
 20 the dsRNA agent includes a sense strand sequence set forth in any one of Tables 1,2, 3, wherein
 the sense strand sequence is fully complementary to the antisense strand sequence in the dsRNA
 agent. In some embodiments, the dsRNA agent includes an antisense strand sequence set forth
 in any one of Tables 1,2, 3. In some embodiments, the dsRNA agent includes the sequences set
 forth as a duplex sequence in any of Tables 1,2, 3.

In some embodiments, the antisense strand of the dsRNA agent is at least substantially
 complementary to any one of a target region of SEQ ID NO: 7 and is provided in any one of
 Tables 1A,2A, 3A. In some embodiments, the antisense strand of the dsRNA agent is fully
 complementary to any one of a target region of SEQ ID NO: 7 and is provided in any one of
 Tables 1A,2A, 3A. In some embodiments, the dsRNA agent includes a sense strand sequence set
 30 forth in any one of Tables 1A,2A, 3A, wherein the sense strand sequence is at least substantially
 complementary to the antisense strand sequence in the dsRNA agent. In certain embodiments,
 the dsRNA agent includes a sense strand sequence set forth in any one of Tables 1A,2A, 3A,
 wherein the sense strand sequence is fully complementary to the antisense strand sequence in
 the dsRNA agent. In some embodiments, the dsRNA agent includes an antisense strand sequence
 set forth in any one of Tables 1A,2A, 3A. In some embodiments, the dsRNA agent includes the
 35 sequences set forth as a duplex sequence in any of Tables 1A,2A, 3A.

In some embodiments, the dsRNA agent includes at least one modified nucleotide. In certain embodiments, all or substantially all of the nucleotides of the antisense strand are modified nucleotides. In some embodiments, at least one of the modified nucleotides comprises: 2'-O-methyl nucleotide, 2'-fluoro nucleotide, 2'-deoxy nucleotide, 2'3'-seco nucleotide mimic, locked nucleotide, unlocked nucleic acid nucleotide (UNA), glycol nucleic acid nucleotide (GNA), 2'-F-Arabino nucleotide, 2'-methoxyethyl nucleotide, abasic nucleotide, ribitol, inverted nucleotide, inverted abasic nucleotide, inverted 2'-Ome nucleotide, inverted 2'-deoxy nucleotide, isomannide nucleotide, 2'-amino-modified nucleotide, 2'-alkyl-modified nucleotide, morpholino nucleotide, and 3'-OME nucleotide, a nucleotide including a 5'-phosphorothioate group, a nucleotide comprising phosphate mimic, or a terminal nucleotide linked to a cholesteryl derivative or dodecanoic acid bisdecylamide group, a 2'-amino-modified nucleotide, a phosphoramidite, or a non-natural base including nucleotide.

In some embodiments, the dsRNA agent includes an E-vinylphosphonate nucleotide at the 5'-end of the antisense strand.

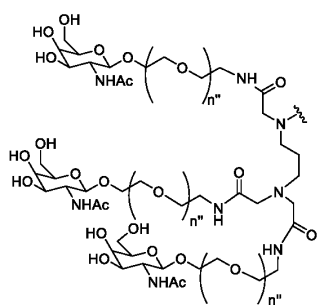
In certain embodiments, the dsRNA agent includes at least one phosphorothioate internucleoside linkage. In certain embodiments, the sense strand includes at least one phosphorothioate internucleoside linkage. In some embodiments, the antisense strand includes at least one phosphorothioate internucleoside linkage. In some embodiments, the sense strand includes 1, 2, 3, 4, 5, or 6 phosphorothioate internucleoside linkages. In certain embodiments, the antisense strand includes 1, 2, 3, 4, 5, or 6 phosphorothioate internucleoside linkages. In some embodiments, at least the terminal two modified or unmodified nucleotides at one end or both ends of the antisense strand are linked through phosphorothioate linkages. In some embodiments, the terminal three modified or unmodified nucleotides at one end or both ends of the antisense strand are linked through phosphorothioate linkages. In some embodiments, at least the terminal two modified or unmodified nucleotides at one end or both ends of the sense strand are linked through phosphorothioate linkages. In some embodiments, the terminal three modified or unmodified nucleotides at one end or both ends of the sense strand are linked through phosphorothioate linkages. In some embodiments, the terminal three modified or unmodified nucleotides at 5' end of the sense strand are linked through phosphorothioate linkages and the terminal two modified or unmodified nucleotides at 3' end of the sense strand are linked through phosphorothioate linkages.

In some embodiments, all or substantially all of the nucleotides of the sense strand and the antisense strand are modified nucleotides. In some embodiments, the antisense strand comprises 15 or more modified nucleotides independently selected from a 2'-O-methyl nucleotide, a 2'-fluoro nucleotide and an UNA modified nucleotide, wherein less than 6 modified nucleotides are 2'-fluoro nucleotides. In some embodiments, the antisense strand comprises 3 or 5 2'-fluoro nucleotides, preferably, the antisense strand comprises 5 2'-fluoro nucleotides. In some embodiments, the sense strand comprises 15 or more modified nucleotides independently selected from a 2'-O-methyl nucleotide and a 2'-fluoro nucleotide, wherein less than 4 modified

nucleotides are 2'-fluoro nucleotides. In certain embodiments, the sense strand comprises 3 2'-fluoro nucleotides. In some embodiments, the antisense strand comprises 15 or more modified nucleotides independently selected from a 2'-O-methyl nucleotide and a 2'-fluoro nucleotide, wherein at least 14 modified nucleotides are 2'-O-methyl nucleotides and the nucleotides at positions 2, 5, 7, 11, 12, 14, 16 and/or 18 counting from the first matching position of the 5' end of the antisense strand are independently a 2'-fluoro nucleotide. In some embodiments, the antisense strand comprises at least one UNA modified nucleotide and 5 2'-fluoro nucleotides. In some embodiments, the antisense strand comprises one UNA modified nucleotide at position 7 and 5 2'-fluoro nucleotides at positions 2, 5, 12, 14 and 16 counting from the first matching position of the 5' end, and the rest 2'-O-methyl nucleotides. In some embodiments, the antisense strand comprises one UNA modified nucleotide at position 7 and 5 2'-fluoro nucleotides at positions 2, 5, 12, 14 and 18 counting from the first matching position of the 5' end, and the rest 2'-O-methyl nucleotides. In some embodiments, the antisense strand comprises one UNA modified nucleotide at position 7 and 5 2'-fluoro nucleotides at positions 2, 5, 11, 14 and 16 counting from the first matching position of the 5' end, and the rest 2'-O-methyl nucleotides. In some embodiments, the antisense strand comprises 5 2'-fluoro nucleotides at positions 2, 7, 12, 14 and 16 counting from the first matching position of the 5' end, and the rest 2'-O-methyl nucleotides. In some embodiments, the antisense strand comprises 5 2'-fluoro nucleotides at positions 2, 7, 11, 14 and 16 counting from the first matching position of the 5' end, and the rest 2'-O-methyl nucleotides. In some embodiments, the antisense strand comprises 5 2'-fluoro nucleotides at positions 2, 5, 12, 14 and 16 counting from the first matching position of the 5' end, and the rest 2'-O-methyl nucleotides. In some embodiments, the antisense strand comprises 5 2'-fluoro nucleotides at positions 2, 5, 11, 14 and 16 counting from the first matching position of the 5' end, and the rest 2'-O-methyl nucleotides. In some embodiments, the sense strand comprises 15 or more modified nucleotides independently selected from a 2'-O-methyl nucleotide and a 2'-fluoro nucleotide, preferably, wherein at least 18 modified nucleotides are 2'-O-methyl nucleotides and the nucleotides at positions 9, 11 and/or 13 counting from the first matching position of the 3' end of the sense strand are 2'-fluoro nucleotides. In some embodiments, the sense strand comprises at least 18 modified nucleotides are 2'-O-methyl nucleotides and the nucleotides at positions 8, 11 and/or 13 counting from the first matching position of the 3' end of the sense strand are 2'-fluoro nucleotides. In some embodiments, the modified sense strand is a modified sense strand sequence set forth in one of Tables 2-3, Tables 2A-3A. In some embodiments, the modified antisense strand is a modified antisense strand sequence set forth in one of Tables 2-3, Tables 2A-3A.

In some embodiments, the dsRNA agent includes at least one modified nucleotide and further includes one or more targeting groups or linking groups. In some embodiments, the one or more targeting groups or linking groups are conjugated to the sense strand. In some embodiments, the targeting group or linking group includes N-acetyl-galactosamine (GalNAc).

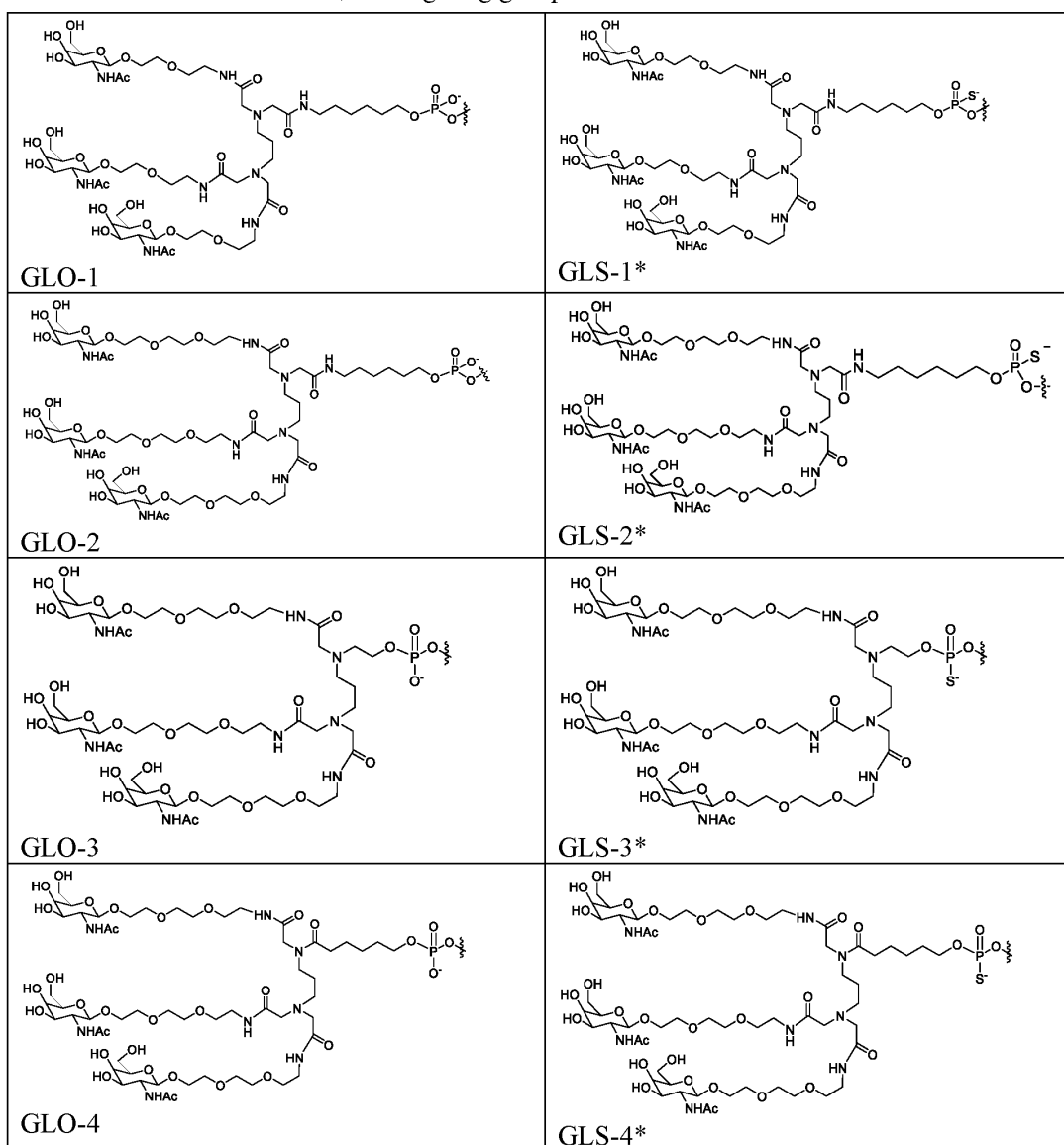
In some embodiments, the targeting group has a structure:

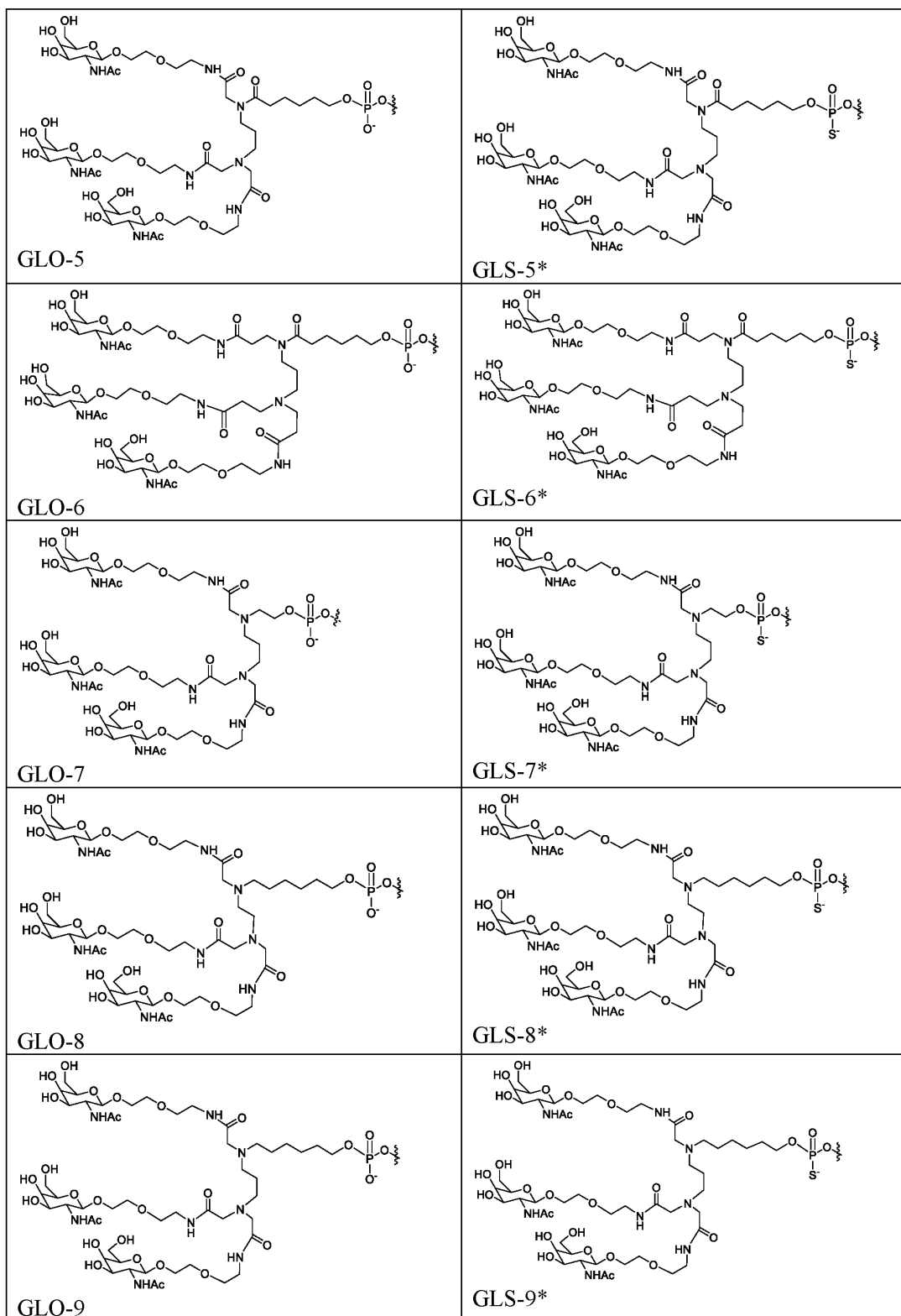


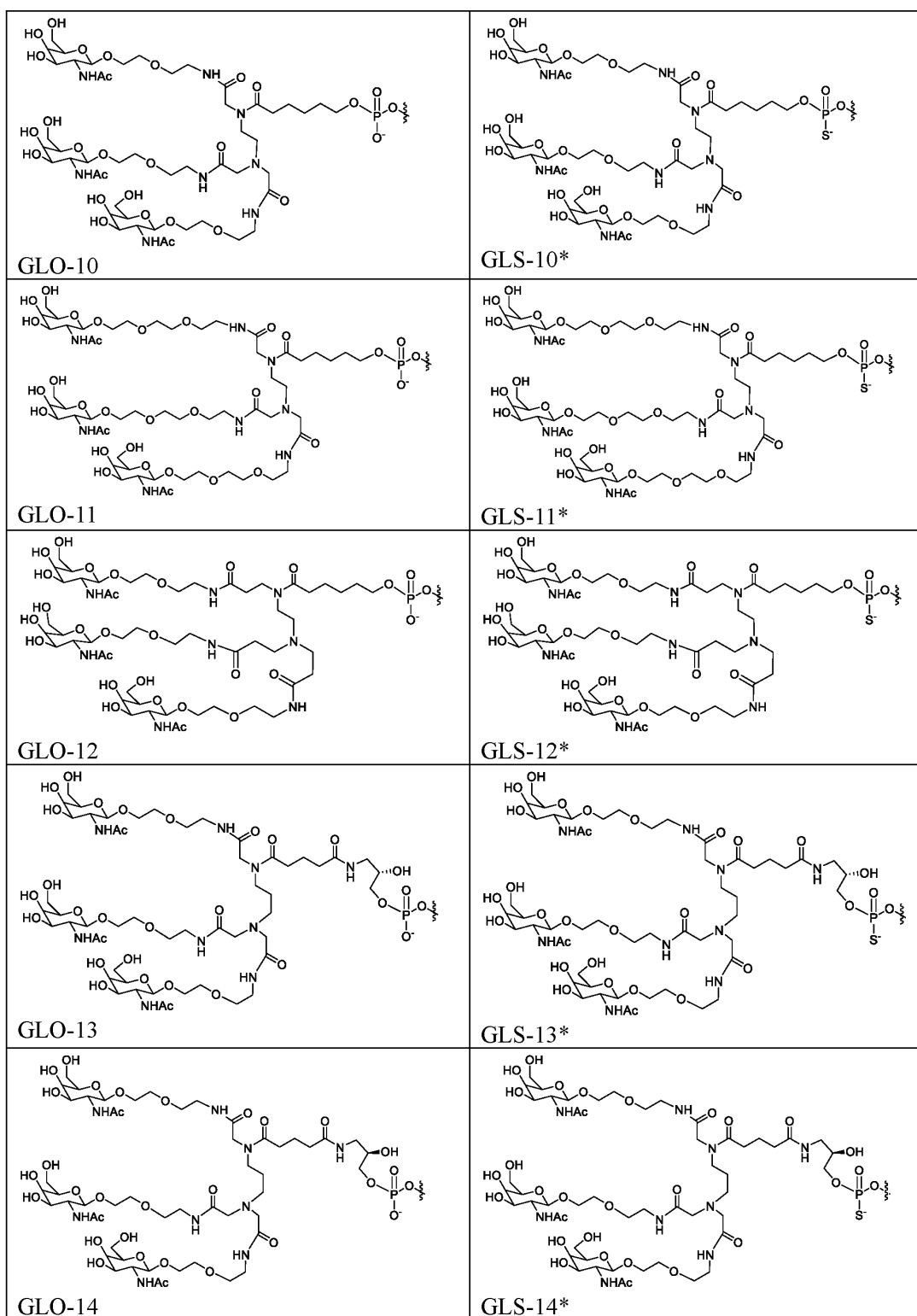
Formula 1

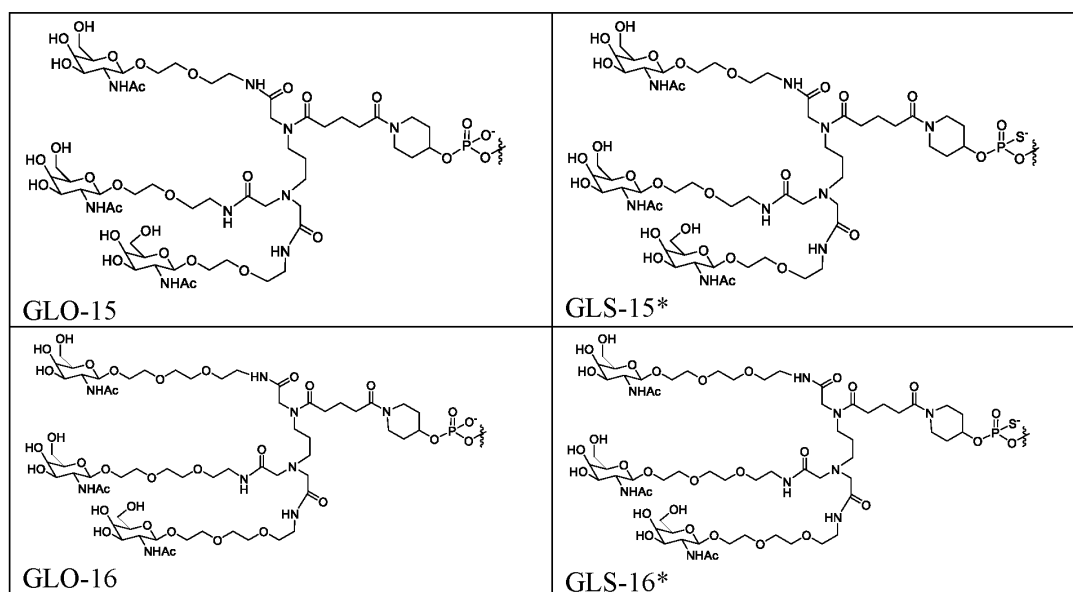
n'' are independently selected from 1 or 2.

In some embodiments, the targeting group has a structure:









In certain embodiments, the dsRNA agent includes a targeting group that is conjugated to the 5'-terminal end of the sense strand. In some embodiments, the dsRNA agent includes a targeting group that is conjugated to the 3'-terminal end of the sense strand.

- 5 In some embodiments, the antisense strand includes one inverted abasic residue at 3'-terminal end.

- In certain embodiments, the sense strand includes one or two inverted abasic residues and/or one or two imann residues at 3' or/and 5' terminal end. In certain embodiments, each end of the sense strand includes one inverted abasic residue. In certain embodiments, each end of the sense strand includes one imann residue. In certain embodiments, each end of the sense strand includes one inverted abasic residue or imann residues at the 5' terminal end of the sense strand, wherein inverted abasic residue or imann residues is linked to an adjacent nucleotide via a phosphorothioate linkage to the 5' terminal end of the nucleotide sequence of the sense strand. In certain embodiments, the sense strand further includes targeting group linked to an inverted abasic residue or imann residues at the 5' terminal end of the sense strand, wherein targeting group is linked to an adjacent inverted abasic residue or imann via a phosphorothioate linkage, and optionally targeting group is N-acetyl-galactosamine (GalNAc). In certain embodiments, each end of the sense strand includes one inverted abasic residue or imann residues at the 3' terminal end of the sense strand, wherein inverted abasic residue or imann residues is linked to an adjacent nucleotide via a phosphorothioate linkage to the 3' terminal end of the nucleotide sequence of the sense strand.

In some embodiments, the dsRNA agent has two blunt ends. In some embodiments, at least one strand includes a 3' overhang of at least 1 nucleotide. In some embodiments, at least one strand includes a 3' overhang of at least 2 nucleotides.

In certain embodiments, the dsRNA comprises a duplex selected from AV04190, AV04183, AV04189, AV04198, AV04181, AV04179, AV04216, AV04187, AV04203, AV04237, AV04211, AV04191, and wherein duplex optionally including a targeting ligand. In certain embodiments, the dsRNA comprises a duplex selected from AD01638, AD01245, AD01246, AD01247, AD01249, AD01926, AD01927, AD01928, AD01929, AD01930, AD01931, AD01932, AD01933.

In some embodiments, a double-stranded ribonucleic acid (dsRNA) agent for inhibiting expression of HTT is provided, wherein the dsRNA agent including a sense strand and an antisense strand, wherein the sense strand is complementary to the antisense strand, wherein the antisense strand comprises a region complementary to part of a HTT RNA transcript, wherein each strand is about 15 to about 30 nucleotides in length, wherein the sense strand comprises sequence may be represented by formula (I):



wherein:

each N'_F represents a 2'-fluoro-modified nucleotide; each N'_{N1} and N'_{N2} independently represents a modified or unmodified nucleotide; each N'_L independently represents a modified or unmodified nucleotide but not a 2'-fluoro-modified nucleotide, and m' and n' are each independently an integer of 0 to 7.

In some embodiments, N'_{N1} and N'_{N2} include only one 2'-Fluorine modified nucleotides.

In some embodiments, N'_{N1} independently represents a 2'-fluoro-modified nucleotide, optionally, N'_{N2} independently represents a 2'-O-methyl -modified nucleotide.

In some embodiments, N'_{N2} independently represents a 2'-fluoro-modified nucleotide, N'_{N1} independently represents a 2'-O-methyl -modified nucleotide.

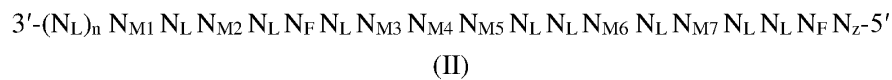
In some embodiments, each N'_L independently represents a 2'-O-methyl nucleotide.

In some embodiments, m' is 2 and n' is 4, or m' is 2 and n' is 2. In some embodiments, m' is 1 and n' is 4, or m' is 1 and n' is 2. In some embodiments, m' is 0 and n' is 4, or m' is 0 and n' is 2.

In some embodiments, the dsRNA agent includes a targeting group that is conjugated to the 5'-terminal end of the sense strand, preferably, the targeting group is any one selected from aforesaid GLO-1 through GLO-16 and GLS-1* through GLS-16*, more preferably, the targeting group is aforesaid GLS-15*. In certain embodiments, the dsRNA agent includes a targeting group that is conjugated to the 3'-terminal end of the sense strand. In certain embodiments, the antisense strand includes one inverted abasic residue at 3'-terminal end. In certain embodiments, the sense strand includes one or two inverted abasic residues and/or one or two imann residues at 3' or/and 5' terminal end. In certain embodiments, each 3' and 5' terminal end of the sense strand independently includes an inverted abasic residue. In certain embodiments, each 3' and 5' terminal end of the sense strand independently includes an imann residue. In certain embodiments, the sense strand includes two inverted abasic residues at 3' and 5' terminal end

and either residue at 3' or 5' terminal end is further conjugated to a targeting group, which preferably is aforesaid GLS-15*. In certain embodiments, the sense strand includes two imann residues at 3' and 5' terminal end and either residue at 3' or 5' terminal end is further conjugated to a targeting group, which preferably is aforesaid GLS-15*. In certain embodiments, each end of the sense strand includes one inverted abasic residue or imann residues at the 5' terminal end of the sense strand, wherein inverted abasic residue or imann residues is linked to an adjacent nucleotide via a phosphorothioate linkage to the 5' terminal end of the nucleotide sequence of the sense strand. In certain embodiments, the sense strand further includes targeting group linked to an inverted abasic residue or imann residues at the 5' terminal end of the sense strand, wherein targeting group is linked to an adjacent inverted abasic residue or imann via a phosphorothioate linkage, and optionally targeting group is N-acetyl-galactosamine (GalNAc). In certain embodiments, each end of the sense strand includes one inverted abasic residue or imann residues at the 3' terminal end of the sense strand, wherein inverted abasic residue or imann residues is linked to an adjacent nucleotide via a phosphorothioate linkage to the 3' terminal end of the nucleotide sequence of the sense strand.

In some embodiments, a double-stranded ribonucleic acid (dsRNA) agent for inhibiting expression of HTT is provided, wherein the dsRNA agent including a sense strand and an antisense strand, wherein the sense strand is complementary to the antisense strand, wherein the antisense strand comprises a region complementary to a HTT RNA transcript, wherein each strand is about 18 to about 30 nucleotides in length, wherein the antisense strand comprises sequence may be represented by formula (II):

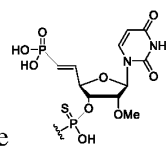


wherein:

each N_F represents a 2'-fluoro-modified nucleotide; each N_{M1} , N_{M2} , N_{M3} , N_{M4} , N_{M5} , N_{M6} , and N_{M7} independently represents a modified or unmodified nucleotide; each N_L and /or N_z independently represents a modified or unmodified nucleotide but not a 2'-fluoro-modified nucleotide, and n is an integer of 0 to 7.

In some embodiments, the modified nucleotide is a modified nucleotide defined above. In some embodiments, N_{M1} , N_{M2} , N_{M3} , N_{M4} , N_{M5} , N_{M6} , and N_{M7} have only three 2'-fluoro-modified nucleotides. In some embodiments, N_{M1} , N_{M2} , N_{M3} , N_{M4} , N_{M5} , N_{M6} , and N_{M7} independently represents a 2'-fluoro-modified nucleotide, a 2'-O-methyl nucleotide, an UNA modified nucleotide or a nucleotide comprising phosphate mimic. In some embodiments, each N_L and/or N_z independently represents a 2'-O-methyl nucleotide.

In some embodiments, N_z a nucleotide comprising phosphate mimic, preferably, wherein said nucleotide comprising vinyl phosphonate.



In some embodiments, Nz is VPu*, which has the structure

In some embodiments, N_{M2}, N_{M3} and N_{M6} each independently represents a 2'-fluoro-modified nucleotide, optionally, N_{M1}, N_{M4}, N_{M5} and N_{M7} independently represents a 2'-O-methyl
5 -modified nucleotide.

In some embodiments, N_{M2}, N_{M4} and N_{M6} each independently represents a 2'-fluoro-modified nucleotide, optionally, N_{M1}, N_{M3}, N_{M4} and N_{M7} independently represents a 2'-O-methyl
-modified nucleotide.

In some embodiments, N_{M1}, N_{M3} and N_{M7} each independently represents a 2'-fluoro-
10 modified nucleotide, optionally, N_{M2}, N_{M4}, N_{M5} and N_{M6} independently represents a 2'-O-methyl
-modified nucleotide.

In some embodiments, N_{M2}, N_{M3} and N_{M7} each independently represents a 2'-fluoro-modified nucleotide, optionally, N_{M1}, N_{M4}, N_{M5} and N_{M6} independently represents a 2'-O-methyl
-modified nucleotide.

15 In some embodiments, N_{M2}, N_{M4} and N_{M7} each independently represents a 2'-fluoro-modified nucleotide, optionally, N_{M1}, N_{M3}, N_{M5} and N_{M6} independently represents a 2'-O-methyl
-modified nucleotide.

In some embodiments, N_{M2}, N_{M5} and N_{M6} each independently represents a 2'-fluoro-modified nucleotide, optionally, N_{M1}, N_{M3}, N_{M4} and N_{M7} independently represents a 2'-O-methyl
20 -modified nucleotide.

In some embodiments, N_{M1}, N_{M3} and N_{M7} each independently represents a 2'-fluoro-modified nucleotide and N_{M6} represents an UNA modified nucleotide, optionally, N_{M2}, N_{M4} and N_{M5} independently represents a 2'-O-methyl -modified nucleotide.

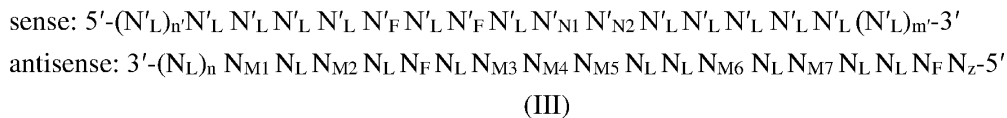
In some embodiments, N_{M2}, N_{M3} and N_{M7} each independently represents a 2'-fluoro-
25 modified nucleotide and N_{M6} represents an UNA modified nucleotide, optionally, N_{M1}, N_{M4} and N_{M5} independently represents a 2'-O-methyl -modified nucleotide.

In some embodiments, N_{M2}, N_{M4} and N_{M7} each independently represents a 2'-fluoro-modified nucleotide and N_{M6} represents an UNA modified nucleotide, optionally, N_{M1}, N_{M3} and N_{M5} independently represents a 2'-O-methyl -modified nucleotide.

30 In some embodiments, n is 1, or n is 2, or n is 3, or n is 5.

In some embodiments, the antisense strand of the dsRNA agent is at least substantially complementary to any one of a target region of SEQ ID NO: 1 and is provided in any one of Tables 1-3. In some embodiments, the antisense strand of the dsRNA agent is at least substantially complementary to any one of a target region of SEQ ID NO: 7 and is provided in any one of Tables 1A-3A.

In some embodiments, a double-stranded ribonucleic acid (dsRNA) agent for inhibiting expression of HTT is provided, wherein the dsRNA agent including a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a dsRNA duplex, wherein said sense strand is complementary to the antisense strand, wherein said antisense strand comprises a region of complementarity to a HTT RNA transcript, wherein the region of complementarity comprises at least 15 contiguous nucleotides, wherein the dsRNA duplex comprises represented by formula (III):



wherein:

each strand is about 18 to about 30 nucleotides in length;

each N_F and N'_F independently represents a 2'-fluoro-modified nucleotide; N_{M1} , N_{M2} , N_{M3} , N_{M4} , N_{M5} , N_{M6} , N_{M7} , N'_{N1} , and N'_{N2} each independently represents a modified or unmodified nucleotide; each N_z , N_L , and N'_L independently represents a modified or unmodified nucleotide but not a 2'-fluoro-modified nucleotide, and m' , n' and n are each independently an integer of 0 to 7.

In some embodiments, N_{M1} , N_{M2} , N_{M3} , N_{M4} , N_{M5} , N_{M6} , and N_{M7} have only three 2'-fluoro-modified nucleotides, N'_{N1} and N'_{N2} include only one 2'-Fluorine modified nucleotides. In some embodiments, N_z , N_{M1} , N_{M2} , N_{M3} , N_{M4} , N_{M5} , N_{M6} , and N_{M7} independently represents a 2'-fluoro-modified nucleotide, a 2'-O-methyl nucleotide, an UNA modified nucleotide or a nucleotide comprising phosphate mimic. In some embodiments, each N_L , and/or N'_L independently represents a 2'-O-methyl nucleotide.

In some embodiments, m' is 2 and n' is 4, m' is 2 and n' is 6, or m' is 2 and n' is 2. In some embodiments, m' is 1 and n' is 4, or m' is 1 and n' is 2. In some embodiments, m' is 0 and n' is 4, or m' is 0 and n' is 2. In some embodiments, n is 1, or n is 2, or n is 3, or n is 5.

In some embodiments, N'_{N1} independently represents a 2'-fluoro-modified nucleotide. , optionally, N'_{N2} independently represents a 2'-O-methyl -modified nucleotide

In some embodiments, N'_{N2} independently represents a 2'-fluoro-modified nucleotide. , optionally, N'_{N1} independently represents a 2'-O-methyl -modified nucleotide

In some embodiments, N_{M2} , N_{M3} and N_{M6} each independently represents a 2'-fluoro-modified nucleotide. optionally, N_{M1} , N_{M4} , N_{M5} and N_{M7} independently represents a 2'-O-methyl-modified nucleotide

In some embodiments, N_{M2} , N_{M4} and N_{M6} each independently represents a 2'-fluoro-modified nucleotide, optionally, N_{M1} , N_{M3} , N_{M5} and N_{M7} independently represents a 2'-O-methyl-modified nucleotide.

In some embodiments, N_{M1} , N_{M3} and N_{M7} each independently represents a 2'-fluoro-modified nucleotide, optionally, N_{M2} , N_{M4} , N_{M5} and N_{M6} independently represents a 2'-O-methyl-modified nucleotide.

In some embodiments, N_{M2} , N_{M3} and N_{M7} each independently represents a 2'-fluoro-modified nucleotide, optionally, N_{M1} , N_{M4} , N_{M5} and N_{M6} independently represents a 2'-O-methyl-modified nucleotide.

In some embodiments, N_{M2} , N_{M4} and N_{M7} each independently represents a 2'-fluoro-modified nucleotide, optionally, N_{M1} , N_{M3} , N_{M5} and N_{M6} independently represents a 2'-O-methyl-modified nucleotide.

In some embodiments, N_{M2} , N_{M5} and N_{M6} each independently represents a 2'-fluoro-modified nucleotide, optionally, N_{M1} , N_{M3} , N_{M4} and N_{M7} independently represents a 2'-O-methyl-modified nucleotide.

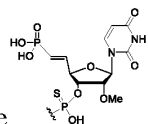
In some embodiments, N_{M1} , N_{M3} and N_{M7} each independently represents a 2'-fluoro-modified nucleotide and N_{M6} represents an UNA modified nucleotide, optionally, N_{M2} , N_{M4} , and N_{M5} independently represents a 2'-O-methyl-modified nucleotide.

In some embodiments, N_{M2} , N_{M3} and N_{M7} each independently represents a 2'-fluoro-modified nucleotide and N_{M6} represents an UNA modified nucleotide, optionally, N_{M1} , N_{M4} , and N_{M5} independently represents a 2'-O-methyl-modified nucleotide.

In some embodiments, N_{M2} , N_{M4} and N_{M7} each independently represents a 2'-fluoro-modified nucleotide and N_{M6} represents an UNA modified nucleotide, optionally, N_{M1} , N_{M3} , and N_{M5} independently represents a 2'-O-methyl-modified nucleotide.

In some embodiments, Nz a nucleotide comprising phosphate mimic, preferably, wherein said nucleotide comprising vinyl phosphonate.

In some embodiments, Nz is VPu*, which has the structure



In some embodiments, the dsRNA agent includes a targeting group that is conjugated to the 5'-terminal end of the sense strand, preferably, the targeting group is any one selected from aforesaid GLO-1 through GLO-16 and GLS-1* through GLS-16*, more preferably, the targeting group is aforesaid GLS-15*.

5 In certain embodiments, the dsRNA agent includes a targeting group that is conjugated to the 5'-terminal end of the sense strand. In certain embodiments, the antisense strand includes one inverted abasic residue at 3'-terminal end. In certain embodiments, the sense strand includes one or two inverted abasic residues and/or one or two imann residues at 3' or/and 5' terminal end. In certain embodiments, each 3' and 5' terminal end of the sense strand independently includes an inverted abasic residue. In certain embodiments, each 3' and 5'

10 terminal end of the sense strand independently includes an imann residue. In certain embodiments, the sense strand includes two inverted abasic residues at 3' and 5' terminal end and either residue at 3' or 5' terminal end is further conjugated to a targeting group, which preferably is aforesaid GLS-15*. In certain embodiments, the sense strand includes two imann residues at 3' and 5' terminal end and either residue at 3' or 5' terminal end is further conjugated

15 to a targeting group, which preferably is aforesaid GLS-15*. In certain embodiments, the dsRNA agent has two blunt ends. In certain embodiments, at least one strand includes a 3' overhang of at least 1 nucleotide. In certain embodiments, at least one strand includes a 3' overhang of at least 2 nucleotides. In certain embodiments, the antisense strand of the dsRNA agent is at least substantially complementary to any one of a target region of SEQ ID NO: 1 and is provided in

20 any one of Tables 1-3. In certain embodiments, the antisense strand of the dsRNA agent is at least substantially complementary to any one of a target region of SEQ ID NO: 7 and is provided in any one of Tables 1A-3A.

In some embodiments, any one of the sense strands in Table 1 may further be modified in a pattern shown in aforesaid Formula (I) or (III).

25 In some embodiments, any one of the antisense strands in Table 1 may further be modified in a pattern shown in aforesaid Formula (II) or (III).

In some embodiments, any one of the duplexes in Table 1 may further be modified in a pattern shown in aforesaid Formula (III).

According to an aspect of the invention, a composition is provided that includes any

30 embodiment of the aforementioned dsRNA agent aspect of the invention. In certain embodiments, the composition also includes a pharmaceutically acceptable carrier. In some embodiments, the composition also includes one or more additional therapeutic agents. In certain embodiments, the composition is packaged in a kit, container, pack, dispenser, pre-filled syringe, or vial. In some embodiments, the composition is formulated for subcutaneous administration, formulated for intrathecally administration, formulated for intracerebroventricular

35 administration, formulated for intrastriatal (IS) administration, or is formulated for intravenous (IV) administration.

According to another aspect of the invention a cell is provided that includes any embodiment of an aforementioned dsRNA agent aspect of the invention. In some embodiments, the cell is a mammalian cell, optionally a human cell, preferentially in CNS (e.g., brain) cells.

According to another aspect of the invention, a method of inhibiting the expression of a
5 HTT gene in a cell, is provided, the method including: (i) preparing a cell including an effective amount of any embodiment of the aforementioned dsRNA agent aspect of the invention or any embodiment of an aforementioned composition of the invention. In certain embodiments, the method also includes: (ii) maintaining the prepared cell for a time sufficient to obtain degradation of the mRNA transcript of a HTT gene, thereby inhibiting expression of the HTT gene in the
10 cell. In some embodiments, the cell is in a subject and the dsRNA agent is administered to the subject by subcutaneously (SQ). In some embodiments, the cell is in a subject and the dsRNA agent is administered to the subject by IV. In some embodiments, the cell is in a subject and the dsRNA agent is administered to the subject by intrathecally. In some embodiments, the cell is in a subject and the dsRNA agent is administered to the subject by intracerebroventricular (ICV)
15 injection. In some embodiments, the cell is in a subject and the dsRNA agent is administered to the subject by intrastriatal (IS) injection. In certain embodiments, the method also includes assessing inhibition of the HTT gene, following the administration of the dsRNA agent to the subject, wherein a means for the assessing comprises: (i) determining one or more physiological characteristics of a HTT-associated disease or condition in the subject and (ii) comparing the
20 determined physiological characteristic(s) to a baseline pre-treatment physiological characteristic of the HTT-associated disease or condition and/or to a control physiological characteristic of the HTT-associated disease or condition, wherein the comparison indicates one or more of a presence or absence of inhibition of expression of the HTT gene in the subject. In some embodiments, the physiological characteristic is one or more of: the HTT mRNA level and
25 the HTT protein level, the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease. s.

According to another aspect of the invention, a method of inhibiting expression of a HTT gene in a subject, is provided, the method including administering to the subject an effective amount of an embodiment of the aforementioned dsRNA agent aspect of the invention or an
30 embodiment of an aforementioned composition of the invention. In some embodiments, the dsRNA agent is administered to the subject by subcutaneously. In certain embodiments, the dsRNA agent is administered to the subject by IV administration. In some embodiments, the dsRNA agent is administered to the subject by intrathecally administration. In some embodiments, the dsRNA agent is administered to the subject by intracerebroventricular (ICV)
35 injection. In some embodiments, the dsRNA agent is administered to the subject by intrastriatal (IS) injection. In some embodiments, the method also includes: assessing inhibition of the HTT gene, following the administration of the dsRNA agent, wherein a means for the assessing comprises: (i) determining one or more physiological characteristics of a HTT-associated disease or condition in the subject and (ii) comparing the determined physiological characteristic(s) to a

baseline pre-treatment physiological characteristic of the HTT-associated disease or condition and/or to a control physiological characteristic of the HTT-associated disease or condition, wherein the comparison indicates one or more of a presence or absence of inhibition of expression of the HTT gene in the subject. In some embodiments, expression of the HTT gene can be assessed based on the level or change in level of any variable associated with HTT gene expression, such as HTT mRNA level, HTT protein level. A reduction in the expression of HTT may also be assessed indirectly by measuring a decrease in biological activity of HTT, the HTT mRNA level and the HTT protein level, e.g., the level of C9orf72 expanded, or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease. HD's one or more of a physical symptom are abnormal body movements called chorea and lack of coordination.

According to another aspect of the invention, a method of treating a disease or condition associated with the presence of HTT protein is provided, the method including: administering to a subject an effective amount of an embodiment of any aforementioned dsRNA agent aspect of the invention or an embodiment of any aforementioned composition of the invention, to inhibit HTT gene expression. In one embodiment, the disorder is a HTT associated disorder. In one embodiment, the disorder is associated with an abnormality of HTT gene encoded protein. In certain embodiments, A "HTT-associated disease" is HD (Huntington's disease).

In some embodiments, the method also includes: administering an additional therapeutic regimen to the subject. In some embodiments, the additional therapeutic regimen includes a treatment for the HTT-associated disease or condition. In certain embodiments, the additional therapeutic regimen comprises: administering to the subject one or more HTT antisense polynucleotides of the invention, administering to the subject a non-HTT dsRNA therapeutic agent, and a behavioral modification in the subject. In some embodiments, the additional therapeutic agent is selected from the group consisting of an oligonucleotide, a small molecule, a monoclonal antibody, a polyclonal antibody and a peptide. other agents or other therapeutic regimens suitable for treating a HTT-associated disease may include a monoamine inhibitor, e.g., tetrabenazine (Xenazine), deutetrabenazine (Austedo), and reserpine, an anticonvulsant, e.g., valproic acid (Depakote, Depakene, Depacon), and clonazepam (Klonopin), an antipsychotic agent, e.g., risperidone (Risperdal), and haloperidol (Haldol), and an antidepressant, e.g., paroxetine (Paxil).

In some embodiments, the dsRNA agent is administered to the subject by subcutaneously. In certain embodiments, the dsRNA agent is administered to the subject by IV administration. In some embodiments, the dsRNA agent is administered to the subject by intrathecally. In certain embodiments, the dsRNA agent is administered to the subject by intracerebroventricular (ICV) injection administration. In certain embodiments, the dsRNA agent is administered to the subject by intrastriatal (IS) injection administration. In some embodiments, the method also includes determining an efficacy of the administered double-stranded ribonucleic acid (dsRNA) agent in the subject.

In some embodiments, a means of determining an efficacy of the treatment in the subject comprises: (i) determining one or more physiological characteristics of the HTT-associated disease or condition in the subject and (ii) comparing the determined physiological characteristic(s) to a baseline pre-treatment physiological characteristic of the HTT-associated disease or condition wherein the comparison indicates one or more of a presence, absence, and level of efficacy of the administration of the double-stranded ribonucleic acid (dsRNA) agent to the subject.

In some embodiments, expression of the HTT gene can be assessed based on the level or change in level of any variable associated with HTT gene expression, such as HTT mRNA level, HTT protein level in the subject, the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease in the subject.

According to another aspect of the invention, a method of decreasing a level of HTT protein in a subject compared to a baseline pre-treatment level of HTT protein in the subject, is provided, the method including administering to the subject an effective amount of an embodiment of any aforementioned dsRNA agent of the invention or an embodiment of any aforementioned composition of the invention, to decrease the level of HTT gene expression. In some embodiments, the dsRNA agent is administered to the subject subcutaneously or is administered to the subject by IV administration. In some embodiments, the dsRNA agent is administered to the subject by intrathecally. In some embodiments, the dsRNA agent is administered to the subject by intracerebroventricular (ICV) injection. In some embodiments, the dsRNA agent is administered to the subject by intrastriatal (IS) injection. In yet another embodiment, the dsRNA agent is administered to the subject intracisternally. A non-limiting exemplary intracisternal administration comprises an injection into the cisterna magna (cerebellomedullary cistern) by suboccipital puncture.

According to another aspect of the invention, a method of altering a physiological characteristic of a HTT-associated disease or condition in a subject compared to a baseline pre-treatment physiological characteristic of the HTT-associated disease or condition in the subject is provided, the method including administering to the subject an effective amount of an embodiment of any aforementioned dsRNA agent of the invention or an embodiment of any aforementioned composition of the invention, to alter the physiological characteristic of the HTT-associated disease or condition in the subject. In some embodiments, the dsRNA agent is administered to the subject subcutaneously or is administered to the subject by IV administration. In some embodiments, the dsRNA agent is administered to the subject by intrathecally. In some embodiments, the dsRNA agent is administered to the subject by intracerebroventricular (ICV) injection administration. In some embodiments, the dsRNA agent is administered to the subject by intrastriatal (IS) injection. In yet another embodiment, the dsRNA agent is administered to the subject intracisternally. A non-limiting exemplary intracisternal administration comprises an injection into the cisterna magna (cerebellomedullary cistern) by suboccipital puncture. By intrathecal administration of the double-stranded RNAi agent, the method can reduce the

expression of an HTT target gene in a brain (e.g., striatum) or spine tissue, for instance, cortex, cerebellum, cervical spine, lumbar spine, and thoracic spine., is formulated for intrathecal administration, is formulated for intracranial administration, is formulated for intraventricular administration, is formulated for intracerebral administration. In some
5 embodiments, the cell is a neuron (e.g., primary sensory neuron). In certain embodiments, the physiological characteristic and symptoms are one or more of: HTT mRNA level, HTT protein level in the subject, the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease. HD's one or more of a physical symptom are abnormal body movements called chorea and lack of coordination.

10 According to another aspect of the invention, the aforementioned dsRNA agent for use in a method of treating a disease or condition associated with the presence of HTT protein is provided. In some embodiments, the disease or condition is HD (Huntington's disease).

According to another aspect of the invention, an antisense polynucleotide agent for inhibiting expression of HTT protein is provided, the agent including from 10 to 30 contiguous
15 nucleotides, wherein at least one of the contiguous nucleotides is a modified nucleotide, and wherein the nucleotide sequence of the agent is about 80% complementary over its entire length to the equivalent region of the nucleotide sequence of SEQ ID NO: 1 and/or SEQ ID NO: 7. In some embodiments, the equivalent region is any one of the target regions of SEQ ID NO: 1 and/or SEQ ID NO: 7, and the complementary sequence is one provided in one of Tables 1-3,

20 Tables 1A-3A. In certain embodiments, the antisense polynucleotide agent includes one of the antisense sequences provided in one of Tables 1-3, Tables 1A-3A.

According to another aspect of the invention, a composition including an embodiment of any aforementioned antisense polynucleotide agents is provided. In some embodiments, the composition also includes a pharmaceutically acceptable carrier. In some embodiments, the
25 composition also includes one or more additional therapeutic agents for treatment of a HTT-associated disease or condition. In certain embodiments, the composition is packaged in a kit, container, pack, dispenser, pre-filled syringe, or vial. In certain embodiments, the composition is formulated for subcutaneous, intracerebroventricular, intrastriatal (IS), intrathecally or IV administration.

30 According to another aspect of the invention a cell that includes an embodiment of any of the aforementioned antisense polynucleotide agents is provided. In some embodiments, the cell is a mammalian cell, optionally a human cell.

According to another aspect of the invention, a method of inhibiting the expression of a HTT gene in a cell is provided, the method including: (i) preparing a cell including an effective
35 amount of an embodiment of any aforementioned antisense polynucleotide agents. In some embodiments, the method also includes (ii) maintaining the cell prepared in (i) for a time sufficient to obtain degradation of the mRNA transcript of a HTT gene, thereby inhibiting expression of the HTT gene in the cell.

According to another aspect of the invention, a method of inhibiting expression of a HTT gene in a subject is provided, the method including administering to the subject an effective amount of an embodiment of any of the aforementioned antisense polynucleotide agent.

5 According to another aspect of the invention, a method of treating a disease or condition associated with the presence of HTT protein, the method including administering to a subject an effective amount of an embodiment of any of the aforementioned antisense polynucleotide agents or an embodiment of any aforementioned composition of the invention, to inhibit HTT gene expression. In certain embodiments, the disease or condition is HD (Huntington's disease).

10 According to another aspect of the invention, a method of decreasing a level of HTT protein in a subject compared to a baseline pre-treatment level of HTT protein in the subject is provided, the method including administering to the subject an effective amount of an embodiment of any of the aforementioned antisense polynucleotide agents or an embodiment of any aforementioned composition of the invention, to decrease the level of HTT gene expression. In certain embodiments, the antisense polynucleotide agent is administered to the subject
15 subcutaneously or by IV administration. In some embodiments, the dsRNA agent is administered to the subject by intracerebroventricular administration. In some embodiments, the dsRNA agent is administered to the subject by intrastriatal (IS) administration. In some embodiments, the antisense polynucleotide agent is administered to the subject by intrathecally. In yet another embodiment, the antisense polynucleotide agent is administered to the subject intracisternally.
20 A non-limiting exemplary intracisternal administration comprises an injection into the cisterna magna (cerebellomedullary cistern) by suboccipital puncture.

According to another aspect of the invention, an antisense polynucleotide agent for inhibiting expression of HTT gene, is provided, the agent including from 10 to 30 contiguous nucleotides, wherein at least one of the contiguous nucleotides is a modified nucleotide, and
25 wherein the nucleotide sequence of the agent is about 80% or about 85% complementary over its entire length to the equivalent region of the nucleotide sequence of SEQ ID NO: 1 and/or SEQ ID NO: 7 .

According to another aspect of the invention, a method of altering a physiological characteristic of a HTT-associated disease or condition in a subject compared to a baseline pre-treatment physiological characteristic of the HTT-associated disease or condition in the subject
30 is provided, the method including administering to the subject an effective amount of an embodiment of any of the aforementioned antisense polynucleotide agents or an embodiment of any aforementioned composition of the invention, to alter the physiological characteristic of the HTT disease or condition in the subject. In some embodiments, the antisense polynucleotide agent is administered to the subject, intracerebroventricular (ICV) , intrastriatal (IS), intrathecally or IV administration. In some embodiments, the antisense polynucleotide agent is administered to the subject by intrathecally. In yet another embodiment, the antisense polynucleotide agent is administered to the subject intracisternally. A non-limiting exemplary intracisternal administration comprises an injection into the cisterna magna (cerebellomedullary
35

cistern) by suboccipital puncture. In certain embodiments, the physiological characteristic and symptoms are one or more of: HTT mRNA level, HTT protein level in the subject, or variable progression of motor, cognitive, and behavioral impairment, or symptoms and hallmarks include abnormal body movements called chorea and lack of coordination.

5

Brief Description of the Sequences

SEQ ID NO: 1 and SEQ ID NO: 2 (reverse complement) are full -length mutant Homo sapiens HTT mRNA [NCBI Reference Sequence: NM_001388492.1].

- 10 SEQ ID NO: 3 and SEQ ID NO: 4 (reverse complement) are exon 1 RNA sequence of the HTT gene (a particular portion from nts. 1-408 of full-length mutant HTT transcrip NM_001388492.1).

- 15 SEQ ID NO: 5 and SEQ ID NO: 6 (reverse complement) are transcript intron 1 (a particular portion from retained in the truncated 5415-12746 of NCBI Reference Sequence: NG_009378.1 (Homo sapiens huntingtin (HTT), RefSeqGene (LRG_763) on chromosome 4)).

- 20 SEQ ID NO: 7 and SEQ ID NO: 8 (reverse complement) are BWS-2a (HTT-1A) transcript comprise exon1 and a particular portion of intron 1(combination of exon1 and retained in the truncated 1-2710 of SEQ ID NO:5 (intron 1)).

SEQ ID NOs: 9-585, 3397-3448 are shown in Table 1 are sense strand sequences. and SEQ ID NOs: 586-1162, 3449-3500 are shown in Table 1 and are antisense strand sequences.

- 25 SEQ ID NOs: 1163-1625, 3391-3393, 3501-3541 are shown in Table 1A are sense strand, and sequences SEQ ID NOs: 1626-2088, 3394-3396, 3542-3582 are shown in Table 1A are antisense strand sequences.

- 30 SEQ ID NOs: 2089-2674 are shown in Table 2 with chemical modifications.

SEQ ID NOs: 2675-3152 are shown in Table 2A with chemical modifications.

- 35 SEQ ID NOs: 3153-3284, 3583-3686 are shown in Table 3. A delivery molecule is indicated as "GLX-__" at the 3' end or 5' end of each sense strand.

SEQ ID NOs: 3285-3356, 3357-3390, 3687-3768 are shown in Table 3A. A delivery molecule is indicated as "GLX-__" at the 3' end or 5' end of each sense strand.

SEQ ID NO: 3397 and SEQ ID NO: 3398(reverse complement) are *Macaca mulatta* (Rhesus monkey) HTT mRNA [NCBI Reference Sequence: XM_028848247.1].

SEQ ID NO:3399 and SEQ ID NO:4000 (reverse complement) are *Mus musculus* HTT mRNA
5 [Chromosome 5, NC_000071.7 (NM_010414.3)].

Detailed Description

The invention in part, includes RNAi agents, for example, though not limited to double stranded (ds) RNAi agents, which are capable of inhibiting HTT gene expression. The
10 invention, in part also includes compositions comprising HTT RNAi agents and methods of use of the compositions. HTT RNAi agents disclosed herein may be attached to delivery compounds for delivery to cells, including to hepatocytes/CNS (e.g., brain). Pharmaceutical compositions of the invention may include at least one dsRNA HTT agent and a delivery compound. In some
15 embodiments of compositions and methods of the invention, the delivery compound is a GalNAc-containing delivery, or compound the delivery compound is a phosphohate miminc-containing delivery compound. HTT RNAi agents delivered to cells are capable of inhibiting HTT gene expression, thereby reducing activity in the cell of the HTT protein product of the gene. dsRNAi agents of the invention can be used to treat HTT-associated diseases and conditions.

20 In some embodiments of the invention reducing HTT expression in a cell or subject treats a disease or condition associated with HTT expression in the cell or subject, respectively. Non-limiting examples of diseases and conditions that may be treated by reducing HTT activity are: alleviation or amelioration of one or more symptoms associated with unwanted or excessive HTT expression, or the level of C9orf72 expanded or levels of the neurotransmitters gamma-
25 aminobutyric acid (GABA) and substance P. "Treatment" can also mean prolonging survival as compared to expected survival in the absence of treatment.

As used herein, "G," "C," "A" and "U" each generally stand for a nucleotide that contains guanine, cytosine, adenine, and uracil as a base, respectively. However, it will be understood that the term "ribonucleotide" or "nucleotide" can also refer to a modified nucleotide, as further
30 detailed below, or a surrogate replacement moiety. The skilled person understands that guanine, cytosine, adenine, and uracil may be replaced by other moieties without substantially altering the base pairing properties of an oligonucleotide comprising a nucleotide bearing such replacement moiety. For example, without limitation, a nucleotide comprising inosine as its base may base pair with nucleotides containing adenine, cytosine, or uracil. Hence, nucleotides
35 containing uracil, guanine, or adenine may be replaced in the nucleotide sequences of the invention by a nucleotide containing, for example, inosine. Sequences comprising such replacement moieties are embodiments of the invention.

As used herein, "HTT" gene, also known as "huntingtin" ; "Huntington Disease Protein", "IT15", "HD", "HD Protein" or "LOMARS", refers to the gene encoding for a protein called

huntingtin protein (HTT) from any vertebrate or mammalian source, including, but not limited to, human, bovine, chicken, rodent, mouse, rat, porcine, ovine, primate, monkey, and guinea pig, unless specified otherwise. That are wild-type transcript, a full-length mutant transcript, required for normal development and the disease gene linked to Huntington's disease, a neurodegenerative disorder characterized by loss of striatal neurons caused by an expanded, unstable trinucleotide (CAG) repeat in the huntingtin gene, which translates as a polyglutamine repeat in the protein product. The term also refers to fragments (for example, a particular portion of a HTT gene, exon 1 RNA sequence of the HTT gene is from nts. 1-408, e.g.,) and variants of native HTT that maintain at least one in vivo or in vitro activity of a native HTT,

Alternatively, fragments, mutant, non-mutant genes or a combination of native HTT linked to Huntington's disease (e.g. Rodriguez-Lebron et al., 2005, Mol Ther. Vol 12 No. 4: 618-633; Franich et al., 2008, Mol Ther, Vol. 16 No. 5; 947-956; Drouet et al., 2009, Annals of Neurology; Vol. 65 No. 3; 276-285 and McBride et al. Mol Ther. 2011 December; 19(12):2152-62; US20080015158, WO2008134646). In the latter case, knock the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease down of the wild type of Huntingtin protein was shown to be beneficial in treating Huntington's disease. The amino acid and complete coding sequences of the reference sequence of the human HTT gene may be found in, for example, GenBank Ref Seq Accession No. NM_001388492.1 (Homo sapiens huntingtin (HTT), transcript variant, SEQ ID NO: 1, full-length mutant transcript include exon1, mRNA, reverse complement, SEQ ID NO: 2); exon 1 RNA sequence of the HTT gene (SEQ ID NO.3, a particular portion from nits. 1-408 of full-length mutant HTT transcript NM_001388492.1, reverse complement, SEQ ID NO: 4); transcript intron 1 (SEQ ID NO:5, a particular portion from retained in the truncated 5415-12746 of NCBI Reference Sequence: NG_009378.1 (Homo sapiens huntingtin (HTT), RefSeqGene (LRG_763) on chromosome 4, reverse complement, SEQ ID NO: 6); BWS-2a transcript comprise exon1 and a particular portion of intron 1 (SEQ ID NO:7, combination of exon1(SEQ ID NO.3) and retained in the truncated 1-2710 of SEQ ID NO:5 (intron 1), reverse complement, SEQ ID NO: 8). No. NM_010414.3 Huntingtin [Mus musculus (house mouse)] Chromosome 5, NC_000071.7 (SEQ ID NO:3367), No. XM_028848247.1 HTT huntingtin [Macaca mulatta (Rhesus monkey)] (SEQ ID NO:3368). The term HTT, as used herein, also refers to variations of the HTT gene including variants provided are readily available using publicly available databases, e.g., GenBank, UniProt, Ensembl and OMIM. It is understood by a skilled artisan that a substitution of a T with a U in any target sequences or mRNA transcripts (e.g., SEQ ID NO:1 to SEQ ID NO: 8) does not count as a difference. As used herein, HTT mRNA sequences U is optionally and independently replaced with T and vice versa

Hence, in one embodiment the double stranded RNA according to the invention is capable of inducing RNA interference to sequence specifically reduce expression of a RNA transcript comprising BWS-2a (SEQ ID NO:7). In a further embodiment, said induction of RNA interference to reduce expression of an RNA transcript comprising SEQ ID NO.7 means

that it is to reduce human Huntingtin gene expression. One can easily determine whether this is the case by using standard luciferase reporter assays and appropriate controls such as described in the examples and as known in the art (Zhuang et al. 2006 *Methods Mol Biol.* 2006; 342:181-7). For example, a luciferase reporter comprising SEQ ID No. 7 can be used to show that the double stranded RNA according to the invention is capable of sequence specific knock down. Furthermore, as shown in the example section, Huntingtin expression can be determined with specific antibodies to determine the amount of expression in a western blot analysis, as can northern blot analysis detecting the amount of RNA transcript. Hence, the double stranded RNA according to the invention is for use in inducing RNA interference. The double stranded RNA according to the invention is for use in reducing expression of transcripts comprising SEQ ID NO.1166, such as for example SEQ ID NO.7 or the like with more than 25 varying number of CAG repeats.

The iRNAs of the invention have been designed to target a HTT gene, including portions of the gene that are conserved in the HTT orthologs of other mammalian species. The iRNAs of the invention have also been designed to target a particular portion of an HTT gene, for example, exon 1 and/or intron 1 e.g., thereby targeting the full-length wild-type transcript, the full-length mutant transcript, the fragments of transcript, as well as the truncated mutant transcript. Without intending to be limited by theory, it is believed that a combination or sub-combination of the foregoing properties and the specific target sites, e.g., exon 1, or the specific modifications in these iRNAs confer to the iRNAs of the invention improved efficacy, stability, potency, durability, and safety.

“Huntington's disease,” also known as HD, Huntington's Chorea, Chorea Major, Chronic Progressive Chorea, and Hereditary Chorea, is an autosomal dominant genetic disorder characterized by choreiform movements and progressive intellectual deterioration, usually beginning in middle age (35 to 50 yr). The disease affects both sexes equally. The caudate nucleus atrophies, the small-cell population degenerates, and levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease. This degeneration results in characteristic “boxcar ventricles” seen on CT scans. Symptoms and signs of HD develop insidiously. HD's most obvious symptoms are abnormal body movements called chorea and lack of coordination, but it also affects a number of mental abilities and some aspects of personality. These physical symptoms commonly become noticeable in a person's forties but can occur at any age. If the age of onset is below 20 years, then it is known as Juvenile HD.

Dementia or psychiatric disturbances, ranging from apathy and irritability to full-blown bipolar or schizophreniform disorder, may precede the movement disorder or develop during its course. Anhedonia or asocial behavior may be the first behavioral manifestation. Motor manifestations include flicking movements of the extremities, a lilting gait, motor impersistence (inability to sustain a motor act, such as tongue protrusion), facial grimacing, ataxia, and dystonia. HD is caused by a trinucleotide repeat expansion in the Huntingtin (HTT) gene and is one of

several polyglutamine expansion (or PolyQ expansion) diseases. This produces an extended form of the mutant Huntingtin protein (mHtt), which causes cell death in selective areas of the brain.

5 The following describes how to make and use compositions comprising HTT single-stranded (ssRNA) and dsRNA agents to inhibit HTT gene expression, as well as compositions and methods for treating diseases and conditions caused by or modulated by HTT gene expression. The term “RNAi” is also known in the art and may be referred to as “siRNA”.

As used herein, the term “RNAi” refers to an agent that comprises RNA and mediates targeted cleavage of an RNA transcript via an RNA-induced silencing complex (RISC) pathway.
10 As is known in the art, an RNAi a target region refers to a contiguous portion of the nucleotide sequence of an mRNA molecule formed during the transcription of a gene, including messenger RNA (mRNA) that is a product of RNA processing of a primary transcription product. The target portion of the sequence will be at least long enough to serve as a substrate for RNAi-directed cleavage at or near that portion. A target sequence may be from 8-30 nucleotides long
15 (inclusive), from 10 - 30 nucleotides long (inclusive), from 12 - 25 nucleotides long (inclusive), from 15 - 23 nucleotides long (inclusive), from 16 -23 nucleotides long (inclusive), or from 18 – 23 nucleotides long (inclusive), including all shorter lengths within each stated range. In some embodiments of the invention, a target sequence is 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or 26 nucleotides long. In certain embodiment a target sequence is between
20 9 and 26 nucleotides long (inclusive), including all sub-ranges and integers there between. For example, though not intended to be limiting, in certain embodiments of the invention a target sequence is 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides long, with the sequence fully or at least substantially complementary to at least part of an RNA transcript of a HTT gene. Some aspects of the invention include pharmaceutical
25 compositions comprising one or more HTT dsRNA agents and a pharmaceutically acceptable carrier. In certain embodiments of the invention, a HTT RNAi as described herein inhibits expression of HTT protein.

As used herein, a “dsRNA agent” means a composition that contains an RNA or RNA-like (e.g., chemically modified RNA) oligonucleotide molecule that is capable of degrading or
30 inhibiting translation of messenger RNA (mRNA) transcripts of a target mRNA in a sequence specific manner. Although not wishing to be limited to a particular theory, dsRNA agents of the invention may operate through the RNA interference mechanism (i.e., inducing RNA interference through interaction with the RNA interference pathway machinery (RNA-induced silencing complex or RISC) of mammalian cells), or by any alternative mechanism(s) or
35 pathway(s). Methods for silencing genes in plant, invertebrate, and vertebrate cells are well known in the art [see, for example, (Sharp et al., Genes Dev. 2001, 15:485; Bernstein, et al., (2001) Nature 409:363; Nykanen, et al., (2001) Cell 107:309; and Elbashir, et al., (2001) Genes Dev. 15:188)], the disclosure of each of which is incorporated herein by reference in its entirety.].

Art-known gene silencing procedures can be used in conjunction with the disclosure provided herein to inhibit expression of HTT.

DsRNA agents disclosed herein are comprised of a sense strand and an antisense strand, and include, but are not limited to: short interfering RNAs (siRNAs), RNAi agents, micro RNAs (miRNAs), short hairpin RNAs (shRNA), and dicer substrates. The antisense strand of the dsRNA agents described herein is at least partially complementary to the mRNA being targeted. It is understood in the art that different lengths of dsRNA duplex structure can be used to inhibit target gene expression. For example, dsRNAs having a duplex structure of 19, 20, 21, 22, and 23 base pairs are known to be effective to induce RNA interference (Elbashir et al., EMBO 2001, 20:6877-6888). It is also known in the art that shorter or longer RNA duplex structures are also effective to induce RNA interference. In some embodiments, the sense strand and the antisense strand may be the same length or different lengths. In some embodiments, each strand is no more than 40 nucleotides in length. In some embodiments, each strand is no more than 30 nucleotides in length. In some embodiments, each strand is no more than 25 nucleotides in length. In some embodiments, each strand is no more than 23 nucleotides in length. In some embodiments, each strand is no more than 21 nucleotides in length. In some embodiments, the sense and antisense strands of the RNAi agents can each be 15 to 49 nucleotides in length. In some embodiments, the antisense strand is independently 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides in length. In some embodiments, the length of the sense strand is independently 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, or 49 nucleotides. In some embodiments, the sense strand and the antisense strand are both 21 nucleotides in length. In some embodiments, the sense strand is complementary or substantially complementary to the antisense strand, and the region of complementarity is between 15 and 23 nucleotides in length. In some embodiments, the region of complementarity is 19-21 nucleotides in length. In some embodiments, the region of complementarity is 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides in length. HTT dsRNAs in certain embodiments of the invention can include at least one strand of a length of minimally 21 nt or may have shorter duplexes based on one of the sequences set forth in any one of Tables 1-3, 1A-3A, but minus 1, 2, 3, or 4 nucleotides on one or both ends may also be effective as compared to the dsRNAs set forth in Tables 1-3, 1A-3A, respectively. In some embodiments of the invention, HTT dsRNA agents may have a partial sequence of at least 15, 16, 17, 18, 19, 20, or more contiguous nucleotides from one or more sequences of Tables 1-3, 1A-3A, and differ in their ability to inhibit the expression of a HTT gene by not more than 5%, 10%, 15%, 20%, 25%, or 30% from the level of inhibition resulting from a dsRNA comprising the full sequence. A sense sequence, an antisense sequence and a duplex disclosed in Tables 1-3 may be referred to herein as a "parent" sequence, meaning that the sequences disclosed in Tables 1-3, 1A-3A, may be modified, shorten, lengthened, include substitutions, etc. as set forth herein, with the resulting sequences retaining all or at least a portion of the efficacy of their parent sequences in methods and compositions of the invention. Sense and antisense

strands included in a dsRNA of the invention are independently selected. As used herein the term “independently selected” means each of two or more like elements can be selected independent of the selection of the other elements. For example, though not intended to be limiting, in preparing a dsRNA of the invention, one may select the “elements” of the two strands to include in the duplex. One selected element, the sense sequence may be SEQ ID NO: 2747 (shown in Table 2A) and the other selected element, the antisense sequence, may be SEQ ID NO:2986, or may be SEQ ID NO: 2986 that is modified, shortened, lengthened, and/or includes 1, 2, or 3 substitutions as compared to its parent sequence SEQ ID NO: 2986. It will be understood that a duplex of the invention need not include both sense and antisense sequences shown as paired in duplexes in Tables 1-3 ,1A-3A. Each sense and antisense strand sequence in the tables is immediately followed by its SEQ ID NO.

Certain embodiments of compositions and methods of the invention comprise a single-strand RNA in a composition and/or administered to a subject. For example, an antisense strand such as one listed in any one of Tables 1-3 ,1A-3A may be a composition or in a composition administered to a subject to reduce HTT polypeptide activity and/or expression of HTT gene in the subject. Tables 1 and Tables 1A shows certain HTT dsRNA agent antisense strand and sense strand core stretch base sequences. A single-strand antisense molecule that may be included in certain compositions and/or administered in certain methods of the invention are referred to herein as a “single-strand antisense agent” or an “antisense polynucleotide agent”. A single-strand sense molecule that may be included in certain compositions and/or administered in certain methods of the invention are referred to herein as a “single-strand sense agent” or a “sense polynucleotide agent”. The term “base sequence” is used herein in reference to a polynucleotide sequence without chemical modifications or delivery compounds. For example, the sense strand UUUUAAACUGCGUUGUGAAGAA (SEQ ID NO: 1233) shown in Table 1A is the base sequence for SEQ ID NO: 2747 in Table 2A and for SEQ ID NO: 3291 in Table 3A, with SEQ ID NO: 2747 and SEQ ID NO: 3291 shown with their chemical modifications, mismatch and a delivery compound. Sequences disclosed herein may be assigned identifiers. For example, a single-stranded sense sequence may be identified with a “Sense strand SS#”; a single stranded antisense sequence may be identified with an “Antisense strand AS#” and a duplex that includes a sense strand and an antisense strand may be identified with a “Duplex AD#/AV#”.

Table 1 and Table 1A includes sense and antisense strands and provides the identification number of duplexes formed from the sense and antisense strand on the same line in Table 1 and Table 1A. In certain embodiments of the invention an antisense sequence includes nucleobase u or nucleobase a in position 1 of the antisense sequence. In certain embodiments of the invention an antisense sequence includes nucleobase u in position 1 of the antisense sequence. As used herein, the term “matching position” in a sense and an antisense strand are the positions in each strand that “pair” when the two strands are duplexed strands. For example, in a 21 nucleobases sense strand and a 21 nucleobases antisense strand, nucleobase in position 1 of the sense strand and position 21 in the antisense strand are in “matching positions”. In yet another non-limiting

example in a 23 nucleobases sense strand and a 23 nucleobases antisense strand, nucleobase 2 of the sense strand and position 22 of the antisense strand are in matching positions. In another non-limiting example, in an 18 nucleobases sense strand and an 18 nucleobases antisense strand, nucleobase in position 1 of the sense strand and nucleobase 18 in the antisense strand are in matching positions, and nucleobase 4 in the sense strand and nucleobase 15 in the antisense strand are in matching positions. A skilled artisan will understand how to identify matching positions in sense and antisense strands that are or will be duplexed strands and paired strands.

The first column in Table 1 and Table 1A indicates a Duplex AV# for a duplex that includes the sense and antisense sequences in the same table row. For example, Table 1A discloses the duplex assigned Duplex AV03373.um, which includes sense strand SEQ ID NO: 1233 and antisense strand SEQ ID NO: 1296. Thus, each row in Table 1A identifies a duplex of the invention, each comprising the sense and antisense sequences shown in the same row, with the assigned identifier for each duplex shown in the final column in the row. The duplexes of the table 1 have been designed to target homo sapiens full-length mutant transcript HTT (SEQ ID NO: 1) ; the duplexes of the table 1A have been designed to target combination of a particular portion of intron1 and exon1 retained in the truncated mutant HTT gene of SEQ ID NO: 7, Wherein the duplexes AV2743--AV02083.um, AV03090.um~AV03095.um of the table 1A have been designed to target exon1(truncated 1-408 of full-length mutant HTT transcript NM_001388492.1), the duplexes AV3373--AV04241.um of the table 1A have been designed to target intro1 ((truncated 1-2710 from SEQ ID NO:5(retained in the truncated 5415-12746 of NCBI Reference Sequence: NG_009378.1), thereby inhibiting expression of the truncated mutant HTT transcript encoding an expanded polyglutamine repeat while sparing full-length wild-type HTT. Without intending to be limited by theory, it is believed that a combination or sub-combination of the foregoing properties and the specific target sites, or the specific modifications in these iRNAs confer to the iRNAs of the invention improved efficacy, stability, potency, durability, and safety.

In some embodiments of methods of the invention, an RNAi agent comprising a polynucleotide sequence shown in any one of Tables 1-3, 1A-3A, is administered to a subject.

In some embodiments of the invention an RNAi agent administered to a subject comprises is a duplex comprising at least one of the base sequences set forth in Table 1, including 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, or 24 sequence modifications. In some embodiments of methods of the invention an RNAi agent comprising a polynucleotide sequence shown in any one of Tables 1-3,1A-3A is attached to a delivery molecule, a non-limiting example of which is a delivery compound comprising a GalNAc compound, or a GLS-15* compound.

Table 1: Unmodified HTT RNAi agent antisense strand and sense strand sequences of full-length mutant (NM_001388492.1) targeting HTT dsRNA Agents. All sequences shown 5' to 3' direction. Duplex AV# are the number assigned to the duplex of the two strands in the same row in the table.

Duplex AV#	Sense Strand	SEQ ID NO	Antisense Strand	SEQ ID NO	Position in NM_001388492.1
AV02731.µm	UCAUAUACACAUUCGUUUUGUA	9	UACAACGGAUUGUAUUUAUGA	586	4399-4419
AV02732.µm	GCUGGUGAAUCCGGAUUCCUGA	10	UCAGGAUUCCGAUUCACCAGC	587	6508-6528
AV02734.µm	UUUCUUCAGCAAAACUCUAUAA	11	UUAUAGAGUUUGCUGAAGAAA	588	2332-2352
AV02736.µm	CGGUACCGACCAACCAGUAUUA	12	UAAUACUUGUUUGCGGUACCG	589	1897-1917
AV02737.µm	AACCUUUCAGAGUUAUUGCA	13	UGCAUUAACUUCUUGAAAGGUU	590	3146-3166
AV02738.µm	CAGUCGUACUCAGUUUUGAAAGA	14	UCUUCAAACUGAGUACGACUG	591	7522-7542
AV02740.µm	UCUGAUAUCGAGAUCCGGAUUGU	15	AACAUCCGAUUCUCGAUUCAGA	592	1508-1528
AV02741.µm	ACAGCAGUGUUGAUUAAAUUUG	16	CAAAUUAUCAACACUCUGU	593	2067-2087
AV02742.µm	CUGCUAGCUCCAUGCUUAAGA	17	UCUUAAGCAUGGAGCUVAGCAG	594	6575-6595
AV02804.µm	GUGCACCGACCAAGAAAGAAA	18	UUCUUUCUUUGGUCGGUCAC	595	398-418
AV02805.µm	GGCACCGACCAAGAAAGAAA	19	UUUCUUUCUUUGGUCGGUGCC	596	399-419
AV02806.µm	CCACCGACCAAGAAAGAAACA	20	UGUUUCUUUCUUUGGUCGGUGG	597	400-420
AV02807.µm	GACCGACCAAGAAAGAAACUA	21	UAGUUUCUUUCUUUGGUCGGUC	598	401-421
AV02808.µm	GCCGACCAAGAAAGAAACUUA	22	UAAGUUCUUUCUUUGGUCGGC	599	402-422
AV02809.µm	GCGACCAAGAAAGAAACUUUA	23	UAAAGUUUCUUUCUUUGGUCGC	600	403-423
AV02810.µm	GGACCAAGAAAGAAACUUUCA	24	UGAAAGUUUCUUUCUUUGGUC	601	404-424
AV02811.µm	CACCAAGAAAGAAACUUUCAA	25	UUGAAAGUUUCUUUCUUUGGUG	602	405-425
AV02812.µm	GCCAAAGAAAGAAACUUUCAGA	26	UCUGAAAGUUUCUUUCUUUGGC	603	406-426
AV02813.µm	GAAAAGAAAGAAACUUUCAGCUA	27	UAGCUGAAAGUUUCUUUCUUUC	604	408-428
AV02814.µm	GAGAAAGAAACUUUCAGCUAA	28	UUAGCUGAAAGUUUCUUUCUUUC	605	409-429
AV02815.µm	GGAACUUUCAGCUACCAAGAA	29	UUCUUUGGUAGCUGAAAGUUUC	606	415-435
AV02816.µm	GAGAAAAGACCGUGUGAAUCAA	30	UUGAUUUCACACGGUCUUUCUC	607	431-451
AV02817.µm	CAAAGACCGUGUGAAUCAUUA	31	UAAUGAUUCACACGGUCUUUG	608	433-453

AV02818.µm	CACCGUGUGAUAUCAUUGUCUA	32	UAGACAUAUGAUUCCACACGGUG	609	437-457
AV02819.µm	GGUGUGAUAUCAUUGUCUGACA	33	UGUCAGACAUAUGAUUCCACACC	610	440-460
AV02820.µm	CUUGAUAUCAUUGUCUGACAA	34	UUGUCAGACAUAUGAUUCCACAG	611	441-461
AV02821.µm	CUGAUAUCAUUGUCUGACAUA	35	UAUUGUCAGACAUAUGAUUCCAG	612	443-463
AV02822.µm	CAUCAUUGUCUGACAUAUA	36	UAUAUUGUCAGACAUAUGAUUUG	613	445-465
AV02823.µm	GUUGUCUGACAUAUUGUGAAAA	37	UUUUACAUAUUGUCAGACAC	614	451-471
AV02824.µm	CUUCGACAUAUUGUGAAAAACA	38	UGUUUUACAUAUUGUCAGAG	615	453-473
AV02825.µm	GUUGCAGAAAAUUCUCCAGAAA	39	UUUCUGGAGAAUUUUCUGACAC	616	486-506
AV02826.µm	GUUCUCCAGAAUUBUCAGAAAA	40	UUUUUCUGAAAAUUCUGGAGAAC	617	495-515
AV02827.µm	GUUCUCCAGAAUUBUCAGAAAA	41	UGUUUCUGAAAAUUCUGGAGAC	618	496-516
AV02828.µm	CCUAUGGAACUUUUUUCUGCUA	42	UAGCAGAAAAAAGUUCCAUAGG	619	527-547
AV02829.µm	GCUCAACAAAGUUAUCAAAAGA	43	UCUUUGAUUAACUUUUGUUGAGC	620	595-615
AV02830.µm	CUUAUCAAAAGCUUUUGAUGGAA	44	UUCCAUCAAAGCUUUUGAUAAG	621	605-625
AV02831.µm	GAUCAAAAGCUUUUGAUGAUA	45	UAAUCCAUCAAAGCUUUUGAUC	622	607-627
AV02832.µm	GAAAGCUUUUGAUGGAUUCUA	46	UUAGAUAUCCAUCAAAGCUUUC	623	610-630
AV02833.µm	GGCUUUUGAUGGAUUCUAUAUCA	47	UGAUUAGAUAUCCAUCAAAGCC	624	613-633
AV02834.µm	CCUUUGAUGGAUUCUAUAUCUA	48	UAGAUUAGAUAUCCAUCAAAGG	625	614-634
AV02835.µm	GUUUUGAUGGAUUCUAUAUCUA	49	UAGAUAUAGAUAUCCAUCAAAC	626	615-635
AV02836.µm	CAUUGGAUUCUAUUCUCCAAAA	50	UUUGGAAGAUUAGAUAUCCAUG	627	619-639
AV02837.µm	CAUUCUAUAUCUUCCAAGGUUA	51	UAACCUUGGAAGAUAUAGAUAUG	628	623-643
AV02838.µm	GUUCUAUAUCUUCCAAGGUUAA	52	UUAAACCUUGGAAGAUAUAGAAC	629	624-644
AV02839.µm	GCUAUAUCUUCCAAGGUUACAA	53	UUGUAACCUUGGAAGAUUAGC	630	626-646
AV02840.µm	GGUUCCCAAAAAUUAUUGGCUUA	54	UAAGCCAUAAUUUUUGGGAACC	631	838-858
AV02841.µm	CUUCCCAAAAAUUAUUGGCUUCA	55	UGAAGCCAUAAUUUUUGGGAAG	632	839-859
AV02842.µm	GCCCCAAAAUUAUUGGCUUCUA	56	UAAAGAAGCCAUAAUUUUUGGGC	633	841-861
AV02843.µm	GUUUGGCUUCUUUUUGGCAUAUA	57	UAUUUGCCAAAAAGAAGCCAUUAC	634	849-869
AV02844.µm	GUUUUGGCAAUUUUGCAAAAUUGA	58	UCAUUUGCAAAAAAUUGCCAAC	635	859-879
AV02845.µm	GUUGUUAAAAAGGCCUUCAUAGA	59	UCUAUGAAGGCCUUUAACAAC	636	895-915
AV02846.µm	GAUAGCGAACCUGAAGUCAA	60	UUUGACUUUCAGGUUUCGCUAUC	637	910-930

AV02847.µm	CACAAAGGAAAGAAAUUGGAAGA	61	UCUUCCAUUUUCUUUCCUUGUG	638	1165-1185
AV02848.µm	GCAAGGAAAGAAAUUGGAAGUA	62	UACUUCCAUUUUCUUUCCUUGC	639	1166-1186
AV02849.µm	GUUGUCCAGGUUUAUGAAACUA	63	UAGUUCAUAAAACCUGGACAAC	640	1205-1225
AV02850.µm	GAGGUUUAUGAACUUGACGUUA	64	UAAAGUCAGUUUAUAAAACUUC	641	1211-1231
AV02851.µm	CGUUUAUGAACUUGACGUUACA	65	UGUAACGUACAGUUCAUAAAACG	642	1213-1233
AV02852.µm	GUGAACUUGACGUUACAUCAUUA	66	UAUGAUUGUAACGUCAGUUCAC	643	1218-1238
AV02853.µm	GGAACUUGACGUUACAUCAUAA	67	UUUAUGAUUGUAACGUCAGUUC	644	1219-1239
AV02854.µm	GUUGACGUUACAUCAUACACAA	68	UUUGUUAUGAUUGUAACGUCAC	645	1223-1243
AV02855.µm	GGGAGUUAUUGUGGAACUUA	69	UUAAAGUUCACAAUACUCC	646	1396-1416
AV02856.µm	CAGUAUUGUGGAACUUAUAGA	70	UCUAUAAAGUUCACAAUACUG	647	1399-1419
AV02857.µm	GAAAGGCAAAAGUUCUUAAGA	71	UCUAAGAGCACUUUUGCCUUC	648	1462-1482
AV02858.µm	GCUCUGAAUUCGAGAUCCGGAUA	72	UAUCCGAUUCUGAUUUCAGAGC	649	1506-1526
AV02859.µm	GUUCAGACAGUUCUGAAAUAUA	73	UAAUUBUCAGAAACUGUCUGAAC	650	1869-1889
AV02860.µm	GAGUUCUGAAAUUGUGUUAAGA	74	UCUAACACAAUUBUCAGAACUC	651	1876-1896
AV02861.µm	GGUUCUGAAAUUGUGUUAAGAA	75	UUCUAACACAAUUBUCAGAAC	652	1877-1897
AV02862.µm	GUUCUGAAAUUGUGUUAAGACGA	76	UUCGUUAACACAAUUBUCAGAC	653	1879-1899
AV02863.µm	CUUGAUAAAUUBUGUGUUGAGA	77	UCUCAACACAAAUUBUAUCAAG	654	2075-2095
AV02864.µm	GGCCUUUAUUCUGCUCUUA	78	UAACGAAAGCAGAUAAAAGGCC	655	2201-2221
AV02865.µm	GUUUAUUCUGCUCUUGUUAUUA	79	UCAAACGAAAGCAGAUAAAAC	656	2205-2225
AV02866.µm	GUUCUGCUCUUGUUAUUGCUAAA	80	UUUAGCAAAAAACGAAAGCAGAC	657	2209-2229
AV02867.µm	GUUCUUCGUUUUUUGCUAACAA	81	UUUGUUAAGCAAAAAACGAAAGCAC	658	2211-2231
AV02868.µm	GGCUUCGUUUUUUGCUAACAGA	82	UCUGUUAAGCAAAAAACGAAAGCC	659	2212-2232
AV02869.µm	GGGAUUCUUUUUCUUCAGCAAAA	83	UUUUUGCUGAAAGAAAGAUUCCC	660	2325-2345
AV02870.µm	CGAAUUCUUUUUCUUCAGCAACA	84	UGUUUGCUGAAAGAAAGAUUUCG	661	2326-2346
AV02871.µm	GUUCAGCAAAACUUCUUAUAAAAG	85	UCUUUAUAAGAGUUUGCUGAAC	662	2335-2355
AV02872.µm	GCAAGCAAAACUUCUUAUAAAAGUUA	86	UAACUUUAUAAGAGUUUGCUUGC	663	2337-2357
AV02873.µm	GGCAAAACUUCUUAUAAAAGUCCA	87	UUGAAACUUUAUAAGAGUUUGGCC	664	2339-2359
AV02874.µm	GUUCUAUAAAAGUUCUUCUUGAA	88	UUCAAGAGGAACUUUAUAAGAC	665	2345-2365
AV02875.µm	GUUCAGACAUUCUUUGAACUACAA	89	UUUGUAGUUCAAGAUUGUCUGAC	666	2395-2415

AV02876.µm	GCAUCCUUGAACUACAUCCGAUA	90	UAUCGAUGUAGUUCUACAAGAUCC	667	2400-2420
AV02877.µm	GUCCUUGAACUACAUCCGAUCAA	91	UUGAUCCGAUGUAGUUCACAAGAC	668	2402-2422
AV02878.µm	GUUGAAACUACAUCCGAUCCAUGA	92	UCAUGAUCCGAUGUAGUUCACAAC	669	2404-2424
AV02879.µm	GCCUCACAGGAAAUACAUUUUA	93	UAAAUUGAUUUUCCUGUGAGGCG	670	2532-2552
AV02880.µm	GAUUCUUUUGCUGCGGAAAAAA	94	UUUUUCCCGCAGCAAAAGGAUUC	671	2566-2586
AV02881.µm	CAGUCUUUCUGUUUACUUGCAAAA	95	UUUGCAAGUAAACAGAGAGACUG	672	2597-2617
AV02882.µm	GCUCUCUGUUACUUGCAAGUUA	96	UAAUCUUGCAAGUAAACAGAAAGC	673	2600-2620
AV02883.µm	CAGGAACUGUGUCAUGAGUCA	97	UGACUCAUGACACAGUUUCCUG	674	2635-2655
AV02884.µm	GGCAGCUACAGUGAGUUAGGA	98	UCCUAACUACUCUGUAGCUGCC	675	2663-2683
AV02885.µm	GUAGAGAAACAGUUCCUAUUGA	99	UCAAUAGGAACUGUUCCUCAC	676	2711-2731
AV02886.µm	GAGCAGAAAAACUUAACACAGAA	100	UUCUGUGUAAAGUUUUUCUGCUC	677	2802-2822
AV02887.µm	GUUUAACAGGGCUUUUAAAAACA	101	UGUUUUUAAAAAGCCCUGUUUAUAC	678	2833-2853
AV02888.µm	GGUGCUCAAUAAUUGUUGUCAA	102	UUGACAACAUUUAUUGAGCACCC	679	2863-2883
AV02889.µm	GAUUAUUGUUGUCAUCCAUUA	103	UAAUGGAUGACAACAUAUUAUUC	680	2869-2889
AV02890.µm	GAUUGUUUGUCAUCCAUUUUCA	104	UGCAAAUUGGAUGACAACAUAUUC	681	2872-2892
AV02891.µm	GCCAUUUUGCUUGGAGAUUGAAAA	105	UUUCAUUCUCCAAAGCAAAUUGGC	682	2883-2903
AV02892.µm	GAUUUUUGCUUGGAGAUUGAGAA	106	UUUCUCAUUCUCCAAAGCAAAUUC	683	2885-2905
AV02893.µm	CAUCAAAAGCAGUGUUUUAACCUA	107	UAGGUAAACACUGCUUUUGAUG	684	3011-3031
AV02894.µm	GAAAGCAGUGUUUUAACCUGAAA	108	UUUCAGGUAAAACACUGCUUUUC	685	3014-3034
AV02895.µm	GAUUAAGAGGCUUAUAACCUACUA	109	UAGUAAGGUUAUAGCCUCUAUUC	686	3095-3115
AV02896.µm	CGAAAAUUAACCUUUUCAAGAGA	110	UUCUUUGAAAAAGGUUAUUUUUCG	687	3139-3159
AV02897.µm	GUUGCAGCAGUUUUCUCAUGAAA	111	UUUCAUGAGAAACUGCUGCAC	688	3162-3182
AV02898.µm	GGAGCACUCACAUUUUGGAUGA	112	UCAUCCAAAUUGUGAGUGCUCC	689	3200-3220
AV02899.µm	GCACAUUUUGGAUUGCUGUAAAA	113	UUUCAACAGCAUUCCAAUUGUGC	690	3207-3227
AV02900.µm	GGCUGUGAAGCUUUUGUGUCUA	114	UAGACACAAAAAGCUUACACAGCC	691	3218-3238
AV02901.µm	CCUGUGAAGCUUUUGUGUCUUA	115	UAAAGACAAAAAGCUUACACAGG	692	3219-3239
AV02902.µm	CUGAAGCUUUUGUGUCUUUUA	116	UAAAGAAGACACAAAAAGCUUCAAG	693	3222-3242
AV02903.µm	CAAGCUUUUGUGUCUUUUCA	117	UGAAAGAAGACACAAAAAGCUUG	694	3224-3244
AV02904.µm	GCCAGUUUUGCAUUUUGGAGUUUA	118	UAAUCUCCAAAUUGCAAAACUUGGC	695	3253-3273

AV02905.µm	GCAGUTUUGCAUUTUGGAGUUUA	119	UAAACUCCAAAUUGCAAAACUUGC	696	3254-3274
AV02906.µm	GAGUUTUGCAUUTUGGAGUUUA	120	UUAACUCCAAAUUGCAAAACUC	697	3255-3275
AV02907.µm	GCUCAGAUAGUCUAGAAGA	121	UCUUCUAGACUCUUCUGAGC	698	3306-3326
AV02908.µm	CCCCAUCAGAUGCUUUGAUA	122	UAUCAAGCAUCUUGAUGGGG	699	3398-3418
AV02909.µm	GUUCUAGACAUCUGAUACCA	123	UGGUUUCAGAUUGUCUAGAAC	700	3771-3791
AV02910.µm	GUCAAGUCCUGUUAACAACAAA	124	UUUGUUGUAACAGGACCUGAC	701	3790-3810
AV02911.µm	GACAACAAGUAAAUCCUCAUA	125	UAUGAGGAUUVACUUGUUGUC	702	3802-3822
AV02912.µm	GAACAAGUAAAUCCUCAUA	126	UUGAUAGGAUUVACUUGUUC	703	3804-3824
AV02913.µm	GCACUGGGAGUUCUCAUCAA	127	UUGAUAGAAACUCCCCAGUGC	704	3821-3841
AV02914.µm	GACUGGGAGUUCUCAUCAA	128	UAUGAUAGAAACUCCCCAGUC	705	3822-3842
AV02915.µm	GUUCUAVCAUCUUCUCCUCAUA	129	UAUGAAGGAAGAUGAUAGAAC	706	3832-3852
AV02916.µm	GUUCUAVCAUCUUCUCCUCAUA	130	UUAUGAAGGAAGAUGAUAGAC	707	3833-3853
AV02917.µm	GUCCUCCUUCAUACCUCAAAA	131	UUUUGAGGUUAUGAAGGAAGAC	708	3840-3860
AV02918.µm	GUACUCAAACUGCAUGAUGA	132	UCAUCAUGCAGUUUGAGGUAC	709	3850-3870
AV02919.µm	GAACUUGCAUGAUGUCCUGAAA	133	UUUCAGGACAUCAUGCAGUUC	710	3857-3877
AV02920.µm	GGAAAUCCUGCUUUAUGUGAA	134	UUCGACUAAAGCAGGAUUUCC	711	4035-4055
AV02921.µm	CAUGGCAACUGUUGUUGUUCA	135	UGAACACAAACAGUUGCCAUUG	712	4063-4083
AV02922.µm	GGGCAACUGUUUGUUGUCAA	136	UUUGAACACAAACAGUUGCCC	713	4065-4085
AV02923.µm	GAACUUGUUUGUUGUCAAACAA	137	UUUGUUUGAACACAAACAGUUC	714	4068-4088
AV02924.µm	GACUGUUUGUUGUCAAACAUA	138	UAUUGUUUGAAACACAAACAGUC	715	4069-4089
AV02925.µm	GUCAACA AUUGUUGAAGACUA	139	UAGUCUUCACAACA AUUGUUGAC	716	4080-4100
AV02926.µm	GCAACA AUUGUUGAAGACUCA	140	UGAGUCUUCACAACA AUUGUUGC	717	4081-4101
AV02927.µm	GUUUGAAGAGACUUCUUCUUGGA	141	UCCAAGAAGAGUCUUCACAACAC	718	4088-4108
AV02928.µm	GCAAAAGAACCGUGCAGAUAAA	142	UUUAUCUGCAGCGUUUCUUUGC	719	4370-4390
AV02929.µm	GACCGUGCAGAUUAAGAUUGCA	143	UGCAUUCUUAUCUGCAGCGGUC	720	4376-4396
AV02930.µm	CCAGAUUAAGAAUUGCUAUUCAA	144	UUGAUUAAGCAUUCUUAUUCUGG	721	4382-4402
AV02931.µm	CAUUAAGAAUUGCUAUUCAAUAAA	145	UUUAUGA AUUAAGCAUUCUUAUG	722	4385-4405
AV02932.µm	GAAGA AUUGCUAUUCAUUAUUA	146	UGAUUAUUGAAUUAAGCAUUCUUC	723	4387-4407
AV02933.µm	CCUAUUCAUUAUUCACAUUUCGA	147	UCGA AUUGU GAUUAUGAAUAGG	724	4394-4414

AV02934.µm	GCAUAAUCACAUUCGUUUUA	148	UACAAACGAUUGAUUUAUGC	725	4399-4419
AV02935.µm	GAUCACAUUCGUUUUGUUUGAA	149	UUCAAACAACGAUUGUGAUC	726	4403-4423
AV02936.µm	GCACAUUCGUUUUGUUUGAACAA	150	UGUUCAAACAACGAUUGUGC	727	4405-4425
AV02937.µm	GCAUUCGUUUUGUUUGAACCUA	151	UAGGUUCAACAACAACGAUUGC	728	4407-4427
AV02938.µm	GUUCGUUUUGUUUGAACCUUA	152	UAGAGGUUCAACAACAACGAAC	729	4409-4429
AV02939.µm	GUUUUUUGAACCUUCUUGUUAUA	153	UAUAAACAAGAGGUUCAACAC	730	4415-4435
AV02940.µm	CUUUUGAACCUUCUUGUUAUAAA	154	UUUUAUAAACAAGAGGUUCAAAAG	731	4417-4437
AV02941.µm	GUUGAACCUUCUUGUUUAUAAAA	155	UUUUUAUAAACAAGAGGUUCAAC	732	4418-4438
AV02942.µm	GGAACCUUCUUGUUUAUAAAAAGA	156	UCUUUUUAUAAACAAGAGGUUCC	733	4420-4440
AV02943.µm	CAACCUUCUUGUUUAUAAAAAGCA	157	UGCUUUUAUAAACAAGAGGUUG	734	4421-4441
AV02944.µm	GGCUUUAAAAACAAGUACACGAA	158	UUCGUUUAUCUUGUUUUAAAGCC	735	4438-4458
AV02945.µm	GCAGAAAGCAGGUUUUAGAUUA	159	UAAUCUAAAAACCUUGCUUCUGC	736	4477-4497
AV02946.µm	CAAGCAGGUUUUAGAUUUUGCA	160	UGCAAUUCUAAAAACCUUGCUUG	737	4480-4500
AV02947.µm	GUCAGUUACGGGUUAAUUVACA	161	UGUAUUUAACCCGUAAACUGAC	738	4512-4532
AV02948.µm	GCAGUUACGGGUUAAUUVACUA	162	UAGUAAUUAAACCCGUAAACUUGC	739	4513-4533
AV02949.µm	CGGUUAAUUAUCUGUCUUCUGA	163	UCAGAAGACAGUAAUUAACCG	740	4521-4541
AV02950.µm	GAUUUACUGUCUUCUGGAUUA	164	UAAUCCAGAAGACAGUAAUUC	741	4525-4545
AV02951.µm	GGUCUUCUGGAUUCAGAUCAA	165	UUGAUUCUGAAUCCAGAAGACC	742	4532-4552
AV02952.µm	CAUUCAGGUUUUAUUGGCUUA	166	UAAGCCAAUAAACACCUUGAUG	743	4547-4567
AV02953.µm	GAGGUUUUAUUGGCUUUUGUA	167	UACAAAAGCCAAUAAAACACCUUC	744	4550-4570
AV02954.µm	GGUUUAUUGGCUUUUGAUUGA	168	UCAAUACAAGGCCAAUUAACCC	745	4554-4574
AV02955.µm	GAUUGGCUUUUGAUUUGAAACA	169	UGUUUCAUACAAAGCCAUUC	746	4558-4578
AV02956.µm	GUUGGCUUUUGAUUUGAAACAGA	170	UCUGUUUCAAUUACAAAGCCAC	747	4560-4580
AV02957.µm	GCAUUCUUUUUCUUCUUGGUAA	171	UUACCAAGAAGAAAAAAGAUGC	748	4632-4652
AV02958.µm	GAUUCUUUUUCUUCUUGGUUAUA	172	UAUACCAAGAAGAAAAAAGAUUC	749	4633-4653
AV02959.µm	GUUUUUUCUUCUUGGUUAUUGAA	173	UGUAUUAACCAAGAAGAAAAAAC	750	4636-4656
AV02960.µm	GUACUUAUCUUAUUGAACGCUAA	174	UUAGCGUUCAUAAAGAUAGUAC	751	4652-4672
AV02961.µm	GACUUAUCUUAUUGAACGCUAUA	175	UAUAGCGUUCAUUAAAGAUAGUUC	752	4653-4673
AV02962.µm	GUUAUCUUUAUGAACGCUAUCAA	176	UUGAUUAAGCGUUCAUAAAGAUAC	753	4655-4675

AV02963.µm	GAUCUUAUGAACGCUAUCAU	177	UAUGAUAAGCGUUCAUAGAUC	754	4656-4676
AV02964.µm	GCUUAUGAACGCUAUCAUUCA	178	UGAAUGAUAAGCGUUCAUAAAGC	755	4658-4678
AV02965.µm	GUUAUGAACGCUAUCAUUCAA	179	UUGAAUGAUAAGCGUUCAUAAAC	756	4659-4679
AV02966.µm	GAUGAACGCUAUCAUUCAAAA	180	UUUUUGAAUGAUAAGCGUUCAUUC	757	4661-4681
AV02967.µm	GACGCUAUCAUUCAAAAACAGA	181	UCUGUUUUUGAAUGAUAAGCGUC	758	4665-4685
AV02968.µm	GCAUUCAAAAACAGAUCAUUGA	182	UCAAUGAUCUGUUUUUGAAUUGC	759	4672-4692
AV02969.µm	GUCAAAAACAGAUCAUUGGAAA	183	UUUUCAAUGAUCUGUUUUUGAAC	760	4675-4695
AV02970.µm	GAAACAGAUCAUUGGAAUUCA	184	UGAAUUCCAUAUGAUCUGUUUC	761	4678-4698
AV02971.µm	GAACAGAUCAUUGGAAUUGCA	185	UGGAAUUCCAUAUGAUCUGUUUC	762	4679-4699
AV02972.µm	GUUGGAAUUCUCAA AAAUCAUA	186	UAUGAUUUUAAGGAAUUCCAAAC	763	4688-4708
AV02973.µm	GAUUCUCAA AAAUCAUUCAGCA	187	UGCUGAAUGAUUUUAAGGAUUC	764	4693-4713
AV02974.µm	GUUCCUAAAAAUCAUUCAGCUA	188	UAAGCUGAAUGAUUUUUAGGAAC	765	4694-4714
AV02975.µm	GCCUCUUUUUAUUAAGAGGAA	189	UUCCUCUUUAUAUACAAGAGGCG	766	4788-4808
AV02976.µm	GGAGGAACAAAUAAAAGCUGAA	190	UUCAAGCUUUUAUUUGUCCUCC	767	4802-4822
AV02977.µm	GGGUUCAAUUGUACUGAGAA	191	UUUCAGUUAACAUAUUGACACCC	768	4857-4877
AV02978.µm	GCAUCAGGUUUUGAGAGAUUA	192	UACAUCUCCAACACCCUGAUGC	769	4888-4908
AV02979.µm	CGUGUUUGAGAUUGUUCAUUCA	193	UGAAUGAACAUCCUCCAACACG	770	4894-4914
AV02980.µm	GGACAUCAUCCUCCCAAUUGUA	194	UACAUUUGGAGAGAUUGAUUCC	771	4978-4998
AV02981.µm	GAGAUGCACAUUGACUUCUCAA	195	UUGAGAGUCAUAUGUGCAUCUC	772	5009-5029
AV02982.µm	GGCACAUUGACUCUCAUGAAAA	196	UUUCAUGAGAGUCAUAUGUGCC	773	5013-5033
AV02983.µm	GACAUUGACUCUCAUGAAGCA	197	UUCUUCAUUGAGAGUCAUUGUC	774	5015-5035
AV02984.µm	GCCUUGGAGUUVUAAAUVACAA	198	UUUUUAUUUAACACUCCCAAGGC	775	5034-5054
AV02985.µm	GCUUGGAGUUVUAAAUVACAU	199	UAUGUAUUUAACACACUCCAAGC	776	5035-5055
AV02986.µm	GUUACGGAUUAUGUUCCGUCAA	200	UUAGCAGAACAUACUCCGUAAAC	777	5101-5121
AV02987.µm	GGUGAGCACUUVUCAAACUGUA	201	UACAGUUUGAACAGUGUCUACCC	778	5140-5160
AV02988.µm	GUUUUUGAGGGUUCUGAUUUCA	202	UGAAAUUCAGAAACCCUCAA AAAC	779	5180-5200
AV02989.µm	GGAUUUUCCCAUGUCAACUGAAA	203	UUUCAGUUUGACUUGGGAUAUCC	780	5193-5213
AV02990.µm	GCAACUGAAGAUUAUUGUUCUA	204	UAGAACAUAUAUCUUCAGUUCC	781	5204-5224
AV02991.µm	GCUGAAGAUUAUUGUUCUUUCA	205	UGAAAGAACAAUAUUCUUCAGC	782	5207-5227

AV02992.µm	GGAUAUUGUUCUUCUCGUAA	206	UUACGAGAAAGAACAUAUCC	783	5212-5232
AV02993.µm	GUUGUUCUUCUCGUAUUCAA	207	UUGAUACGAGAAAGAACAAAC	784	5216-5236
AV02994.µm	GAGAAUUGCCAGAAAGAAACA	208	UGUUUCUUCUGGCAAAUUCUC	785	5342-5362
AV02995.µm	GAGAAAGAAACAUUUCCAAGGA	209	UCCUUGAAAUUGUUUCUUCUC	786	5352-5372
AV02996.µm	GGAAGAAACAUUUCCAAGGUA	210	UACCUUGAAAAUUGUUUCUUC	787	5353-5373
AV02997.µm	GUUUUCAAGGUUUCUAUUAACA	211	UGUAUUAAGAAACCUUGAAAAAC	788	5362-5382
AV02998.µm	GAAGGUUUUAUUAACAACUGA	212	UCAGUUUGUAUUAAGAAACCUUC	789	5367-5387
AV02999.µm	CGUUGUAUUUCUUUUAGAAGA	213	UCUUUAAGAAAGAUUACCAACG	790	5386-5406
AV03000.µm	GUUGUAUUUCUUUUAGAAGACA	214	UGUCUUUAAGAAAGAUUACACAC	791	5388-5408
AV03001.µm	GGGUAAUUCUUUUAGAAGACAA	215	UUGUCUUUAAGAAAGAUUACCC	792	5389-5409
AV03002.µm	GUAGAAGACAUUUGUACAATAA	216	UUUUUAACAUAUUGUCUUCUAC	793	5399-5419
AV03003.µm	GAGACAUUUGUACAATAACAGA	217	UCUGUUUUUAACAUAUUGUCUC	794	5403-5423
AV03004.µm	CAGCAGCAACAUAUUCUUAACA	218	UUAGAAAGUAUUGUUGCUGCUG	795	5441-5461
AV03005.µm	GGCAACAUAUUCUUAUUGCA	219	UGCAAUUAAGAAAGUAUUGGCC	796	5445-5465
AV03006.µm	CCAACAUAUUCUUAUUGCCA	220	UGGCAUUAAGAAAGUAUUGUUG	797	5446-5466
AV03007.µm	GACACUGCUAAUUGUGUCUGAA	221	UUCAGACACAUAUAGCAGUGUC	798	5476-5496
AV03008.µm	GUUCUAAUUGUGUCUGAUCCAA	222	UUUGAUUCAGACACAUAUAGCAC	799	5480-5500
AV03009.µm	GCAGCACAAAAGUUACUUAUGUA	223	UACUAAAGUAACUUUUGUGCUGC	800	5736-5756
AV03010.µm	GAGCACAAAAGUUACUUAUGUCA	224	UGACUAAAGUAACUUUUGUGCUC	801	5737-5757
AV03011.µm	CCAGCCAAAACUUUGGAUUGUGA	225	UCCACAUUCCAAAAGUUUGGCUUG	802	5792-5812
AV03012.µm	GACUUUGAAAUUGUGCAAUAGAA	226	UUCUAUUUGACACAUAUCCAAGUC	803	5799-5819
AV03013.µm	CUGCAAUAGAGAAAUAGUACA	227	UGUACUAUUUCUCUAUUGCAG	804	5809-5829
AV03014.µm	GUUCUAUUCUUCUUCUGUGAUA	228	UAUCACAGAAAGAGAAUUGAGAC	805	5838-5858
AV03015.µm	GAUUUCUUCUUCUGUGAUUAUGA	229	UCAUAAUUCACAGAAAGAGAAUUC	806	5842-5862
AV03016.µm	GUUCUUCUUCUGUGAUUAUUGUA	230	UACAUAUUCACAGAAAGAGAAAC	807	5843-5863
AV03017.µm	GCUUUCUGUAUUAUGUCUGUA	231	UACAGACAUAUUAUCACAGAAAGC	808	5847-5867
AV03018.µm	GUUCUGUAUUAUGUCUGUCAA	232	UUAGACAGACAUAUUAUCACAGAC	809	5849-5869
AV03019.µm	GUUGUAUUAUGUCUGUCAGAA	233	UUUCGACAGACAUAUUAUCACAC	810	5851-5871
AV03020.µm	CUGAUUAUUGUCUGUCAGAACAA	234	UUGUUUCGACAGACAUAUUAUCAG	811	5853-5873

AV03021.µm	GUUUCAGAAACCUCCAUGACUA	235	UAGUCAUGGAGGUUCUGACAC	812	5863-5883
AV03022.µm	GUUAAACGUGGCUCAUUGUAAA	236	UUUACAUGAGCCACGUUAAAC	813	5890-5910
AV03023.µm	GACGUGGCUCAUUGUAAAUCA	237	UGAUUUUACAUAUGAGCCACGUC	814	5893-5913
AV03024.µm	CUUGGCUCAUUGUAAAUCACAA	238	UUUGAUUUUACAUAUGAGCCAG	815	5896-5916
AV03025.µm	GUCAUUGUAAAUCACAUUCAA	239	UUGAAUGUGAUUUUACAUGAC	816	5900-5920
AV03026.µm	GGUAAAUCACAUUCCAAGAUCA	240	UGAUCUUUGAAUUGUAAUUUACC	817	5905-5925
AV03027.µm	GUCAGUCUCGUGUGAAAAACA	241	UGUUUUACACAACGAGACUGAC	818	6015-6035
AV03028.µm	GUGAAGAAAAACUCUUCAGUGA	242	UCACUGAAAGAGUUUUUCUUCAC	819	6053-6073
AV03029.µm	GUGGCUGCAAAUUVUACAGAGA	243	UCUCUGUAAAUVUUGCAGCCAC	820	6203-6223
AV03030.µm	CGCUGCAAAAUUUACAGAGCAA	244	UUGCUCUGUAAAUUUUGCAGCG	821	6205-6225
AV03031.µm	GCUCAACAGAAUCCAGGAUUA	245	UAUUCCUGGAUUCUGUUUGAGC	822	6250-6270
AV03032.µm	GGACACCAAAAGGCUUUAUUA	246	UGAAUAGAGCCUUUGGUUCC	823	6296-6316
AV03033.µm	GCAUUGCAAGACUCACUUAUGUA	247	UACUAAAGUGAGUCUUUGCAUAGC	824	6342-6362
AV03034.µm	GACGUUCAUCUUGUCAAAUCA	248	UGAUUUUGACAAGAUUGAACGUUC	825	6443-6463
AV03035.µm	CUUGGACCAAGUUCAGAUUCUA	249	UAGAAUUCUGACCUGGUCCAAG	826	6468-6488
AV03036.µm	GAUCCGAUUCUCUGCUGAAGAA	250	UUUUUCAGCAGGAUUCGGAUUC	827	6515-6535
AV03037.µm	GUUCCUGCUGAAGAUUAUGAAA	251	UUUCAUUAUCUUCAAGCAGGAAC	828	6521-6541
AV03038.µm	GUAGGGAUUGAGUGAAAUUUCA	252	UGAAAUUUUCACUCAUCCCUAC	829	6596-6616
AV03039.µm	GGGGAUUGAGUGAAAUUUCUGA	253	UCAGAAAUUUUCACUCAUUCCCC	830	6598-6618
AV03040.µm	GUUGAAGCAAGUUUGAAUUGAUCA	254	UGAUUCAUUCAACUUGCUCCAC	831	6748-6768
AV03041.µm	CAGGAAAGUAGAUCCAAAACACA	255	UGUGUUUGGAUUCUACUUCUUG	832	7175-7195
AV03042.µm	GUUGGAGAUUGGUGGCAGAAAA	256	UUUUUCGCCACCAUCUCACAC	833	7222-7242
AV03043.µm	CCCUUUGGUGCAUAAAAGGAAA	257	UUUUUUUUUAUUGACCCCAAGGG	834	7268-7288
AV03044.µm	GAAGGAAAGUCUUUAAAGAGUA	258	UACUCCUUUAAAAGACUUCUUUC	835	7471-7491
AV03045.µm	GAGGAAAGUCUUUAAAGAGUUA	259	UAAUCUUUUAAAAGACUUUCCUC	836	7472-7492
AV03046.µm	CAAGUCUUUAAAGAGUUAUA	260	UAUGAACUCCUUUAAAAGACUUUG	837	7475-7495
AV03047.µm	CUUCUUUAAAGAGUUCAUUCUAA	261	UUAGAUAUAACUCCUUUAAAAGAG	838	7478-7498
AV03048.µm	CUUCGUACUCAGUUUUGAAGAAA	262	UUUUUUUCAAAACUGAGUACGAG	839	7524-7544
AV03049.µm	GCGUACUCAGUUUUUGAAGAAAA	263	UUUUUUUCAAAACUGAGUACGC	840	7525-7545

AV03050.µm	GGUACUCAGUUUUUGAAGAAACA	264	UGUUUUCUUCACAAACUGAGUACC	841	7526-7546
AV03051.µm	CGAGCAAGAGAUUUCAGCAAAA	265	UUUGCUUGAAUUCUCUUGCUCG	842	7807-7827
AV03052.µm	CAGCAAGAGAUUUCAGCAAUUA	266	UAUUGCUUGAAUUCUCUUGCUG	843	7808-7828
AV03053.µm	CAGAUUUCAGCAAUUGUUUCA	267	UGAAACCAUUGCUUGAAUUCUG	844	7814-7834
AV03054.µm	GGAUUUCAGCAAUUGUUUCA	268	UUGAAACCAUUGCUUGAAUUC	845	7815-7835
AV03055.µm	CAUUCAGCAAUUGUUUCAAAA	269	UUUGAAACCAUUGCUUGAAUUG	846	7816-7836
AV03056.µm	GCAAGCAAUUGUUUCAAAAAGAA	270	UUUUUUUGAAACCAUUGCUUGC	847	7819-7839
AV03057.µm	GUCCACUCCUUGUUCCGCAGUUA	271	UAAACUGCGAACAAGGAGUUGGAC	848	8147-8167
AV03058.µm	GAGCAUUCAAUAUACAGAUUA	272	UCAUCUGUAUUAUUAUUGAUUGCUC	849	8700-8720
AV03059.µm	GGCAUUCAAUAUUAACAGAUUA	273	UACAUCUGUAUUAUUAUUGAUUGCC	850	8701-8721
AV03060.µm	GACCCCCUCCAUUCAUUUACCA	274	UUGUAAAUUGAUUGGAGGGGGUC	851	8752-8772
AV03061.µm	CUAUCUUGUUUUUUUUUGAUAGA	275	UCUAUUCAAAAAAGAACAGAUUAG	852	9017-9037
AV03062.µm	GCUUUUUUUUUUUUGAUAGGAUA	276	UAUCCUUAUCAAAGAAAGAACAGC	853	9020-9040
AV03063.µm	GCAAGACAUCAUUGAACAAAGA	277	UUCUUUUUCAUUGAUUGUCCUUGC	854	9115-9135
AV03064.µm	CGUUGUAUAAAGUUUUUUCAGAA	278	UUCUGAAACACCCUUUAUACACG	855	9190-9210
AV03065.µm	CGACGUGAACCUUUUUUCGCCA	279	UUGCAGAAAAAGUUUUCACGUCG	856	9403-9423
AV03066.µm	GGCCACAGACUUUCUACAGACA	280	UGUCUGUAGAAAGUUCUGGCCC	857	9427-9447
AV03067.µm	CGCUUGCUGACUUUUUUUACGAA	281	UUCGUAAACAAGUACAAGCAGCG	858	9528-9548
AV03068.µm	GUUGCUGACUUUUUUUACGAAAA	282	UUUUUUGUAAACCAAGUCAGCAC	859	9530-9550
AV03069.µm	GGCUGACUUUUUUUACGAAAAUA	283	UAUUUUUGUAAAAACAAGUCAGCC	860	9531-9551
AV03070.µm	CCUGACUUUUUUUACGAAAAUGA	284	UCAUUUUUGUAAACAAGUUCAGG	861	9532-9552
AV03071.µm	GGUUUACGAAAUUGUCCACAAA	285	UUUGUGGACAUUUUCGUAAACC	862	9539-9559
AV03072.µm	GCCAUUUUUUUUUUUUCUCUUA	286	UAAGAGAGAAAGGAGAAUUGGC	863	10099-10119
AV03073.µm	GUUUUUUUUUUUUUUUCAGGAUA	287	UAUCCUGAGAAAGAAAAAGAGAC	864	10112-10132
AV03074.µm	GCUAUUUCAUUAUUCACAUUCGA	288	UCGAUUGUGAUUAUUGAAUAGC	865	4394-4414
AV03077.µm	CCGGUACAGUUUCUUGCUUUUAA	289	UUAAAAAGCAGAAACCUAGACCGG	866	29-49
AV03078.µm	AGGCCUUCAUAGCGAAACCUGA	290	UCAGGUUUCGUUAUUGAAGGCCU	867	903-923
AV03079.µm	GCAACCAAGACCAACAUAUUGUA	291	UCAACAUUUGUGGUUUUGGUGC	868	1243-1263
AV03080.µm	CAGGUUUUAUGAACUGAGGUUA	292	UAACGUCAGUUUCAUUAACCUUG	869	1211-1231

AV03081.µm	UUACGGAGU AUGUUCGUCACA	293	UGUGACGAACAUACUCCGUAA	870	5102-5122
AV03082.µm	AUCCACAUUCGUUUGUUUGAAAA	294	UUUCAACAAACGAUUGUGAU	871	4404-4424
AV03083.µm	UCUGAUUUCCCAAGUCAACUGA	295	UCAGUUGACUGGAAAUUCAGA	872	5191-5211
AV03084.µm	GCAAUUCAGUCUCGUGUGUGAA	296	UUCACACGAGACUGAAUUGC	873	6011-6031
AV03085.µm	GUUCGACAUCCUUGCUUGUCGA	297	UCGACAAGCAAGGAUUGUCGAC	874	6167-6187
AV03086.µm	CUUCUAGCUCCAUUGCUUAAGA	298	UCUUAAAGCAUGGAGCUAGCAG	875	6575-6595
AV03087.µm	CUGACUUGUUUACGAAAAUGUA	299	UACAUUUCGUAAAAACAAGUCAG	876	9533-9553
AV03088.µm	UCAUGAACAAAAAGUUCGGA	300	UUCCGAUGACUUUGUUCAUGA	877	9123-9143
AV03089.µm	AGAACTUUCAGACCCUAAUCCA	301	UGGAUUAGGGUCUGAAGUUCU	878	8954-8974
AV02804-19-1.µm	GCACCGACCAAAAGAAAGAA	302	UUCUUUUCUUUGGUCGGUGC	879	400-418
AV02805-19-1.µm	CACCGACCAAAAGAAAGAAA	303	UUUCUUUCUUUGGUCGGUG	880	401-419
AV02806-19-1.µm	ACCGACCAAAAGAAAGAACAA	304	UGUUUCUUUCUUUGGUCGGU	881	402-420
AV02807-19-1.µm	CCGACCAAAAGAAAGAACUA	305	UAGUUUCUUUCUUUGGUCGG	882	403-421
AV02808-19-1.µm	CGACCAAAAGAAAGAACUUA	306	UAAGUUCUUUCUUUGGUCG	883	404-422
AV02809-19-1.µm	GACCAAAAGAAAGAACUUUA	307	UAAAGUUCUUUCUUUGGUC	884	405-423
AV02810-19-1.µm	ACCAAAAGAAAGAACUUUCA	308	UGAAAGUUUCUUUCUUUGGU	885	406-424
AV02811-19-1.µm	CCAAAGAAAGAAACUUUCA	309	UUGAAAGUUUCUUUCUUUGG	886	407-425
AV02812-19-1.µm	CAAAAGAAAGAACUUUCAGA	310	UCUGAAAGUUUCUUUCUUUG	887	408-426
AV02813-19-1.µm	AAGAAAGAACUUUCAGCUA	311	UAGCUGAAAGUUUCUUUCUU	888	410-428
AV02814-19-1.µm	AGAAAAGAACUUUCAGCUAA	312	UUAGCUGAAAGUUUCUUUCU	889	411-429
AV02815-19-1.µm	AACUUUCAGCUAACCAAGAA	313	UUUUUGGUAGCUGAAAGUU	890	417-435
AV02816-19-1.µm	GAAAGACCGUGUGAUAUCAA	314	UUGAUUCACACGGUCUUUC	891	433-451
AV02817-19-1.µm	AAGACCGUGUGAUAUCAAUA	315	UAAUGAUUCACACGGUCUU	892	435-453
AV02818-19-1.µm	CCGUUGUGAUAUCAAUUGCUA	316	UAGACAUAUGAUUCACACGG	893	439-457
AV02819-19-1.µm	UGUGAUAUCAAUUGCUUGACA	317	UGUCAGACAUAUGAUUCACA	894	442-460
AV02820-19-1.µm	GUUGAUAUCAAUUGCUUGACAA	318	UUGUCAGACAUAUGAUUCAC	895	443-461
AV02821-19-1.µm	GAUUCAUUUGUCUGACAAUA	319	UAUUUGUCAGACAUAUGAUUC	896	445-463
AV02822-19-1.µm	AUCAUUUGUCUGACAUAUA	320	UAUAUUUGUCAGACAUAUGAU	897	447-465
AV02823-19-1.µm	GUUCUGACAUAUAUGUGAAAA	321	UUUUUCACAUAUAUUGUCAGAC	898	453-471

AV02824-19-1.µm	CUGACAUAUUGUGAAAACA	322	UGUUUUUCACAUAUUGUCAG	899	455-473
AV02825-19-1.µm	GUCCAGAAAUUCUCCAGAAA	323	UUUUCUGGAGAAUUUCUGAC	900	488-506
AV02826-19-1.µm	UCUCCAGAAUUCACAGAAAA	324	UUUUUCGAAAUUUCUGGAGA	901	497-515
AV02827-19-1.µm	CUCCAGAAUUUCAGAAAACA	325	UGUUUCUGAAAAUUUCUGGAG	902	498-516
AV02828-19-1.µm	UAUGGAACUUUUUCUGCUA	326	UAGCAGAAAAAGUUCCAUVA	903	529-547
AV02829-19-1.µm	UCAACAAAAGUUUAUCAAAGA	327	UUUUUGAUAAACUUUGUUGA	904	597-615
AV02830-19-1.µm	UAUCAAAGCUUUUGAUGGAA	328	UUCCAUCCAAAGCUUUUGAUA	905	607-625
AV02831-19-1.µm	UCAAAAGCUUUUGAUGGAUUA	329	UAAUCCAUCCAAAGCUUUUGA	906	609-627
AV02832-19-1.µm	AAGCUUUUGAUGGAUUCUAA	330	UUAGAUAUCCAUAAGCUU	907	612-630
AV02833-19-1.µm	CUUUUGAUGGAUUCUAAUACA	331	UGAUUUAGAUAUCCAUAUCAAAG	908	615-633
AV02834-19-1.µm	UUUGAUGGAUUCUAAUUCUA	332	UAGAUUAGAUAUCCAUAUCAA	909	616-634
AV02835-19-1.µm	UUUGAUGGAUUCUAAUUCUA	333	UAGAUAUUAGAUAUCCAUAUCAA	910	617-635
AV02836-19-1.µm	UGGAUUUCUAAUUCUCCAAA	334	UUUGGAAGAUUAGAUAUCCA	911	621-639
AV02837-19-1.µm	UUUCUAAUUCUCCAAAGGUUA	335	UAACCUUGGAAAGAUUAGAA	912	625-643
AV02838-19-1.µm	UCUAAUUCUCCAAAGGUUAA	336	UUAACCUUUGGAAGAUUAGA	913	626-644
AV02839-19-1.µm	UAUUCUUCCAAAGGUUACAA	337	UUGUAAACCUUGGAAGAUUA	914	628-646
AV02840-19-1.µm	UUCCCAAAAUAUUGGCUUA	338	UAAGCCAUUAUUUUUGGGAA	915	840-858
AV02841-19-1.µm	UCCCAAAAUAUUGGCUUCA	339	UGAAGCCAUAUUUUUGGGA	916	841-859
AV02842-19-1.µm	CCAAAUAUUAUGGCUUCUUA	340	UAAGAAGCCAUAUUUUUGG	917	843-861
AV02843-19-1.µm	AUUGGCUUCUUUUUGGCAAUUA	341	UAUUUGCCA AAAAAGAACCAU	918	851-869
AV02844-19-1.µm	UUUGCAAUUUUGCAAAUUGA	342	UCAUUUGCAAAAUAUUUGCCAA	919	861-879
AV02845-19-1.µm	UGUUAAAAGGCCUUCAUVAGA	343	UCUAUGAAGGCCUUUAACA	920	897-915
AV02846-19-1.µm	UAGCGAAACCUUGAAGUCAAA	344	UUUGACUUUCAGGUUCGCUA	921	912-930
AV02847-19-1.µm	CAAGGAAAAGAAAUGGAAGA	345	UCUUCCAUUUUUCUUUCCUUG	922	1167-1185
AV02848-19-1.µm	AAGGAAAAGAAAUGGAAUGUA	346	UACUUCCAUUUUUCUUUCCUU	923	1168-1186
AV02849-19-1.µm	UGUCCAGGUUUUAUGAACUA	347	UAGUUCAUAAAACCUUGGACA	924	1207-1225
AV02850-19-1.µm	GGUUUAUGAACUGACGUUA	348	UAACGUCAGUUCAUAAAACC	925	1213-1231
AV02851-19-1.µm	UUUAUGAACUGACGUUACA	349	UGUAACGUCAGUUCAUAAA	926	1215-1233
AV02852-19-1.µm	GAACUGACGUUACAUCAUA	350	UAUGAUUGUAACGUCAGUUUC	927	1220-1238

AV02853-19-1.µm	AACUGACGUAUACAUCAUAA	351	UUUAUGAUGUAACGUCAGUU	928	1221-1239
AV02854-19-1.µm	GACGUUACAUCAUACACAA	352	UUGUGUAUGAUGUAACGUC	929	1225-1243
AV02855-19-1.µm	GGAGUAUUGUGGAACUUA	353	UUAAAGUCCACAAUACUCC	930	1398-1416
AV02856-19-1.µm	GUUUAUUGUGGAACUUAUAGA	354	UCUAUUAAGUUCACAAUAC	931	1401-1419
AV02857-19-1.µm	AAGGCAAAAGUGUCUUAAGA	355	UCUAAGAGCACUUUGCCUU	932	1464-1482
AV02858-19-1.µm	UCUGAAUCCGAGAUCCGAAUA	356	UAUCCGAVUCUGAUUCAGA	933	1508-1526
AV02859-19-1.µm	UCAGACAGUUCUGAAAUUA	357	UAAUUUCAGAACUGUCUGA	934	1871-1889
AV02860-19-1.µm	GUUUCGAAAUUGUGUUAAGA	358	UCUAACACAAUUCACAGAAC	935	1878-1896
AV02861-19-1.µm	UUCUGAAAUUGUGUUAAGAA	359	UUCUAACACAAUUCACAGAA	936	1879-1897
AV02862-19-1.µm	CUGAAAUUGUGUUAAGACGA	360	UCCGUCUAACACAAUUCACAG	937	1881-1899
AV02863-19-1.µm	UGAUAAAUUGUGUUAAGAA	361	UCUCAACACAAAUUUAUCA	938	2077-2095
AV02864-19-1.µm	CCUUUUUAUUCUGCUUCCGUUA	362	UAAACGAAGCAGAUAAAAAGG	939	2203-2221
AV02865-19-1.µm	UUUAUUCUGCUUCGUUUUUGA	363	UCAA AAAACGAAAGCAGAUAA	940	2207-2225
AV02866-19-1.µm	CUUGCUUCGUUUUUGCUAAA	364	UUUAGCAAAAAACGAAACAG	941	2211-2229
AV02867-19-1.µm	GCUUCGUUUUUUGCUAACAA	365	UUUGUAGCAAAAAACGAAAGC	942	2213-2231
AV02868-19-1.µm	CUUCGUUUUUUGCUAACAGA	366	UCUGUUAGCAAAAAACGAAAG	943	2214-2232
AV02869-19-1.µm	GAUUCUUUUUCUACGCAAAAA	367	UUUUUGCUGAAAGAAAGAUUC	944	2327-2345
AV02870-19-1.µm	AAUUCUUUUUCUACGCAAAACA	368	UGUUUGCUGAAAGAAAGAUU	945	2328-2346
AV02871-19-1.µm	UCAGCAAAACUCUAUAAAAGA	369	UCUUUAUAGAGUUUUGCUGA	946	2337-2355
AV02872-19-1.µm	AGCAAAACUCUAUAAAAGUUA	370	UAACUUUUAUAGAGUUUGCU	947	2339-2357
AV02873-19-1.µm	CAAACUUCUAUAAAAGUCCA	371	UGGAACUUUAUAGAGUUUG	948	2341-2359
AV02874-19-1.µm	CUAUAAGUUUCCUUCUUGAA	372	UUCAAGAGGAACUUUAUAG	949	2347-2365
AV02875-19-1.µm	CAGACAUUCUUUGAACUACAA	373	UUGUAGUUCAAAGAUUGUCUG	950	2397-2415
AV02876-19-1.µm	AUUCUUUGAACUACAUUCGAUA	374	UAUCGAUUGUAUUUCAAGAU	951	2402-2420
AV02877-19-1.µm	CUUUGAACUACAUUCGAUCAA	375	UUUGAUCGUAUUGAUUCAAG	952	2404-2422
AV02878-19-1.µm	UGAACUACAUUCGAUUCAUUA	376	UCAUGAUUCGAUUGAUUCA	953	2406-2424
AV02879-19-1.µm	CUCACAGGAAAUUACAUUUA	377	UAAA AUUGUAUUUCCUGUGAG	954	2534-2552
AV02880-19-1.µm	UUCCUUUUGCUGCGGAAAAAA	378	UUUUUCCCGCAGCAAAAGGAA	955	2568-2586
AV02881-19-1.µm	GUUCUUUCUUGUACUUUGCAAA	379	UUUGCAAGUAACAGAGAAGAC	956	2599-2617

AV02882-19-1.µm	UUCUGUUAUUGCAAGUUA	380	UAACUUGCAAGUAAACAGAA	957	2602-2620
AV02883-19-1.µm	GGAACUGUGUCAUGAGUCA	381	UGACUCAUGACACAGUCC	958	2637-2655
AV02884-19-1.µm	CAGCUACAGUGAGUUAAGGA	382	UCCUAAACUACUUGUAGCUG	959	2665-2683
AV02885-19-1.µm	GAGGAACAGUUCUCCAUUUGA	383	UCAUAUAGGAACUGUCCUC	960	2713-2731
AV02886-19-1.µm	GCAGAAAAACUUAACACAGAA	384	UUCUGUGUAAAGUUUUCUUGC	961	2804-2822
AV02887-19-1.µm	AUACAGGGCUUUUAAAAACA	385	UGUUUUAAAAAGCCCUGUAU	962	2835-2853
AV02888-19-1.µm	UGCUCAAUAAUUGUUGUCAA	386	UUGACAACAUUAUUGAGCA	963	2865-2883
AV02889-19-1.µm	AUAAUUGUUUGCAUCCAUUA	387	UAAUUGG AUGACAACAUAU	964	2871-2889
AV02890-19-1.µm	AUGUUUGCAUCCAUUUUGCA	388	UGCAAAUUGGAUGACAACAU	965	2874-2892
AV02891-19-1.µm	CAUUUUGCUUGGAGAUUGAAA	389	UUUCAUCCCAAGCAAAUG	966	2885-2903
AV02892-19-1.µm	UUUGCUUGGAGAUUGAAGAA	390	UUCUUCAUUCUCCAAGCAAA	967	2887-2905
AV02893-19-1.µm	UCAAAAGCAGUGUUUACCUA	391	UAGGUAAACACUGCUUUUGA	968	3013-3031
AV02894-19-1.µm	AAGCAGUGUUUUAACCUGAAA	392	UUUCAGGUAAAACACUGCUU	969	3016-3034
AV02895-19-1.µm	UAGAGGCUAUAAACCUACUA	393	UAGUAGGUUAUAGCCUCUA	970	3097-3115
AV02896-19-1.µm	AAAAUAAACCUUUUCAAGAGA	394	UCUCUUUGAAAAGGUUAUUUU	971	3141-3159
AV02897-19-1.µm	GCAGCAGUUUUUCUAUGAAA	395	UUUCAUUGAGAAACUGCUGC	972	3164-3182
AV02898-19-1.µm	AGCACUCACAUUUUGGAUGA	396	UCAUCCAAAUUGUGAGUGCU	973	3202-3220
AV02899-19-1.µm	ACAUUUUGAUUGCUUGGAAA	397	UUUCACAGCAUCCAAAUUGU	974	3209-3227
AV02900-19-1.µm	CUUGUGAAGCUUUUGUUCUA	398	UAGACACAAAAGCUUCACAG	975	3220-3238
AV02901-19-1.µm	UGUGAAAGCUUUUGUUCUA	399	UAAGACACAAAAGCUUCACA	976	3221-3239
AV02902-19-1.µm	GAAGCUUUUGUUCUUCUA	400	UAAAGAAGACACAAAAGCUUC	977	3224-3242
AV02903-19-1.µm	AGCUUUUGUUCUUCUUA	401	UGAAAAGAAGACACAAAAGCU	978	3226-3244
AV02904-19-1.µm	CAGUUUUGCAUUUUGAGUUA	402	UAAUCUCCAUAUUGCAAAACUG	979	3255-3273
AV02905-19-1.µm	AGUUUUGCAUUUUGAGUUUA	403	UAAAACUCCAUAUUGCAAAACU	980	3256-3274
AV02906-19-1.µm	GUUUUGCAUUUUGGAUUUUA	404	UUAAAACUCCAUAUUGCAAAAC	981	3257-3275
AV02907-19-1.µm	UCAGAUUGAGUCUAGGAAGA	405	UUCUUCCUAGACUCAUCUGA	982	3308-3326
AV02908-19-1.µm	CCAUCAAAGAUUGCUUUUGAUA	406	UAUCAAAGCAUUCUUGAUGG	983	3400-3418
AV02909-19-1.µm	UCUAGACAUAUCUGAUACCA	407	UUGUAUUCAGAUUUGUCUAGA	984	3773-3791
AV02910-19-1.µm	CAGGUCCUUGUUAACAACAAA	408	UUUGUUUGUAACAGGACCUUG	985	3792-3810

AV02911-19-1.µm	CAACAAGUAAAUCCUCAUA	409	UAUGAGGAUUVACUUGUG	986	3804-3822
AV02912-19-1.µm	ACAAGUAAAUCCUCAUCAA	410	UUGAUGAGGAUUVACUUGU	987	3806-3824
AV02913-19-1.µm	ACUGGGGAGUUUCUUAUCAA	411	UUGAUGAAGAAACUCCCCAGU	988	3823-3841
AV02914-19-1.µm	CUGGGGAGUUUCUUAUCAUA	412	UAUGAUGAAGAAACUCCCCAG	989	3824-3842
AV02915-19-1.µm	UCUAUCAUCUUCUUCUCAUA	413	UAUGAAGGAAGAUUGAUGAGA	990	3834-3852
AV02916-19-1.µm	CUAUCAUUCUUCUUCUAUAA	414	UUAUGAAGGAAGAUUGAUGAG	991	3835-3853
AV02917-19-1.µm	CUUCCUUCUAUACCUCAAAA	415	UUUUUGAGGUUAUGAAGGAAG	992	3842-3860
AV02918-19-1.µm	ACCUCAAAACUGCAUUGAUGA	416	UCAUCAUGGCAGUUUUGAGGU	993	3852-3870
AV02919-19-1.µm	ACUUGCAUUGAUGUCCUGAAA	417	UUUCAGGACAUUCAUUGCAGU	994	3859-3877
AV02920-19-1.µm	AAAUCCUGCUUUUAGUCCGAA	418	UUUGACUAAAGCAGGAUUUU	995	4037-4055
AV02921-19-1.µm	UGGCAACUGUUUUUGUUUCA	419	UGAACACACAACAGUUUGCCA	996	4065-4083
AV02922-19-1.µm	GCAACUGUUUUUGUUUCAAAA	420	UUUGAACACACAACAGUUUGC	997	4067-4085
AV02923-19-1.µm	ACUGUUUUUGUUUCAACAAA	421	UUUGUUUGAACACACAACAGU	998	4070-4088
AV02924-19-1.µm	CUUGUUUUUGUUUCAACAAUA	422	UAUUUUUGAACACACAACAG	999	4071-4089
AV02925-19-1.µm	CAACAUUUUUGUAAAGACUA	423	UAGUCUUCAACAUAUUUGUUG	1000	4082-4100
AV02926-19-1.µm	AACAUAUUUUUGAAGACUCA	424	UGAGUCUUUCAACAUAUUUGUU	1001	4083-4101
AV02927-19-1.µm	GUUGAAAGACUCUCUUUGGA	425	UCCAAAGAGAGUCUUCUCAAAC	1002	4090-4108
AV02928-19-1.µm	AAAGAACCUGGACAGAUAAA	426	UUUAUCUUGCACGGUUUCUUU	1003	4372-4390
AV02929-19-1.µm	CCGUGCAGAUAAAGAAUUGCA	427	UGCAUUCUUAUUCUGCACGG	1004	4378-4396
AV02930-19-1.µm	AGAUAAAGAAUUGCUAUUCAA	428	UUGAUUAAGCAUUCUUAUUCU	1005	4384-4402
AV02931-19-1.µm	UAAGAAUUGCUAUUUCAUAAA	429	UUUAUUGAAUUAAGCAUUCUUA	1006	4387-4405
AV02932-19-1.µm	AGAAUUGCUAUUUCAUAAUCA	430	UGAUUAUGAAUUAAGCAUUCU	1007	4389-4407
AV02933-19-1.µm	UAUUCAUUAUUCACAUUUGCA	431	UUGAAUUGUUAUUAUGAAUUA	1008	4396-4414
AV02934-19-1.µm	AUAAUUCACAUUCGUUUUGUA	432	UACAAACGAAUUGUUAUUAU	1009	4401-4419
AV02935-19-1.µm	UCACAUUCGUUUUGUUUGAA	433	UUCAAAACAACGAUUGUGA	1010	4405-4423
AV02936-19-1.µm	ACAUUUCGUUUUGUUUGAACA	434	UUUUUCAAAACAACGAUUGU	1011	4407-4425
AV02937-19-1.µm	AUUUCGUUUUGUUUGAAACCUA	435	UAGUUUCAAAACAACGAUUGU	1012	4409-4427
AV02938-19-1.µm	UCGUUUUGUUUGAAACCUCA	436	UAGAGGUUCAAAACAACGA	1013	4411-4429
AV02939-19-1.µm	GUUUUGAAACCUUUUGUUAUA	437	UAUAAACAAGAGGUUCAAAC	1014	4417-4435

AV02940-19-1.µm	UUGAACCUUUGUUUAUAAA	438	UUUAUAACAAGAGUUCAA	1015	4419-4437
AV02941-19-1.µm	UGAACCUUUGUUUAUAAAA	439	UUUUUAACAAGAGGUUCA	1016	4420-4438
AV02942-19-1.µm	AACCUUUGUUUAUAAAAAGA	440	UUCUUUAUAACAAGAGGUU	1017	4422-4440
AV02943-19-1.µm	ACCUUUGUUUAUAAAAAGCA	441	UUCUUUUUAACAAGAGGU	1018	4423-4441
AV02944-19-1.µm	CUUUAAAAACAGUACACGAA	442	UUCGUGUACUGUUUUAAAG	1019	4440-4458
AV02945-19-1.µm	AGAAAGCAGUUUUAGAUUA	443	UAAUCUAAAAACUUGCUUCU	1020	4479-4497
AV02946-19-1.µm	AGCAGGUUUUAGAUUUUGCA	444	UGCAAAUUCUAAAAACCUGCU	1021	4482-4500
AV02947-19-1.µm	CAGUUACGGGUUAUUACA	445	UGUAAUUAAACCGUAACTUG	1022	4514-4532
AV02948-19-1.µm	AGUUACGGGUUAUUACUA	446	UAGUAAUUAAACCGUAACTU	1023	4515-4533
AV02949-19-1.µm	GUUAAAUUACUGUUCUUGA	447	UCAGAAGACAGUAAUUAAAC	1024	4523-4541
AV02950-19-1.µm	AUUACUUGUUCUUGGAUUUA	448	UAAUCCAGAAGACAGUAAU	1025	4527-4545
AV02951-19-1.µm	UCUUUCUGGAUUCAGAUCAA	449	UUGAUUCUGAAUCCAGAAGA	1026	4534-4552
AV02952-19-1.µm	UCAGGUUUUUUUUGGCUUA	450	UAAGCCAAUAAACACCUUGA	1027	4549-4567
AV02953-19-1.µm	GGUUUUUUUUUUGGCUUUUA	451	UACAAAGCCAAUAAAAACACC	1028	4552-4570
AV02954-19-1.µm	UUUAUUUGGCUUUUGAUUGA	452	UCAAUACAAGCCAAUAAAA	1029	4556-4574
AV02955-19-1.µm	UUUGGCUUUUGAUUGAAAACA	453	UGUUUCAUUAACAAGCCAA	1030	4560-4578
AV02956-19-1.µm	GGCUUUUGAUUGAAAAACAGA	454	UCUGUUUCAAUACAAGGCC	1031	4562-4580
AV02957-19-1.µm	AUCCUUUUUUUUUGGUUAA	455	UUACCAAGAAGAAAAAGAU	1032	4634-4652
AV02958-19-1.µm	UCUUUUUUUUUUUGGUUUA	456	UAUACCAAGAAGAAAAAGA	1033	4635-4653
AV02959-19-1.µm	UUUUUUUUUUUUUGGUUAUACA	457	UGUAAUUAACCAAGAAAGAAA	1034	4638-4656
AV02960-19-1.µm	ACUUAUCUUUAUGAACGCUAA	458	UUAGCGUUCAUAAAGAUAGU	1035	4654-4672
AV02961-19-1.µm	CUAUCUUUAUGAACGCUAUA	459	UAUAGCGUUCAUAAAGAUAG	1036	4655-4673
AV02962-19-1.µm	AUCCUUAUGAACGCUAUCAA	460	UUGAUUAGCGUUCAUAAAGAU	1037	4657-4675
AV02963-19-1.µm	UCUUUAUGAACGCUAUCAUUA	461	UAUGAUUAGCGUUCAUAAAGA	1038	4658-4676
AV02964-19-1.µm	UUUAUGAACGCUAUCAUUCA	462	UGAAUUGAUAGCGUUCAUAA	1039	4660-4678
AV02965-19-1.µm	UAUGAACGCUAUCAUUCAA	463	UUGAAUUGAUUAGCGUUCAUUA	1040	4661-4679
AV02966-19-1.µm	UGAAACGCUAUCAUUCAAAAA	464	UUUUUGAAUUGAUUAGCGUUC	1041	4663-4681
AV02967-19-1.µm	CGCUAUCAUUCAAAAAACAGA	465	UCUGUUUUUGAAUUGAUUAGCG	1042	4667-4685
AV02968-19-1.µm	AUUCAAAAACAGAUUCAUUUA	466	UCAAUGAUUCUGUUUUUGAAU	1043	4674-4692

AV02969-19-1.µm	CAAAACAGAUCAUUGGAAA	467	UUUCCAUGAUCUGUUUG	1044	4677-4695
AV02970-19-1.µm	AACAGAUCAUUGGAUUA	468	UGAAUUBCCAUAUGAUCUGUU	1045	4680-4698
AV02971-19-1.µm	ACAGAUCAUUGGAUUBCCA	469	UGGAUUBCCAUAUGAUCUGU	1046	4681-4699
AV02972-19-1.µm	UGGAUUBCCUAAAAUUA	470	UAUGAUUUUAGGAUUBCCA	1047	4690-4708
AV02973-19-1.µm	UUCUAAAAAUCAUUBCAGCA	471	UGCUGAAUGAUUUUAGGAA	1048	4695-4713
AV02974-19-1.µm	UCCUAAAAAUCAUUBCAGCUA	472	UAGCUGAAUGAUUUUAGGA	1049	4696-4714
AV02975-19-1.µm	CUCCUUUGUAUUAAGAGGAA	473	UUCCUUAUAUACAAGAG	1050	4790-4808
AV02976-19-1.µm	AGGAACAUAUAAGCUGAA	474	UUCAGCUUUUUAUUUGUCCU	1051	4804-4822
AV02977-19-1.µm	GUUGCAUUGUUAACUGAGAA	475	UUCUCAGUAACAUUGACAC	1052	4859-4877
AV02978-19-1.µm	AUCAGGUGUUGGAGAUUA	476	UACAUCUCCAACACCUGAU	1053	4890-4908
AV02979-19-1.µm	UGUUGGAGAUUGUUAUUA	477	UGAAUGAACAUUCUCCAACA	1054	4896-4914
AV02980-19-1.µm	ACAUCAUUCCUCCCAUUGUA	478	UACAUBGGGAGGAUUGAUUGU	1055	4980-4998
AV02981-19-1.µm	GAUUGCACAUUGACUCUCAA	479	UUGAGAGUCAAUUGUGCAUC	1056	5011-5029
AV02982-19-1.µm	CACAUUGACUCUCAUGAAA	480	UUUCAUGAGAGUCAUUGUG	1057	5015-5033
AV02983-19-1.µm	CAUUGACUCUCAUGAAGCA	481	UGCUUCAUGAGAGUCAUUG	1058	5017-5035
AV02984-19-1.µm	CUUGGAGUGUUAUAUACAA	482	UUGUAUUUAACACUCCAAG	1059	5036-5054
AV02985-19-1.µm	UUGGAGUGUUAUAUACAUUA	483	UAUGUAUUUAACACUCCAAG	1060	5037-5055
AV02986-19-1.µm	UACGGAUUAUUGUUCGUCAA	484	UUGACGAACAUAUACUCCGUA	1061	5103-5121
AV02987-19-1.µm	UGAGCACUGUUAACUUGUA	485	UACAGUUGAACAGUGCUCA	1062	5142-5160
AV02988-19-1.µm	UUUGAGGUGUUCUGAUUUA	486	UGAAAUCAAGAAUCCUCAA	1063	5182-5200
AV02989-19-1.µm	AUUUCCCAAGUCAACUGAAA	487	UUUCAGUUGACUGGGAUUAU	1064	5195-5213
AV02990-19-1.µm	AACUGAAGAUUAUUGUUCUA	488	UAGAACAUAUUCUUCAGUU	1065	5206-5224
AV02991-19-1.µm	UGAAGAUUAUUGUUCUUA	489	UGAAGAAACAUAUUCUUA	1066	5209-5227
AV02992-19-1.µm	AUAUUGUUCUUCUUCGUAA	490	UUACGAGAAAGAAACAUAUUAU	1067	5214-5232
AV02993-19-1.µm	UGUUCUUUUUCUGUAUUA	491	UUGAUUAAGAGAAAGAACAA	1068	5218-5236
AV02994-19-1.µm	GAUUAUUGCCAGAGAAACA	492	UGUUAUUGUUGGCAAUUUC	1069	5344-5362
AV02995-19-1.µm	GAAAGAAACAUAUUAAGGA	493	UCCUUGAAAUUGUUUUCUUC	1070	5354-5372
AV02996-19-1.µm	AAGAAACAUAUUAAGGUA	494	UACCUUGAAAUUGUUUUCU	1071	5355-5373
AV02997-19-1.µm	UUUCAAGGUUUCUAUUA	495	UGUAUUAAGAAACCUUGAAA	1072	5364-5382

AV02998-19-1.µm	AGGUUUCUAAUACAACUGA	496	UCAGUUGUAUAGAACC	1073	5369-5387
AV02999-19-1.µm	UUUGUAAUUCUUUAGAAGA	497	UCUUUCAAAGAUAACCA	1074	5388-5406
AV03000-19-1.µm	GGUAAUUCUUUUAGAAGACA	498	UGUCUUUAAAAAGAAUACC	1075	5390-5408
AV03001-19-1.µm	GUAAUUCUUUAGAAGACAA	499	UUUGCUUCUAAAAAGAAUAC	1076	5391-5409
AV03002-19-1.µm	AGAAAGACAUUGUUACAATA	500	UUUUUAAACAUAUGUCUUU	1077	5401-5419
AV03003-19-1.µm	GACAUUGUUACAATAACAGA	501	UUCUUUUUUUAACAUAUGUC	1078	5405-5423
AV03004-19-1.µm	GCAGCAACAUACUUUCUAA	502	UUAGAAGUAUUGUUGCUGC	1079	5443-5461
AV03005-19-1.µm	CAACAUACUUUCUAAUUGCA	503	UGCAAUAGAAGUAUUGUUU	1080	5447-5465
AV03006-19-1.µm	AACAUACUUUCUAAUUGCCA	504	UGGCAUAGAAGUAUUGUU	1081	5448-5466
AV03007-19-1.µm	CACUUCUAAUUGUUCUGAA	505	UUCAGACACAUUAGCAGUG	1082	5478-5496
AV03008-19-1.µm	GCUAAUUGUUCUGAUCCAA	506	UUUGAUUCAGACACAUUAGC	1083	5482-5500
AV03009-19-1.µm	AGCACAAAAGUUAUUAUUA	507	UACUAAAGUAACUUUUGUGCU	1084	5738-5756
AV03010-19-1.µm	GCACAAAAGUUAUUAUUA	508	UGACUAAAGUAAACUUUUGUGC	1085	5739-5757
AV03011-19-1.µm	AGCCAAACUUUGGAUUGUA	509	UCCACAUUCCAAAGUUUGCU	1086	5794-5812
AV03012-19-1.µm	CUUUGAAUUGUGCAUUAAGA	510	UUCUAAUUGCACAUAUCCAAAG	1087	5801-5819
AV03013-19-1.µm	GCAUUAAGAGAAAUAGUACA	511	UGUACUAAUUCUUAUUGC	1088	5811-5829
AV03014-19-1.µm	CUCAUUCUUCUUCUGUGUA	512	UAUCACAGAAAGAGAAUGAG	1089	5840-5858
AV03015-19-1.µm	UUCUCUUUCUGUGAUUAUGA	513	UCAUAAUUCACAGAAAGAGAA	1090	5844-5862
AV03016-19-1.µm	UUCUCUUUCUGAUUAUUGUA	514	UACAUAUUCACAGAAAGAGA	1091	5845-5863
AV03017-19-1.µm	UUUCUGUAAUUAUGUCUGUA	515	UACAGACAUAAUCCACAGAA	1092	5849-5867
AV03018-19-1.µm	CUUGUAAUUAUGUCUGCAA	516	UUGACAGACAUAAUCCACAG	1093	5851-5869
AV03019-19-1.µm	GUUGAUUAUGUUCUUCAGAA	517	UUCUGACAGACAUAAUCCAC	1094	5853-5871
AV03020-19-1.µm	GAUUAUUGUUCUGUCAGACA	518	UGUUUCUGACAGACAUAAUCC	1095	5855-5873
AV03021-19-1.µm	GUCAAGAACCUCCAUGACUA	519	UAGUCAUUGAGGUUUCUGAC	1096	5865-5883
AV03022-19-1.µm	UAACGUUGGCUCAUUGUAAA	520	UUUACAUAUGAGCCACGUUA	1097	5892-5910
AV03023-19-1.µm	CGUUGGCUCAUUGUAAAUA	521	UGAUUUUACAUAUGAGCCAG	1098	5895-5913
AV03024-19-1.µm	GGCUCAUUGUAAAUAUCACAA	522	UUUGAUUUUACAUAUGAGCC	1099	5898-5916
AV03025-19-1.µm	CAUUGUAAAUAUCACAUUCA	523	UUGAUUGUGAUUUUAACAUG	1100	5902-5920
AV03026-19-1.µm	UAAAUCACAUUCACAAGAUCA	524	UGAUUUUUGAAUUGUUAUUA	1101	5907-5925

AV03027-19.1.µm	CAGUCUCGUUGUGAAAACA	525	UGUUUUUCACACGAGACUG	1102	6017-6035
AV03028-19.1.µm	GAAGAAAACUCUVCAGUGA	526	UCACUGAAGAGUUUUUCUUC	1103	6055-6073
AV03029-19.1.µm	GGCUGCAAAUUBUACAGAGA	527	UCUCUGUAAAUUUUGCAGCC	1104	6205-6223
AV03030-19.1.µm	CUGCAAAUUBUACAGAGCAA	528	UUGCUCUGUAAAUUUUGCAG	1105	6207-6225
AV03031-19.1.µm	UCAACAGAAUCCAGGAUUA	529	UAUUCCUGGAUUCUGUUUA	1106	6252-6270
AV03032-19.1.µm	ACACCAAAAGCUCUUAUUA	530	UGAAUAGAGCCUUUGGUGU	1107	6298-6316
AV03033-19.1.µm	AUCCAAGACUCACUUAAGUA	531	UACUAAAGUGAGUCUUGCAU	1108	6344-6362
AV03034-19.1.µm	CGUUCAUUCUUGUCAAAUCA	532	UGAUUUUGACAAGAUUGAACG	1109	6445-6463
AV03035-19.1.µm	UGGACCAGGUCAGAUUCUA	533	UAGAAUUCUGACCUGGUCCA	1110	6470-6488
AV03036-19.1.µm	UCCGAUUUCCUGCUGAAAGAA	534	UUUUUCCAGCAGGAUUCGGA	1111	6517-6535
AV03037-19.1.µm	UCCUUGCUGAAGAUUUGAAA	535	UUUCAUUAUCUUACAGCAGGA	1112	6523-6541
AV03038-19.1.µm	AGGGAUUGAGUGAAAUUUUA	536	UGAAAUUUUCACUCAUCCCU	1113	6598-6616
AV03039-19.1.µm	GGAUUGAGUGAAAUUUUCUGA	537	UCAGAAAUUUUCACUCAUCC	1114	6600-6618
AV03040-19.1.µm	GGAGCAAGUUGAUAUUGAUCA	538	UGAUCAUUCACACUUGCUCC	1115	6750-6768
AV03041-19.1.µm	GGAAAUAGAUUCCAAACACA	539	UGUGUUUGGAUUCUACUUC	1116	7177-7195
AV03042-19.1.µm	GUUGAGAUUGGUGCAGAAAAA	540	UUUUUCUGCCACCACUUCAC	1117	7224-7242
AV03043-19.1.µm	CUUGGGUCAUAAAAGGAAAA	541	UUUCCUUUAUUGACCCCAAG	1118	7270-7288
AV03044-19.1.µm	AGGAAGUCUUUUAAAGAGUA	542	UACUCCUUAAAAGACUUCU	1119	7473-7491
AV03045-19.1.µm	GGAAGUCUUUUAAAGAGUUA	543	UAACUCCUUAAAAGACUUC	1120	7474-7492
AV03046-19.1.µm	AGUCUUUUAAAGAGUUCUA	544	UAUGAACUCCUUAAAAGACU	1121	7477-7495
AV03047-19.1.µm	CUUUAAAGAGUUCUUA	545	UUAGAUGAACUCCUUAAAAG	1122	7480-7498
AV03048-19.1.µm	CGUACUCAGUUUUGAAGAAA	546	UUUCUUCAAAACUGAGUACG	1123	7526-7544
AV03049-19.1.µm	GUACUCAGUUUUGAAGAAAA	547	UUUUUCUUCAAAACUGAGUAC	1124	7527-7545
AV03050-19.1.µm	UACUCAGUUUUGAAGAAAA	548	UGUUUCUUCAAAACUGAGUA	1125	7528-7546
AV03051-19.1.µm	AGCAAGAGAUUUCAGCAAAA	549	UUUGCUUGAAUUCUUCUUGCU	1126	7809-7827
AV03052-19.1.µm	GCAAGAGAUUUCAGCAAUUA	550	UAUUUCUUUGAAUUCUUCUGC	1127	7810-7828
AV03053-19.1.µm	GAUUCAAGCAAUUGGUUCA	551	UGAAACCAUUGCUUGAAUUC	1128	7816-7834
AV03054-19.1.µm	AUUCAAGCAAUUGGUUCA	552	UUGAAACCAUUGCUUGAAU	1129	7817-7835
AV03055-19.1.µm	UUCAAGCAAUUGGUUCAAA	553	UUUGAAACCAUUGCUUGAA	1130	7818-7836

AV03056-19-1.µm	AAGCAUUGUUUCAAAAGA	554	UUUUUUGAAACCAUUGCUU	1131	7821-7839
AV03057-19-1.µm	CCACUCCUUGUUCCGAGUUA	555	UAAUCGCGAACAGAGUGG	1132	8149-8167
AV03058-19-1.µm	GCAUCAAUAUACAGAUUA	556	UCAUCUGUAUUAUUGAUGC	1133	8702-8720
AV03059-19-1.µm	CAUCAUAUAUACAGAUUA	557	UACAUCUGUAUUAUUGAUG	1134	8703-8721
AV03060-19-1.µm	CCCCCUCCAUUUUACCA	558	UGGUAAAUUGAUGGAGGGG	1135	8754-8772
AV03061-19-1.µm	AUCUGUUCUUUUUGAUA	559	UCUAUCAAAAAAGACAGAU	1136	9019-9037
AV03062-19-1.µm	UGUUUUUUUUUGAUA	560	UAUCCUAUCAA AAAAGACA	1137	9022-9040
AV03063-19-1.µm	AGGACAUCAUGAAACAAAG	561	UCUUUUUUUCAUUGUCCU	1138	9117-9135
AV03064-19-1.µm	UGUAUAAGGUGUUUCAGAA	562	UUCUGAAACACCUUAUACA	1139	9192-9210
AV03065-19-1.µm	ACGUGAAACCUUUUCCGCCA	563	UGGCAGAAAAAGGUUCACGU	1140	9405-9423
AV03066-19-1.µm	CCACAGACUUUCUACAGACA	564	UGUCUGUAAGAAAGUCUGUG	1141	9429-9447
AV03067-19-1.µm	CUGCUGACUUUGUUUACGAA	565	UUCGUAAACAAGUCAGCAG	1142	9530-9548
AV03068-19-1.µm	GCUGACUUUGUUUACGAAAA	566	UUUUUGUAAAAACAAGUCAGC	1143	9532-9550
AV03069-19-1.µm	CUGACUUUGUUUACGAAAA	567	UAUUUUCGUAAAAACAAGUCAG	1144	9533-9551
AV03070-19-1.µm	UGACUUUGUUUACGAAAAUGA	568	UCAUUUUCGUAAAAACAAGUCA	1145	9534-9552
AV03071-19-1.µm	UUUACGAAAUUGUCCACAAA	569	UUUGUGACAUUUUGUAAA	1146	9541-9559
AV03072-19-1.µm	CAUUCUCCCUUUUCUCUUA	570	UAAAGAGAGAAAGGAGAAUG	1147	10101-10119
AV03073-19-1.µm	CUUUUUUUUUUCUACAGAUUA	571	UAUCCUGAGAGAAAGAAAAGAG	1148	10114-10132
AV03074-19-1.µm	UAUUCAUUAUUCACAUUUGA	572	UCGAUUGUGAUUAUGAUA	1149	4396-4414
AV03077-19-1.µm	GGUCAGGUUUUCUUUUUA	573	UUAAAAAGCAGAAACCUGACC	1150	31-49
AV03078-19-1.µm	GCCUUCAUAGCGAAACCUGA	574	UCAGGUUCCGUUAUGAAGGC	1151	905-923
AV03079-19-1.µm	ACCAAGACCACAUAUUGUUA	575	UCAACAUUUGUGUCUUUGU	1152	1245-1263
AV03080-19-1.µm	GGUUUAUUGAACUGACGUUA	576	UAAAGUCAGUUUCAUAAACC	1153	1213-1231
AV03081-19-1.µm	ACGGAGUAUUGUUCGUCACA	577	UGUGACGAAACAUACUCCGU	1154	5104-5122
AV03082-19-1.µm	CACAUUUCGUUUUUUGAAAA	578	UUUCAAAACAAGCAAAUUGUG	1155	4406-4424
AV03083-19-1.µm	UGAUUUUCCAGUUCACUGA	579	UCAGUUUGACUGGGAUAUCA	1156	5193-5211
AV03084-19-1.µm	AAUUCAGUCUCUGUUUGGAA	580	UUCAACAACGAGACUCAAUU	1157	6013-6031
AV03085-19-1.µm	CGACAUCCUUUGCUUGGA	581	UCGACAAGCAAGGAUUGUCG	1158	6169-6187
AV03086-19-1.µm	GCUAGCUCCAUUGCUUAAGA	582	UCUUAAAGCAUUGGAGCUAGC	1159	6577-6595

AV03087-19-1.µm	GACUUGUUUACGAAAUUGUA	583	UACAUUUUCGUAAACAAGUC	1160	9535-9553
AV03088-19-1.µm	AUAGAACAAAGUCAUCGGAA	584	UUCCGAVGACUUTUGUCAU	1161	9125-9143
AV03089-19-1.µm	AACUUCAGACCCCUAAUCCA	585	UGGAUUAGGGUCUCUGAAGUU	1162	8956-8974
AD03542.µm	GGGUGCCAAGAUGGACGGCCA	3397	UGGCCGUCCAUCUUGGACCC	3449	11-31
AD03543.µm	GCCUUGAAAAAGCUUGAUGAGA	3398	UCUUCAUCAGCUUUUCCAGGC	3450	153-173
AD03544.µm	CAAAAGCUUGAUGAAGCCUUA	3399	UAAAGCCUUCAUCAAGCUUUUG	3451	158-178
AD03545.µm	GCGGCUUGGCGUGAGGAGCCA	3400	UGGCUCCUCAGCCACAGCCGC	3452	377-397
AD03546.µm	GUGCACCGACCAAGAAAAAGAA	3401	UUCUUUUUUUGGUCGGUGCAC	3453	398-418
AD03547.µm	GCCGACCAAAAGAAAGAACTUA	3402	UAAGUUUCUUUCUUUGGUCGGC	3454	402-422
AD03548.µm	GCGACCAAAAGAAAGAACTUUA	3403	UAAAGUUUUUUUUUUUGGUCGC	3455	403-423
AD03549.µm	CACCAAAAGAAAGAACTUUCAA	3404	UUGAAAGUUUUUUUUUUUGGUG	3456	405-425
AD03550.µm	GCCAAAGAAAGAACTUUCAGA	3405	UCUGAAAGUUUUUUUUUUUGGC	3457	406-426
AD03551.µm	CAUUCAUUGUCUGACAUAUUA	3406	UAUAUUUGUCAGACAUAUGAUUG	3458	445-465
AD03552.µm	CUUCUGACAUAUUGUGAAAAACA	3407	UGUUUUUCACAUUAUUGUCAGAG	3459	453-473
AD03553.µm	GUUUUGAUGGAUUCUUAUUCUA	3408	UAAGAUUAGAUAUCCAUCAAAC	3460	615-635
AD03554.µm	CAUUCUAAUUCUUCCAAGGUUA	3409	UAAACUUUGGAAGAUAUAGAAUG	3461	623-643
AD03555.µm	GGUUCCCAAAAUAUUAUGGCUUA	3410	UAAGCCAUUAUUUUUGGGAACC	3462	838-858
AD03556.µm	GUUGUUAAAAGGCCUUCAUAGA	3411	UCUAUUGAAGGCCUUUAACAAC	3463	895-915
AD03557.µm	GAUAGCGAACCUGAAGUCAAA	3412	UUUGACUUUCAGGUUCCGCUAUC	3464	910-930
AD03558.µm	GUGAACUUGACGUUACAUCAUUA	3413	UAUGAUUGUAACGUCAGUUCAC	3465	1218-1238
AD03559.µm	GGAACUUGACGUUACAUCAUAA	3414	UUUAUGAUUGUAACGUCAGUUC	3466	1219-1239
AD03560.µm	GUUCGAAAAUUGUUGUUAAGACGA	3415	UCGUCUAAACACAUAUUUCAGAC	3467	1879-1899
AD03561.µm	GGCUUCCGUUUUUUGCUAAACAGA	3416	UCUGUUUAGCAAAAAACGAAGCC	3468	2212-2232
AD03562.µm	GCAUUCUUUGAACUACAUCCGAUA	3417	UAUCCGAVUGUAGUUUCAAGAUCC	3469	2400-2420
AD03563.µm	GUUCUUUGAACUACAUCCGACAA	3418	UUGAUCCGAVUGUAGUUUCAAGAC	3470	2402-2422
AD03564.µm	GCCUCACAGGAAAUUACAUAUUA	3419	UAAAUUGUAUUUUCCUGUGAGGC	3471	2532-2552
AD03565.µm	GCCUCACAGGAAAUUACAUAUUA	3420	UAAAUUGUAUUUUCCUGUGAGGC	3472	2532-2552
AD03566.µm	GUAGAGGAACAGUUCUUAUUGA	3421	UCAAUAGGAACUGUUUCCUCAC	3473	2711-2731
AD03567.µm	GAAAGCAGUGUUUUAACCUGAAA	3422	UUUCAGGUAAACACUCUGCUUUC	3474	3014-3034

AD03568.µm	GACUGGGGAGUUUUCUAVCAUA	3423	UAUGAUAAGAAACUCCCCAGUC	3475	3822-3842
AD03569.µm	GUUCUCCUUCAUUACCUCAAAA	3424	UUUUUGAGGUUAUGAAGGAAGAC	3476	3840-3860
AD03570.µm	GAACUGUUUGUGUUCACAACAAA	3425	UUUGUUUGAAACACAAAACAGUUC	3477	4068-4088
AD03571.µm	CCUAVUCCAUAAUCCACAUUCGA	3426	UCGAAUUGGAUUAUAGAUAUAGG	3478	4394-4414
AD03572.µm	GCAUAAUCCACAUUCCGUUUUA	3427	UACAACGGAUUGUAUUAUUGC	3479	4399-4419
AD03573.µm	GUUCGUUUUGUUUGAACCUCUA	3428	UAGAGGUUCAAAACAAGCAACGAAC	3480	4409-4429
AD03574.µm	GGAACCUUCUUUUUAUAAAAAGA	3429	UCUUUUUAUAACAAGAGGUUCC	3481	4420-4440
AD03575.µm	GUCAGUUACGGGUUAUUAUACA	3430	UGUAAUUUAACCCGUAAACUIGAC	3482	4512-4532
AD03576.µm	GCAGUUACGGGUUAUUAUACUA	3431	UAGUAAUUUAACCCGUAAACUIGC	3483	4513-4533
AD03577.µm	GAUUUACUGUCUUCUGGAUUUA	3432	UAAUCCAGAAAGACAGUAUUAUUC	3484	4525-4545
AD03578.µm	GGUCUUCUGGAUUUCCAGAUCAA	3433	UUGAUCCUGAAUCCAGAAAGACC	3485	4532-4552
AD03579.µm	GUUGCUUUUGUAUUUGAAACAGA	3434	UCUGUUUCCAUAUACAAGCCAC	3486	4560-4580
AD03580.µm	GAUUCUUUAUGAACCGCUAUCAUA	3435	UAUGAUAAGCGUUCAUUAAGAUUC	3487	4656-4676
AD03581.µm	GUUGGAUUUCCUAAAAUCAUA	3436	UAUGAUUUUAAGGAUUUCCAAC	3488	4688-4708
AD03582.µm	GUUCCUAAAAAUCAUUCAGCUA	3437	UAGCUGAUUGAUUUUUAAGGAAC	3489	4694-4714
AD03583.µm	GAGAAUUUUGCCAGAAAGAAACA	3438	UGUUUUCUUCUGGCAAAUUCUC	3490	5342-5362
AD03584.µm	GAGAAAGAAACAUUUUCCAAGGA	3439	UCCUUGAAGAAUUGUUUCUUCUC	3491	5352-5372
AD03585.µm	GACUUUGGAUUGUGCAUUAAGAA	3440	UUCUAUUUGACAUUCCCAAGUC	3492	5799-5819
AD03586.µm	GUUGUCAGAACCUCCAUUGACUA	3441	UAGUCAUUGGAGGUUUCUGACAC	3493	5863-5883
AD03587.µm	CUUGCUCAUUUGUAAAUCCACAA	3442	UUUGUAUUUACAUAUAGGCCAG	3494	5896-5916
AD03588.µm	GUGAAGAAAAACUCCUCCAGUGA	3443	UCACUGAAGAGUUUUUCUUCAC	3495	6053-6073
AD03589.µm	GUUGCUCGCAAAUUVUACAGAGA	3444	UCUCUGUAAAUUVUCCAGCCAC	3496	6203-6223
AD03590.µm	CGCUGCAAAAUUVUACAGAGCAA	3445	UUGCUCUGUAAAUUVUCCAGCG	3497	6205-6225
AD03591.µm	GCAAGCAAUUGUUUCAAAGAA	3446	UUUUUUUGAAACCAUUGCUUUGC	3498	7819-7839
AD03592.µm	CUAUCUUGUUUUUUUGAUAAGA	3447	UCUAUCAAAGAAAGAACAGAUAG	3499	9017-9037
AD03593.µm	GCUUGUUUUUUUUUGAUAAGAUUA	3448	UAUCCUAUCAAAGAAAGACAGC	3500	9020-9040

Table 1A: Unmodified HTT RNAi agent antisense strand and sense strand sequences of BW5-2a transcript (SEQ ID NO:7, combination of exon1 and retained in the truncated 1-2710 of SEQ ID NO:5 (intron 1)) targeting HTT dsRNA Agents. All sequences shown 5' to 3' direction. Duplex AV# are the number assigned to the duplex of the two strands in the same row in the table.

Duplex AV#	Sense Strand	SEQ ID NO	Antisense Strand	SEQ ID NO	Position in SEQ ID NO:7	Position in NM_001388492.1
AV02733.µm	GCCGCUCAGGUCUUCGCUUUA	1163	UAAAAGCAGAACCUGAGCGGC	1626	28-48	28-48
AV02735.µm	GGACGGCCGCUCAGGUCUGA	1164	UCAGAACCUAGAGCGGCCGUC	1627	23-43	23-43
AV02739.µm	GGUUCUGCUUUUACCUGCCGA	1165	UCCGCAGGUAAAAGCAGAACCC	1628	36-56	36-56
AV02743.µm	CCCGGACGGGUCCAAAGUA	1166	UCAUCUUUGAACCCGUCGCCGG	1629	4-24	4-24
AV02744.µm	GGGGUCCAAGAUUGAGCGCCA	1167	UGGCCGUCCAUUCUUGGACCCC	1630	11-31	11-31
AV02745.µm	GGGACGGCCGCUCAGUUCUA	1168	UAGAACCUAGAGCGGCCGUC	1631	22-42	22-42
AV02746.µm	CCCGCUCAGGUCUUCGUUUUA	1169	UAAAAGCAGAACCUGAGCGGG	1632	28-48	28-48
AV02747.µm	GGCUCAGGUCUUCGUUUUACA	1170	UGUAAAAGCAGAACCUGAGCC	1633	30-50	30-50
AV02748.µm	CCUCAGGUCUUCGUUUUACCA	1171	UGGUAAAAGCAGAACCUGAGG	1634	31-51	31-51
AV02749.µm	GUCAAGUUCUGCUUUUACCUA	1172	UAGGUAAAAGCAGAACCUGAC	1635	32-52	32-52
AV02750.µm	GCAAGUUCUGCUUUUACCUGA	1173	UCAGGUAAAAGCAGAACCUGC	1636	33-53	33-53
AV02751.µm	GAGGUUCUGCUUUUACCUGCA	1174	UGCAGGUAAAAGCAGAACCUC	1637	34-54	34-54
AV02752.µm	GGGUUCUGCUUUUACCUGCCA	1175	UCCGAGGUAAAAGCAGAACC	1638	35-55	35-55
AV02753.µm	CGUUCUGCUUUUACCUGCCGA	1176	UCCGCAGGUAAAAGCAGAACG	1639	36-56	36-56
AV02754.µm	GUUCUUUUUACCUGCCGCCAA	1177	UUGGGCCGCAGGUAAAAGCAC	1640	40-60	40-60
AV02755.µm	GCAGAGCCCCCAUUCAUUGCCA	1178	UGGCAUUGAAUUGGGGCUUGC	1641	57-77	57-77
AV02756.µm	GGCCCCAUUCAUUGCCCCGA	1179	UCCGGGGCAAUUGAUGGGGCC	1642	61-81	61-81
AV02757.µm	CCCCCAUUCAUUGCCCCGUA	1180	UACCGGGGCAAUUGAUGGGGG	1643	62-82	62-82
AV02758.µm	GGCCCCGUGUGCUGAGCGCGCA	1181	UCCGCCGUCAGCACCCGGGGCC	1644	73-93	73-93
AV02759.µm	CGUGCUGAGCGCGCGCGCGAA	1182	UUCCGGCGCGCCGUCAGCACG	1645	79-99	79-99
AV02760.µm	CGCGCCGCGAGUCGGCCCCGAA	1183	UUCGGGCGGACUCCGGCGCG	1646	89-109	89-109
AV02761.µm	GGCCCGCAGAGUCGGCCCGAGGA	1184	UCCUCGGGCGCGACUCCGGGCC	1647	91-111	91-111
AV02762.µm	GGGGCCGAGGCCUCCGGGGAA	1185	UUCCCCGAGGCCUCGCGGCC	1648	101-121	101-121
AV02763.µm	CGCCCGAGGCCUCCGGGGACA	1186	UGUCCCCGGAGGCCUCGCGCG	1649	102-122	102-122

AV02764.µm	GGAGGCCUCCGGGACUGCCA	1187	UGGCAGUCCCCGGAGGCCUCC	1650	106-126	106-126
AV02765.µm	GCUCCGGGAGACUGCCGUGCCA	1188	UGGCACGGCAGUCCCCGGAGC	1651	111-131	111-131
AV02766.µm	GCCGGGAGACUGCCGUGCCGGA	1189	UCCGGCACGGCAGUCCCCGGC	1652	113-133	113-133
AV02767.µm	GCUGCCGUGCCGGGGCGGAGA	1190	UCUCCCGCCCGGCACGGCAGC	1653	120-140	120-140
AV02768.µm	CGGCGGAGACCCGCCAUGGCA	1191	UGCCAUGGCGGUCUCCCGCCG	1654	131-151	131-151
AV02769.µm	CCGGGAGACCGCCAUUGGCGAA	1192	UUGGCCAUUGGCGGUCUCCCGG	1655	133-153	133-153
AV02770.µm	CGAGACCGCCAUUGGCGACCCA	1193	UGGGUCGCCAUUGGCGGUCUCG	1656	136-156	136-156
AV02771.µm	CACCGCCAUUGGCGACCCUGGA	1194	UCCAGGGUCGCCAUUGGCGGUG	1657	139-159	139-159
AV02772.µm	GAUGGCGACCCUUGGAAAAAGCA	1195	UGCUUUUCCAGGGGUCGCCAUC	1658	145-165	145-165
AV02773.µm	GGACCCUGGAAAAAGCUGAUGA	1196	UCAUCAGCUIIUUCCAGGGUCC	1659	150-170	150-170
AV02774.µm	CACCCUGGAAAAAGCUGAUGAA	1197	UUCAUCAGCUIIUUCCAGGGUG	1660	151-171	151-171
AV02775.µm	GCCCUUGGAAAAAGCUGAUGAAA	1198	UUUCAUCAGCUIIUUCCAGGGC	1661	152-172	152-172
AV02776.µm	GCCUGGAAAAAGCUGAUGAAGA	1199	UCUUCAUCAAGCUIIUUCCAGGC	1662	153-173	153-173
AV02777.µm	GCUGGAAAAAGCUGAUGAAGGA	1200	UCCUUCAUCAAGCUIIUUCCAGC	1663	154-174	154-174
AV02778.µm	GUUGAAAAAGCUGAUGAAGGCA	1201	UGCCUUCAUCAAGCUIIUUCCAC	1664	155-175	155-175
AV02779.µm	CGAAAAAGCUGAUGAAGGCCUA	1202	UAGGCCUUCAUCAAGCUIIUUCG	1665	157-177	157-177
AV02780.µm	CAAAAAGCUGAUGAAGGCCUUA	1203	UAAAGCCUUCAUCAAGCUIIUUG	1666	158-178	158-178
AV02781.µm	GAAAGCUGAUGAAGGCCUUCGA	1204	UCGAAGGCCUUCAUCAAGCUIUC	1667	160-180	160-180
AV02782.µm	GAGCUGAUGAAGGCCUUCGAA	1205	UUCGAAAGCCUUCAUCAAGCUC	1668	161-181	161-181
AV02783.µm	CCUGAUGAAGGCCUUCGAGUA	1206	UACUCGAAGGCCUUCAUUCAGG	1669	163-183	163-183
AV02784.µm	GGAUGAAGGCCUUCGAGUCCA	1207	UGGACUCCGAAGGCCUUCAUUCC	1670	165-185	165-185
AV02785.µm	CAAGGCCUUCGAGUCCCUCAA	1208	UUAGGGGACUCCGAAGGCCUUG	1671	169-189	169-189
AV02786.µm	GUUCGAGUCCCUCAAGUCCUA	1209	UAGGACUUGAGGGACUCCGAAC	1672	175-195	175-195
AV02787.µm	CAGUCCCUCAAGUCCCUUCCAA	1210	UUUGAAGGACUUGAGGGACUUG	1673	179-199	179-199
AV02788.µm	GGUCCCUCAAGUCCCUUCCAGA	1211	UCUGGAAGGACUUGAGGGACC	1674	180-200	180-200
AV02789.µm	CUCCCUCAAGUCCCUUCCAGCA	1212	UGCUUGGAAGGACUUGAGGGAG	1675	181-201	181-201
AV02790.µm	GCCCUCAAGUCCCUUCCAGCAA	1213	UUUCUGGAAGGACUUGAGGGC	1676	182-202	182-202
AV02791.µm	GCCUCAAGUCCCUUCCAGCAGA	1214	UCUGCUUGGAAGGACUUGAGGC	1677	183-203	183-203

AV02792.µm	GCUCAAGUCCUUCACGACGA	1215	UGCUGCUGGAAGACUUGAGC	1678	184-204	184-204
AV02793.µm	GAGUCCUUCACGACGACGACAA	1216	UUGCUGCUGCUGGAAGGACUC	1679	188-208	188-208
AV02794.µm	CCCUCCUACAGCUUCCUCACAGA	1217	UGCUGAAGGAAGCUGAGGAGGG	1680	286-306	286-306
AV02795.µm	GCUCCUCAGCUCUCCUCAGCCA	1218	UGGCUGAGGAAGCUGAGGAGC	1681	287-307	287-307
AV02796.µm	GCGCCGACAGGACACAGCCGCUA	1219	UAGCGGCUUGGCCUGCGCGCGC	1682	308-328	308-328
AV02797.µm	GGCAGGCACAGCCGCUGCUGA	1220	UCAGCAGCGGCUUGGCCUGCC	1683	312-332	312-332
AV02798.µm	GAGGCACAGCCGCUUGCUGCCA	1221	UGGCAGCAGCGGCUUGCCUC	1684	314-334	314-334
AV02799.µm	CGCACAGCCGCUUGCCUCA	1222	UGAGGACAGCAGCGGCUUGCG	1685	316-336	316-336
AV02800.µm	GGGCCCCGCUUGGCUUGAGGA	1223	UCCUCAGCCACAGCCGGGCC	1686	373-393	373-393
AV02801.µm	GCGGCUUGGCUAGGAGGCCA	1224	UGGCUCUCAGCCACAGCCGC	1687	377-397	377-397
AV02802.µm	CUGGCUAGGAGCCGCUGCAA	1225	UUGCAGCGGCUCCUCAGCCAG	1688	383-403	383-403
AV02803.µm	GGAGGAGCCGCUGCACCGACA	1226	UGUCGGUGCAGCGGCUCCUC	1689	388-408	388-408
AV03090.µm	CGACCCUGGAAAAAGCUGAU	1227	AUCAGCUCUUCCAAGGUCG	1690	150-170	150-170
AV03091.µm	GGGACGGGUCCAAGAUUGGA	1228	UCCAUCUUGGACCCGUC	1691	7-27	7-27
AV03092.µm	UGGCGACCCUGGAAAAAGCU	1229	AGCUCUUGCCAGGGUCGCCA	1692	147-167	147-167
AV03093.µm	GCCGCGACGGGCUCCAAGAU	1230	AUCUUGGACCCGUC	1693	4-24	4-24
AV03094.µm	UGCCCCGGUGCUGAGCGGC	1231	GCCGCUCAGCACCGGGCA	1694	73-93	73-93
AV03095.µm	CGUGCCGGGCGGAGACCG	1232	CGGUCUCCCGCCCGGCACG	1695	125-145	125-145
AV03373.µm	UUUUAAACUGCGUUGUGAAGAA	1233	UUUCUACACAACGACAGUUAAAA	1696	777-797	
AV03374.µm	GGAUAGACAUAAUGCUUUUAGA	1234	UCUAAAAAGCAUUAUGUCAUCC	1697	923-943	
AV03375.µm	AUGACAUAAUGCUUUUAGGAA	1235	UUCCUAAAAAGCAUUAUGUCAU	1698	925-945	
AV03376.µm	UGACAUAAUGCUUUUAGGACA	1236	UGUCCUAAAAAGCAUUAUGUCA	1699	926-946	
AV03377.µm	AUGGGAGAUUUUCUUUUCCUAA	1237	UUAGGAAAAAGAAUUCUCCAU	1700	999-1019	
AV03378.µm	CCUAGUGGCACUUA AAAACAGA	1238	UCUGUUUUAAAGUGCCACUAGG	1701	1015-1035	
AV03379.µm	GAGGCUUCUCCUACAUUUGUA	1239	UGACAAUUGUAGGAAGAGCCUC	1702	1045-1065	
AV03380.µm	UUCCUACAUUUGUCAGGACAUUA	1240	UAUGUCCUGACAAUUGUAGGAA	1703	1052-1072	
AV03381.µm	UUUCAUUUAGUUCAUUGAUCAA	1241	UUGAUCAUGAACUAAAUUGAAA	1704	1071-1091	
AV03382.µm	CAUGAUCACGGGUGGUAGUAAA	1242	UUUACUACCAACCGUGAUCAUG	1705	1083-1103	

AV03383.µm	CACGGUGGUAGUAAACAGUA	1243	UAUCGUGUACUACCACCGUG	1706	1089-1109	
AV03384.µm	UAGUAAACACGALUUTUUAAGCAA	1244	UUGCUUAAAAUUCGUGUACUA	1707	1097-1117	
AV03385.µm	CUAAGAAGALUCUGCUCAUUA	1245	UUAGAUUGAGCAGAUUCUCUAG	1708	1121-1141	
AV03386.µm	AAGAGAUUCUGCUCAUUAAGA	1246	UCUUAAGAUAGAGCAGAUUCUCU	1709	1123-1143	
AV03387.µm	UCAUCUAAAGCCUAAAGUUGGUA	1247	UACCAACUUAAGGCUUAGAUGA	1710	1134-1154	
AV03388.µm	UGAGUUGUGGUGGUGCCAAGUAA	1248	UUACUUGGCAACCAACAUCUA	1711	1169-1189	
AV03389.µm	GUGAACUUAACGUGGUGAUUAA	1249	UUAAUACACACGUAAGUUCAC	1712	1194-1214	
AV03390.µm	AACUUAACGUGGUGAUUAAUGA	1250	UCAUUAUACACCACGUAAGUU	1713	1197-1217	
AV03391.µm	UUACGUGGUGAUUAAUAGAAAA	1251	UUUUCAUUAUUAUACACCAAGUAA	1714	1200-1220	
AV03392.µm	AUUAGGAAGAGUUGAUUUGAAA	1252	UUUCAUUCAAACUCUUCUAAU	1715	1231-1251	
AV03393.µm	UGAAGUUUUUUGCCUAAUGUA	1253	UCACAUAAGGCAAAAAACUUA	1716	1247-1267	
AV03394.µm	UUGCCUAAUGUGUGUUGGGA	1254	UUUCCCAACACACAUAGGCAA	1717	1256-1276	
AV03395.µm	GAAUGAAUGAGGUGAUCAUUUA	1255	UAAAUGUACACCCUCAUUCAU	1718	1317-1337	
AV03396.µm	GAGGUGUACAUUUUUACCAAGUA	1256	UACUGGUAAAAAUUGUACACCUC	1719	1324-1344	
AV03397.µm	GGUGUACAUUUUACCAAGUAUA	1257	UAUACUGGUAAAAAUUGUACACC	1720	1326-1346	
AV03398.µm	CAGUGAAAGGGUUUUUCUUGUA	1258	UAAACAGAAAAACCCUUUCACUG	1721	1406-1426	
AV03399.µm	AGUGAAAAAGGUGUUUCUUGUA	1259	UCAAACAGAAAAACCCUUUCACU	1722	1407-1427	
AV03400.µm	CAGCUUGUUACUUUUUUGGAAA	1260	UUUCCAAAAAAGUAAACAAGCUG	1723	1439-1459	
AV03401.µm	AGCUUGUUACUUUUUUGGAGA	1261	UCUUCCAAAAAAGUAAACAAGCU	1724	1440-1460	
AV03402.µm	GUUUUCUGUUUGCUUUUCUUGA	1262	UCAAGAACAAGCAACAGAAAC	1725	1466-1486	
AV03403.µm	UUUCUUGUUUGCUUGUUUCUUGA	1263	UCCAAGAACAAGCAACAGAAA	1726	1467-1487	
AV03404.µm	GGGAGAUAUUUUUUGAAAAAGA	1264	UCUGUUUCAAAAAAUUCUCCCC	1727	1485-1505	
AV03405.µm	GAGACCAUUAAAAACAUCUAGA	1265	UCUAGAUUGUUUUAUUGGUCUC	1728	1512-1532	
AV03406.µm	CAGUUCAAGCCUUUUUCUUUA	1266	UUAAAGAGAAAAAGCCUUGAAACUG	1729	1602-1622	
AV03407.µm	UUUCUUAACCUUCUAGUAUA	1267	UAUACUAGAGAGGUAAAGAGAAA	1730	1613-1633	
AV03408.µm	UCUCUUAACCUUCUAGUAUA	1268	UGAAUACUAGAGAGGUAAAGAGA	1731	1615-1635	
AV03409.µm	CCAGAUUGGCAUUUGGUAAAGAA	1269	UUUCUUAACCAAAUUGCCAUUCUGG	1732	1656-1676	
AV03410.µm	UUUAGUAAUUAUUUCUUGUUCA	1270	UGAACAAGAAAAUUAUUACUAAA	1733	1701-1721	

AV03411.µm	UUCUGUUAUGAUCCUUGCUA	1271	UAGACAAGGAUCAUAACAGAA	1734	1726-1746	
AV03412.µm	UAUGAUCCUUGUCUCGUCUUA	1272	UAAGACGAGACAAGGADUCAUA	1735	1732-1752	
AV03413.µm	UCCUUGUCUGUCUCUCAAAGA	1273	UCUUGAAGACGAGACAAGGA	1736	1737-1757	
AV03414.µm	CUUGUCUCGUCUCUCAAAGUUA	1274	UAACUUGAAGACGAGACAAG	1737	1739-1759	
AV03415.µm	UUGUCUCGUCUCUCAAAGUUA	1275	UAAACUUUGAAGACGAGACAA	1738	1740-1760	
AV03416.µm	GUUGUAAGCUUAUUUUGUGGAA	1276	UCCAACAUAUAAGCUAACAC	1739	1784-1804	
AV03417.µm	UGUUAAGCUUAUUUUGUGGAAA	1277	UUUCCAACAUAUAAGCUAACAA	1740	1785-1805	
AV03418.µm	GUUAGCUUAUUUUGUGGAAUA	1278	UAUUCCAACAUAUAAGCUAAC	1741	1786-1806	
AV03419.µm	AUUCUAAAAGGALUGGAAAAACA	1279	UGUUUUUCCAUCCUUUAAGAAU	1742	1824-1844	
AV03420.µm	AACAUAUUUGGCUUAUCUCUUA	1280	UAAGAGAUUAAGCCAAAUUGUU	1743	1870-1890	
AV03421.µm	UUUGGCUUAUCUCUCUACAGUAA	1281	UUACUGAAGAGAUUAAGCCAAA	1744	1875-1895	
AV03422.µm	GCUUAUCUCUCUUCAGUAAAGUAA	1282	UUACUUAACUGAAGAGAUUAAGC	1745	1879-1899	
AV03423.µm	UAUCUCUCUACAGUAAAGUAAUA	1283	UAAUUAACUUAACUGAAGAGAUUA	1746	1882-1902	
AV03424.µm	GUAAUUUUCUCAUCCAGAAAUUA	1284	UAUUUCUGGAUGAGAAAUUAC	1747	1896-1916	
AV03425.µm	AUCCAGAAAAUUAUCUGUAGUA	1285	UACUACAGUAAAAUUAUCUGGAU	1748	1906-1926	
AV03426.µm	UAAGGAGGUAAGGUGUCAUAAAA	1286	UUUUUAUGACACCUCUACCUCCUA	1749	1933-1953	
AV03427.µm	AAAAGUUCACACAUAUUGCAUGUA	1287	UACAUGCAAUUGUGGAACUUU	1750	1951-1971	
AV03428.µm	AGUUCACACAUAUUGCAUGUUA	1288	UAUACAUUGCAAUUGUGGAACU	1751	1953-1973	
AV03429.µm	CACACAUAUUGCAUUGAUCUUA	1289	UCAAGAUACAUUGCAAUGUGUG	1752	1957-1977	
AV03430.µm	UUGCAUUGUAUUCUUGUGUAAAA	1290	UUUUACACAAGAUACAUUGCAA	1753	1963-1983	
AV03431.µm	UGCAUUGUAUUCUUGUGUAAAA	1291	UGUUUAACAACAAGAUACAUUGCA	1754	1964-1984	
AV03432.µm	CAUGUAUUCUUGUAAAAACA	1292	UGUGUUUACACAAGAUACAUUG	1755	1966-1986	
AV03433.µm	UGUAUUCUUGUGUAAAAACACUAA	1293	UUAGUGUUUACACAAGAUACAA	1756	1968-1988	
AV03434.µm	CUUCAGACACAUAUUGAUCAUUA	1294	UGAAUGAUUCAAGUGUCUGAAG	1757	2030-2050	
AV03435.µm	UUCAGACACUUGAUCAUUCUA	1295	UAGAUAUGAUAAGUGUCUGAA	1758	2031-2051	
AV03436.µm	AAAAAUUAUGCCUUCUCUUAUCA	1296	UGAAAGAGAAAGGCAUAUUUUU	1759	2051-2071	
AV03437.µm	AAAAUAUGCCUUCUCUUAUCA	1297	UAGAAAGAGAAAGGCAUAUUUU	1760	2052-2072	
AV03438.µm	UAUGCCUUCUCUUAUUGA	1298	UCAUAAGAAAGAGAAAGGCAUA	1761	2056-2076	

AV03439.µm	AUGCCUUCUUCUUCUUAUGCA	1299	UGCAUUAAGAAAGAGAAGGCAU	1762	2057-2077	
AV03440.µm	CUUUCUUUAUGCUGAUUUGACA	1300	UGUCAAUUCAGCAUAAGAAAAG	1763	2066-2086	
AV03441.µm	UUUAUGCUGAUUUGACAGACA	1301	UGUUCUUGUCAAAUUCAGCAUAA	1764	2071-2091	
AV03442.µm	AUUUGACAGAACCUUGCAUUUA	1302	UAAAUUGCAGGUUUCUGUCAAAU	1765	2079-2099	
AV03443.µm	CAGAACCUGCAUUUGCUUAUA	1303	UAUAAGCAAAUUGCAGGUUCUG	1766	2085-2105	
AV03444.µm	AGAACCUGCAUUUGCUUAUCA	1304	UGAUUAAGCAAAUUGCAGGUUCU	1767	2086-2106	
AV03445.µm	CUGCAUUUGCUUAUCUUCAAA	1305	UUUGAAGAUAAAGCAAAUUGCAG	1768	2091-2111	
AV03446.µm	UAUCUUCAAAAUUAUGGUAUA	1306	UAUACCCAUAUUUUGAAGAUUA	1769	2102-2122	
AV03447.µm	UCUUCAAAAUUAUGGUAUCAA	1307	UUGAUACCCAUAUUUUGAAGA	1770	2104-2124	
AV03448.µm	AUAGAUUUUUGUUUCAUUACUA	1308	UAGUAAUGAAACAACAAUUCUAU	1771	2155-2175	
AV03449.µm	UUACUUUAAGGUAAUUAUUAUGA	1309	UCAUAUAUUACCUUAAAGUAA	1772	2170-2190	
AV03450.µm	UUAAAGGUAAUUAUUAUGAUUA	1310	UGUAUUCAUUAUUAUUAACCUAA	1773	2175-2195	
AV03451.µm	AAGGUAAUUAUUAUGAUUACCUA	1311	UAGGUAAUUAUUAUUAUUAACCUU	1774	2177-2197	
AV03452.µm	UGCAUUAAGUUAUUAUUAUGACA	1312	UGUCAUUGUUAUUAUUAUUAUGCA	1775	2527-2547	
AV03453.µm	CAUUGACAUUGAUUACAUAUUA	1313	UGAAUUUUUGAUUAUUAUUAUGCAUUG	1776	2540-2560	
AV03454.µm	GAUACAUAUUUCUGUAAUUAACA	1314	UGUAUUUAACAGAAUUUUUGUAUC	1777	2549-2569	
AV03455.µm	AAUUUCUGUAAUUAUUAUUAAGGA	1315	UCCUUUUUGUAAUUUAUUAUUAAGAAUU	1778	2555-2575	
AV03456.µm	UUUCCUUCUGAGUUAACCUAACUA	1316	UAGUUAGGUACUACAGAGGAAA	1779	2605-2625	
AV03457.µm	CUUCGAGUACCUAACUUUUGUA	1317	UACAAGUUUAAGGUACUCAGAGAG	1780	2609-2629	
AV03458.µm	CUCAUUGUAUCCUUGCCAGAUAA	1318	UUAUUCUUGGCAGGAUUAUUAUUAAG	1781	2656-2676	
AV03459.µm	CCUGUUCAUAUUUGUAAAGAUAA	1319	UUAUUCUUACAUAUAUUAUUAAGACAGG	1782	2679-2699	
AV03460.µm	UGUUCAUAUUUGUAAAGAUAGAA	1320	UUCUAUUCUUACAUAUAUUAUUAAGACA	1783	2681-2701	
AV03461.µm	GUAAAGAUAGAUUUUAAAAUUGCA	1321	UGCAUUUUUAAAAUUCUAUUCUUAAC	1784	2691-2711	
AV03462.µm	GAGAUUGUAGUUCUACACAUUUGUA	1322	UACAUAUGUGAGACUAUACAUUCUC	1785	2758-2778	
AV03463.µm	UCUUAGCAUUGCUUCUGAAAUUCA	1323	UGAUUUUACAGAGCAUUGCUAAGA	1786	3059-3079	
AV03464.µm	UUAGCAUUGCUUCUGAAAAUUCAAA	1324	UUUGAUUUUACAGAGCAUUGCUAA	1787	3061-3081	
AV03465.µm	CUGAAAAUUCACUUGCAUUUAGGA	1325	UCCUAAUUGCAGGUUGAUUUUCAG	1788	3071-3091	
AV03466.µm	AAUCAACUGCAUUUAGGUUUAA	1326	UUAAACCUAAUUGCAGUUUGAUUU	1789	3075-3095	

AV03467.µm	AUCAACUGCAUUVAGGUUUUA	1327	UAUAAACCUAAUUGCAGUUGAU	1790	3076-3096	
AV03468.µm	UGUGUCCCGAGAUGGCAUUUA	1328	UAAAUGCCAUUCUGGGACACA	1791	1649-1669	
AV03469.µm	AGGC AUUUUGUUAAGAUAUUCU	1329	AGAUUUCUUAACCAAAUGCCU	1792	1660-1680	
AV03470.µm	CAUUVCAUUVUAGUUCAUUGAA	1330	UUCAUGAACUAAAUAGAUAUG	1793	1068-1088	
AV03471.µm	ACCCGCUCCCUACAUUGGGUA	1331	UACCCAAGUGAGGGAGCGGGU	1794	595-615	
AV03472.µm	GGCUCUUCUACA UUGUCA	1332	UUGACA UGUAGGAAGAGCC	1795	1046-1066	
AV03473.µm	AGAGGGGAGGCAGAGCCUUGA	1333	UCAAGGCUCUGCCUCCCU	1796	632-652	
AV03474.µm	AGUGCCACUUCUCCUUCUA	1334	UAGAAGAGGGAAGUGGCACU	1797	822-842	
AV04179.µm	GGAACUUAACGUGGUUAUAAA	1335	UUUAUUCACCACGUAAGUUC	1798	1195-1215	
AV04180.µm	CAACUUAACGUGGUUAUAAUA	1336	UAUUAUUCACCACGUAAGUUG	1799	1196-1216	
AV04181.µm	GCUUACGUGGUUAUAAUGAA	1337	UUCAUUAUUCACCACGUAAGC	1800	1198-1218	
AV04182.µm	GUUACGUGGUUAUAAUGAAA	1338	UUUCAUUAUUCACCACGUAAC	1801	1199-1219	
AV04183.µm	CUGGUUAUUAUUGAAAUAUA	1339	UAUAAUUAUUAUUAUUCACCAG	1802	1204-1224	
AV04184.µm	GAUCUUAUAUUAUAGGAAGAA	1340	UUUUUUUAUUAUUAUUAAGAU	1803	1221-1241	
AV04185.µm	GAAUUAUUAUUAUAGGAAGUA	1341	UAUCAACUUCUUAUUAUUAUUC	1804	1227-1247	
AV04186.µm	GAUUAAGGAAGAUUGAUUGAA	1342	UUCAUUAUUAUUAUUAUUAUUC	1805	1230-1250	
AV04187.µm	GAGGAAGAUUGAUUGAAAGUA	1343	UACUUAUUAUUAUUAUUAUUC	1806	1233-1253	
AV04188.µm	GGGAAGAGUUGAUUGAAAGUA	1344	UAACUUAUUAUUAUUAUUAUUC	1807	1234-1254	
AV04189.µm	CGAAGAGUUGAUUGAAAGUUA	1345	UAAACUUAUUAUUAUUAUUAUUC	1808	1235-1255	
AV04190.µm	GUGAUUUGAAAGUUUUUUGCUA	1346	UAGGCAAAAAACUUAUUAUUAUUC	1809	1242-1262	
AV04191.µm	GGUACA UUUUACCAAGUAUUA	1347	UGAAUUAUUAUUAUUAUUAUUAUUC	1810	1328-1348	
AV04192.µm	CUACA UUUUACCAAGUAUUA	1348	UGGAUUAUUAUUAUUAUUAUUAUUC	1811	1329-1349	
AV04193.µm	GUUCUACA UUGUCCAGUAGAAA	1349	UUUACA UUGGACAUUCUGAGAC	1812	1393-1413	
AV04194.µm	GCUACA UUGUCCAGUAGAAA	1350	UUUUACA UUGGACAUUCUGAGAC	1813	1394-1414	
AV04195.µm	CCCAGUAGAAAGGGUUUUUCUUA	1351	UACAGAAACCCUUUAUUAUUAUUC	1814	1404-1424	
AV04196.µm	GCAGUAGAAAGGGUUUUUCUUA	1352	UAACAGAAACCCUUUAUUAUUAUUC	1815	1405-1425	
AV04197.µm	CUGAAAGGGUUUUUCUUGCA	1353	UGCAAAACAGAAACCCUUUAUUAUUC	1816	1408-1428	
AV04198.µm	GAAAGGUUUUCUUGUUUGCUUA	1354	UGAAGCAAAACAGAAACCCUUUC	1817	1411-1431	

AV04199.µm	CUUUCUGUUUGCUUCAUUGCA	1355	UGCAUUGAAGCAAAACAGAAAG	1818	1416-1436	
AV04200.µm	GUUCAUUGCUGACAGCUUGUA	1356	UACAAGCUGUCAGCAUUGAAC	1819	1427-1447	
AV04201.µm	GUCAUUGCUGACAGCUUGUA	1357	UAACAAGCUGUCAGCAUUGAC	1820	1428-1448	
AV04202.µm	GCAUUGCUGACAGCUUGUAA	1358	UUAACAAGCUGUCAGCAUUGC	1821	1429-1449	
AV04203.µm	GUUCUGACAGCUUGUACUUA	1359	UAAGUAAACAAGCUGUCAGCAC	1822	1432-1452	
AV04204.µm	CACAGCUUGUACUUUUUGGA	1360	UCCAAAAAGUAAACAAGCUGUG	1823	1437-1457	
AV04205.µm	GCAGCUUGUACUUUUUGGAA	1361	UUCCAAAAAGUAAACAAGCUGC	1824	1438-1458	
AV04206.µm	GGUUACUUUUUGGAAAGCUAGA	1362	UCUAGCUUCCAAAAAGUAAACC	1825	1444-1464	
AV04207.µm	GGUCUCGUCUUCACAAAGUUAA	1363	UUAAACUUUGAAGACGAGACC	1826	1741-1761	
AV04208.µm	GAAUUAAGAAAAUUGAUUCGGAA	1364	UUCCGAAUACAUUUUCUAAUUC	1827	1759-1779	
AV04209.µm	CAUUCGAGAGACAGUGUAGA	1365	UCUAAACACUGCUCUCCGAAUG	1828	1771-1791	
AV04210.µm	GCGGAGAGCAGUGUAGCUUA	1366	UAGCUAACACUGCUCUCCGCG	1829	1774-1794	
AV04211.µm	CGAAGACAGUGUAGCUUAUA	1367	UAUAAGCUAAACACUGCUCUG	1830	1776-1796	
AV04212.µm	CAGAGCAGUGUAGCUUAUUA	1368	UAUUAAGCUAAACACUGCUCUG	1831	1777-1797	
AV04213.µm	CAGCAGUGUAGCUUAUUUGA	1369	UCAAAUUAAGCUAAACACUGCUG	1832	1779-1799	
AV04214.µm	GGCAGUGUAGCUUAUUUGUA	1370	UACAAAUAAGCUAAACACUGCC	1833	1780-1800	
AV04215.µm	GGUGUAGCUUAUUUUGUGGA	1371	UCCAACAUAUUAAGCUAAACACC	1834	1783-1803	
AV04216.µm	GAGCUUAUUUGUUGGAAUAAA	1372	UUUAUUCCAACAUAUUAAGCUC	1835	1788-1808	
AV04217.µm	GGUUGGAUUAUAAAUUUAGGAA	1373	UUCCUAAAUUUUAUUCCAACC	1836	1797-1817	
AV04218.µm	GUGGAUUAUAAAUUUAGGAUUA	1374	UAUUCCUAAAUUUUAUUCCAC	1837	1799-1819	
AV04219.µm	GUUAUUUCUAAAGGAUUGAAAA	1375	UUUUCCAUCUCUUAAGAAUAAAC	1838	1821-1841	
AV04220.µm	GUUAUUUCUAAAGAUUGAAAAA	1376	UUUUUCCAUCUCUUAAGAUUAC	1839	1822-1842	
AV04221.µm	GGGAUUGGAAAAACUUUUUGGA	1377	UCCAAAAAGUUUUUCCAUCGCC	1840	1831-1851	
AV04222.µm	GUUGAAAAAACUUUUUUGGAUAA	1378	UUAUCCAAAAAAGUUUUUCCAC	1841	1834-1854	
AV04223.µm	GAAACUUUUUUGGAUUAUUUGGA	1379	UCCAUAUUAUCCAAAAAAGUUUC	1842	1839-1859	
AV04224.µm	GUUUGGAUUAUUUGGAGAAAUUA	1380	UAUUUCUCCAUAUUAUCCAAC	1843	1845-1865	
AV04225.µm	GUUUAAAAACAUAUUUGCUIAA	1381	UUAAGCCAAAUUUGUUUUAAAC	1844	1864-1884	
AV04226.µm	GUUAAAAACAUAUUUGCUUAUA	1382	UAUAAGCCAAAUUUGUUUUAAC	1845	1865-1885	

AV04227.µm	GUAAAAACAUUUGGCUUAVCA	1383	UGAUAAAGCCAAAUUGUUUAC	1846	1866-1886	
AV04228.µm	GAAACAUAUUUGGCUUAVUCUA	1384	UGAGAUAAAGCCAAAUUGUUUC	1847	1868-1888	
AV04229.µm	GUUGCUGAUUUGACAGAACCUA	1385	UAGGUUUCUGUCAAAUUCAGCAC	1848	2073-2093	
AV04230.µm	CAUUUGACAGAACCUUGCAUUA	1386	UAAUUGCAGGUUCUGUCAAAUG	1849	2078-2098	
AV04231.µm	GUGACAGAAACCUUGCAUUUGCA	1387	UGCAAAUUGCAGGUUCUGUCAC	1850	2081-2101	
AV04232.µm	GGACAGAAACCUUGCAUUUGCUA	1388	UAGCAAAUUGCAGGUUCUGUCC	1851	2082-2102	
AV04233.µm	GCAGAAACCUUGCAUUUGCUUAA	1389	UUAAGCCAAAUUGCAGGUUCUGC	1852	2084-2104	
AV04234.µm	CAACCUGCAUUUGCUUAVUCUA	1390	UAGAUAAAGCAAAUUGCAGGUUG	1853	2087-2107	
AV04235.µm	GACCUGCAUUUGCUUAVUCUUA	1391	UAAGAUAAAGCAAAUUGCAGGUC	1854	2088-2108	
AV04236.µm	GCCUGCAUUUGCUUAVUCUUA	1392	UGAAGAUAAAGCAAAUUGCAGGC	1855	2089-2109	
AV04237.µm	GCUGCAUUUGCUUAVUCUCAA	1393	UUGAAGAUAAAGCAAAUUGCAGC	1856	2090-2110	
AV04238.µm	GGCAUUUGCUUAVUCUCAA AAA	1394	UUUUUGAAGAUAAAGCAAAUUGCC	1857	2092-2112	
AV04239.µm	GUUUUGCUUAVUCUCAA AAAUAA	1395	UUAUUUUGAAGAUAAAGCAAAAC	1858	2095-2115	
AV04240.µm	GUUGCUUAVUCUCAA AAAUAVUA	1396	UAUAUUUUUGAAGAUAAAGCAAC	1859	2096-2116	
AV04241.µm	GUUCUUAUUCUCAA AAAUAVUGA	1397	UCAUAVUUUUUGAAGAUAAAGCAC	1860	2097-2117	
AV02743-19-1.µm	CGGGACGGGUCCAAAGAU GA	1398	UCAUCUUUGACCCCGUCCCG	1861	6-24	6-24
AV02744-19-1.µm	GGUCCAAAGAUUGGACGGCCA	1399	UGGCCGUCCAUUCUUUGGACC	1862	13-31	13-31
AV02745-19-1.µm	GACGGCCGCU CAGGUUCUA	1400	UAGAACCU GAGCGGCCGUC	1863	24-42	24-42
AV02746-19-1.µm	CGCU CAGGUUCUGCUUUUA	1401	UAAAAGCAGAAACCU GAGCG	1864	30-48	30-48
AV02747-19-1.µm	CU CAGGUUCUGCUUUUACA	1402	UGUAAAAGCAGAACCU GAG	1865	32-50	32-50
AV02748-19-1.µm	UCAAGGUUCUGCUUUUACCA	1403	UGGUAAAAGCAGAACCU GA	1866	33-51	33-51
AV02749-19-1.µm	CAGGUUCUGCUUUUAVACUA	1404	UAGGUAAAAGCAGAACCU G	1867	34-52	34-52
AV02750-19-1.µm	AGGUUCUGCUUUUAVACCU GA	1405	UCAGGUAAAAGCAGAACCU	1868	35-53	35-53
AV02751-19-1.µm	GGUUCUGCUUUUAVACCU GA	1406	UGCAGGUAAAAGCAGAACCC	1869	36-54	36-54
AV02752-19-1.µm	GUUCUGCUUUUAVACCU GGA	1407	UCCGAGGUAAAAGCAGAAAC	1870	37-55	37-55
AV02753-19-1.µm	UUCUGCUUUUAVACCU GCGGA	1408	UCCG CAGGUAAAAGCAGAAA	1871	38-56	38-56
AV02754-19-1.µm	GCUUUUUAVACCU GCGGCCCAA	1409	UUUGGCCG CAGGUAAAAGC	1872	42-60	42-60
AV02755-19-1.µm	AGAGCCCCCAUUCAUUGCCA	1410	UGGCAUUGAAUUGGGGCU CU	1873	59-77	59-77

AV02756-19-1.µm	CCCCAUAUUAUUGCCCCGGA	1411	UCCGGGGCAUAUGAUGGGG	1874	63-81	63-81
AV02757-19-1.µm	CCCAUUAUUAUUGCCCCGGUA	1412	UACCGGGGCAUAUGAUAUGGG	1875	64-82	64-82
AV02758-19-1.µm	CCCCGGUUGCUGAGCGCGGA	1413	UCCCGCUCACAGCACCGGGG	1876	75-93	75-93
AV02759-19-1.µm	UGCUAGAGCGGCGCGCGGAA	1414	UUCGCGGCGCGCGCUCAGCA	1877	81-99	81-99
AV02760-19-1.µm	CGCCGCGAGUCGCGCCCGGAA	1415	UUCGGGCGGACUCGCGGCG	1878	91-109	91-109
AV02761-19-1.µm	CCGCGAGUCGCGCCCGAGGA	1416	UCCUCGGGCGGACUCGCGG	1879	93-111	93-111
AV02762-19-1.µm	GCCCCGAGGCCUCCGGGGAA	1417	UUCCCCGAGGCCUCCGGGC	1880	103-121	103-121
AV02763-19-1.µm	CCCGAGGCCUCCGGGGACA	1418	UGUCCCCGAGGCCUCCGGG	1881	104-122	104-122
AV02764-19-1.µm	AGGCCUCCGGGGACUAGCA	1419	UGGCAGUCCCCGAGGCCU	1882	108-126	108-126
AV02765-19-1.µm	UCCGGGACUAGCCGUGCCA	1420	UGGCACGGCAGUCCCCGGA	1883	113-131	113-131
AV02766-19-1.µm	CGGGGACUAGCCGUGCCGA	1421	UCCGGCACGGCAGUCCCCG	1884	115-133	115-133
AV02767-19-1.µm	UGCCGUGCCGGGGCGGGAGA	1422	UCUCCCCCGCGGCACGGCA	1885	122-140	122-140
AV02768-19-1.µm	GCGGAGAGACCGCCAUAGCA	1423	UGCCAUGGCGGUUCCCCGC	1886	133-151	133-151
AV02769-19-1.µm	GGGAGACCGCCAUGGCGAA	1424	UUCGCCAUUGCGGUUCCCC	1887	135-153	135-153
AV02770-19-1.µm	AGACCGCCAUUGGCGACCCA	1425	UGGGUCGCCAUUGCGGUU	1888	138-156	138-156
AV02771-19-1.µm	CCGCCAUUGCGGACCCUGGA	1426	UCCAGGGUCCGCCAUUGCGG	1889	141-159	141-159
AV02772-19-1.µm	UGGCGACCCUGGAAAAAGCA	1427	UGCUUUUCCAGGGUCCGCA	1890	147-165	147-165
AV02773-19-1.µm	ACCCUGGAAAAAGCUGAUGA	1428	UCAUCAGCUUUUCCAGGGU	1891	152-170	152-170
AV02774-19-1.µm	CCCUAGGAAAAAGCUGAUGAA	1429	UUCAUACGCUUUUCCAGGG	1892	153-171	153-171
AV02775-19-1.µm	CCUUGAAAAAGCUGAUGAAA	1430	UUUCAUCAGCUUUUCCAGG	1893	154-172	154-172
AV02776-19-1.µm	CUUGAAAAAGCUGAUGAAGA	1431	UCUUAUCAGCUUUUCCAG	1894	155-173	155-173
AV02777-19-1.µm	UGGAAAAAGCUGAUGAAGGA	1432	UCCUUAUCAGCUUUUCCA	1895	156-174	156-174
AV02778-19-1.µm	GGAAAAAGCUGAUGAAGGCA	1433	UGCCUUAUCAGCUUUUCC	1896	157-175	157-175
AV02779-19-1.µm	AAAAAGCUGAUGAAGGCCUA	1434	UAGGCCUUAUCAGCUUUU	1897	159-177	159-177
AV02780-19-1.µm	AAAGCUGAUGAAGGCCUUA	1435	UAAGGCCUUAUCAGCUUU	1898	160-178	160-178
AV02781-19-1.µm	AGCUGAUGAAGGCCUUCGA	1436	UCGAAGGCCUUAUCAGCU	1899	162-180	162-180
AV02782-19-1.µm	GCUGAUGAAGGCCUUCGAA	1437	UUCGAAGGCCUUAUCAGC	1900	163-181	163-181
AV02783-19-1.µm	UGAUGAAGGCCUUCGAGUA	1438	UACUCGAAGGCCUUAUCA	1901	165-183	165-183

AV02784-19-1.µm	AUGAAGGCCUUCGAGUCCA	1439	UGGACUUCGAAGGCCUUCAU	1902	167-185	167-185
AV02785-19-1.µm	AGGCCUUCGAGUCCCUCAA	1440	UUGAGGACUCCGAAGGCCU	1903	171-189	171-189
AV02786-19-1.µm	UCGAGUCCCCUCAAGUCCUA	1441	UAGGACUUGAGGGACUCGA	1904	177-195	177-195
AV02787-19-1.µm	GUCCCCUCAAGUCCCUCCAA	1442	UUGGAAGGACUUGAGGGAC	1905	181-199	181-199
AV02788-19-1.µm	UCCCUCAAGUCCUCCAGAGA	1443	UCUGGAAGGACUUGAAGGA	1906	182-200	182-200
AV02789-19-1.µm	CCCUCAAGUCCUCCAGAGA	1444	UGCUGGAAGGACUUGAAGG	1907	183-201	183-201
AV02790-19-1.µm	CCUCAAGUCCUCCAGCAA	1445	UUGCUGGAAGGACUUGAGG	1908	184-202	184-202
AV02791-19-1.µm	CUCAAGUCCUCCAGCAGA	1446	UCUGCUGGAAGGACUUGAG	1909	185-203	185-203
AV02792-19-1.µm	UCAAGUCCUCCAGCAGCA	1447	UGCUGCUUGGAAGGACUUGA	1910	186-204	186-204
AV02793-19-1.µm	GUCCUUCGAGCAGCAGCAA	1448	UUGCUGCUGCUUGGAAGGAC	1911	190-208	190-208
AV02794-19-1.µm	CUCCUCAAGCUUCCUCAGCA	1449	UGCUGAGGAAGCUUGAGGAG	1912	288-306	288-306
AV02795-19-1.µm	UCCUCAGCUUCCUCAGCCA	1450	UGGCUGAGGAAGCUUGAGGA	1913	289-307	289-307
AV02796-19-1.µm	GCCGCAAGCACAAGCCGCUA	1451	UAGCGGCUUGCCUGCGGC	1914	310-328	310-328
AV02797-19-1.µm	CAGGCACAGCCGCUUGCUGA	1452	UCAGCAGCGGCUUGGCCUG	1915	314-332	314-332
AV02798-19-1.µm	GGCACAGCCGCUUGCCCA	1453	UGGCAGCAGCGGCUUGGCC	1916	316-334	316-334
AV02799-19-1.µm	CACAGCCGCUUGCUCCUCA	1454	UGAGCCAGCAGCGGCUUG	1917	318-336	318-336
AV02800-19-1.µm	GCCCGGCUUGGCUUGAGGA	1455	UCCUCAGCCACAGCCGGGC	1918	375-393	375-393
AV02801-19-1.µm	GGCUUGGCUUGAGGAGCCA	1456	UGGCUCCUCAGCCACAGCC	1919	379-397	379-397
AV02802-19-1.µm	GGCUGAGGAGCCGCUGCAA	1457	UUGCAGCGGCUCCUCAGCC	1920	385-403	385-403
AV02803-19-1.µm	AGGAGCCGCUGCAACCGACA	1458	UGUCGGUGCAGCGGCUCCU	1921	390-408	390-408
AV03373-19-1.µm	UUAACTUGCGUUGUGAAGAA	1459	UUCUUCACAACGCAGUUA	1922	779-797	
AV03374-19-1.µm	AUGACAUAUUGCUUUVAGA	1460	UCUAAAAGCAUUAUUGCAU	1923	925-943	
AV03375-19-1.µm	GACAUAAUGCUUUVAGGAA	1461	UUCUAAAAGCAUUAUGUC	1924	927-945	
AV03376-19-1.µm	ACAUAAUGCUUUAAGGACA	1462	UGUCCUAAAAGCAUUAUGU	1925	928-946	
AV03377-19-1.µm	GGGAGAUUUUCUUUCCUAA	1463	UUAGGAAAAAGAAAUUCUCC	1926	1001-1019	
AV03378-19-1.µm	UAGUGGACCUUAAAAACAGA	1464	UCUUVUUUAAGUGCCACUA	1927	1017-1035	
AV03379-19-1.µm	GGCUCUUCUACAUUGUCA	1465	UGACAUAUGUAGGAAGAGCC	1928	1047-1065	
AV03380-19-1.µm	CCUACAUUUGUCAGGACAUA	1466	UAUGUCCUGACAUAUGUAGG	1929	1054-1072	

AV03381-19-1.µm	UCAUUUUAGUUCAUUGAUCAA	1467	UUGAUUCAUGAACUAAAUGA	1930	1073-1091	
AV03382-19-1.µm	UGAUCCACGGUGGUAGUAAA	1468	UUUACUACCACCGUGAUCA	1931	1085-1103	
AV03383-19-1.µm	CGUGUGUAGUAAACACGAUA	1469	UAUCGUGUUACUACCACCG	1932	1091-1109	
AV03384-19-1.µm	GUAAACACGAUUUUAAAGCAA	1470	UUUCUUAAAAUUCGUGUUAU	1933	1099-1117	
AV03385-19-1.µm	AAGAGAUUCUCUCUACUCAA	1471	UUAGAUAGACGAGAUUCUCU	1934	1123-1141	
AV03386-19-1.µm	GAGAUUCUGCUCUACUUAAGA	1472	UCUUAGAUAGACGAGAUUCUC	1935	1125-1143	
AV03387-19-1.µm	AUCUAAAGCCUAAAGUUGGUA	1473	UACCAACUUAGGCUUAGAU	1936	1136-1154	
AV03388-19-1.µm	AGUUUGUGGUUGCCAAGUAA	1474	UUACUUUGGCAACCACACACU	1937	1171-1189	
AV03389-19-1.µm	GAAUCUACGUGGUGAUUAA	1475	UUAAUCCACCACGUAAGUUC	1938	1196-1214	
AV03390-19-1.µm	CUUACGUGGUGAUUAAUAGA	1476	UCAUUAAUCCACCACGUAAG	1939	1199-1217	
AV03391-19-1.µm	ACGUGGUGAUUAAUAGAAAA	1477	UUUUCAUUAAUCCACCACGU	1940	1202-1220	
AV03392-19-1.µm	UAGGAAGAGUUGAUUAGAAA	1478	UUUCAUCCAACTUUCUUA	1941	1233-1251	
AV03393-19-1.µm	AAGUUUUUUGCCUAAUGUA	1479	UCACAUAGGCAAAAAAACUU	1942	1249-1267	
AV03394-19-1.µm	GCCUAAUGUGUGUUGGAAAA	1480	UUUUCCCAACACACAUAGGC	1943	1258-1276	
AV03395-19-1.µm	UGAAUUGAGGUGUACAUUUA	1481	UAAAUUGUACACCUCAUUA	1944	1319-1337	
AV03396-19-1.µm	GGUGUACAUUUUACCAAGUA	1482	UACUGGUAAAAAUGUACACC	1945	1326-1344	
AV03397-19-1.µm	UGUACAUUUUACCAAGUUA	1483	UAUACUUGGUAAAAUUGUACA	1946	1328-1346	
AV03398-19-1.µm	GUGAAGGGGUUUUCUGUUUA	1484	UAAACAGAAAAACCCUUCAC	1947	1408-1426	
AV03399-19-1.µm	UGAAAAAGGUUUUCUGUUUA	1485	UCAAAACAGAAAAACCCUUA	1948	1409-1427	
AV03400-19-1.µm	GCUUGUUACUUUUUUGAAAA	1486	UUUCCAAAAAAGUAAACAAGC	1949	1441-1459	
AV03401-19-1.µm	CUUGUUACUUUUUUGGAAGA	1487	UCUUCCAAAAAAGUAAACAAG	1950	1442-1460	
AV03402-19-1.µm	UUCUGUUUGCUUUGUUCUUA	1488	UCAAGAACAAGCAACAGAA	1951	1468-1486	
AV03403-19-1.µm	UUCUGUUUGCUUUGUUCUUGA	1489	UCCAAGAACAAAGCAACAGAA	1952	1469-1487	
AV03404-19-1.µm	GGAGAAUUUUUUUGAAAACAGA	1490	UCUGUUUUCAAAAAAUUCUCC	1953	1487-1505	
AV03405-19-1.µm	GACCAUUAAAAACAUCUAGA	1491	UCUAGAUUGUUUUAAUUGGUC	1954	1514-1532	
AV03406-19-1.µm	GUUCAGGCGCUUUUCUUAUA	1492	UUAAAGAGAAAGGCCUGAAC	1955	1604-1622	
AV03407-19-1.µm	UCUCUUUACCUUCUCAGUUAU	1493	UAUACUUGAGAGGUAAGAGA	1956	1615-1633	
AV03408-19-1.µm	UCUUUACCUUCUCAGUUAUUA	1494	UGAAUUAUCUAGAGGUUAAGA	1957	1617-1635	

AV03409-19-1.µm	AGAUGGCAUUTUGGUAAGAA	1495	UUUUVACCAAAUUGCCAUUCU	1958	1658-1676	
AV03410-19-1.µm	UAGUAUAUUTUCUUGUUA	1496	UGAACAGAAGAAUAUUAUUA	1959	1703-1721	
AV03411-19-1.µm	CUUUAUAUGAUCCUUGUUA	1497	UAGACAAGGAUUAUAACAG	1960	1728-1746	
AV03412-19-1.µm	UGAUCCUUGUCUCUGUUA	1498	UAAGACGAGACAAGGAUUA	1961	1734-1752	
AV03413-19-1.µm	CUUGUCUCUGUCUUAAGA	1499	UCUUUGAAAGACGAGACAAG	1962	1739-1757	
AV03414-19-1.µm	UGUCUCUGUCUUAAGUUA	1500	UAACUUUGAAAGACGAGACA	1963	1741-1759	
AV03415-19-1.µm	GUUCUCGUCUUAAGUUUA	1501	UAAACUUUGAAAGACGAGAC	1964	1742-1760	
AV03416-19-1.µm	GUUAGCUUAUUUGUUAGAA	1502	UUCCAACAUAUAAAGCUAAC	1965	1786-1804	
AV03417-19-1.µm	UUAGCUUAUUUGUUAGAAA	1503	UUUCCAACAUAUAAAGCUAA	1966	1787-1805	
AV03418-19-1.µm	UAGCUUAUUUGUUAGAAUA	1504	UAUUCCAACAUAUAAAGCUA	1967	1788-1806	
AV03419-19-1.µm	UCUAAAAGGAUGGAAAAACA	1505	UGUUUUUCCAUCCUUUAGA	1968	1826-1844	
AV03420-19-1.µm	CAAUUUUGGCUUAUCUCUUA	1506	UAAGAGAUAAAGCCAAAUUG	1969	1872-1890	
AV03421-19-1.µm	UGGCUUAUCUCUUAAGUAA	1507	UUACUGAAAGAGAUAAAGCCA	1970	1877-1895	
AV03422-19-1.µm	UUAUUCUCUUAAGUAAAGUAA	1508	UUACUUACUUGAAAGAGAUAA	1971	1881-1899	
AV03423-19-1.µm	UCUCUUAAGUAAAGUAAUUA	1509	UAAUUAUUAUUAAGAGAGA	1972	1884-1902	
AV03424-19-1.µm	AAUUUCUUAUUAAGAAAUUA	1510	UAUUUCUUGAUUGAGAAAUUU	1973	1898-1916	
AV03425-19-1.µm	CCAGAAAUUUUACUUGUAGUA	1511	UACUACAGUAAAUUUUCUGG	1974	1908-1926	
AV03426-19-1.µm	GGAGGUAGGUGUUAUAAAA	1512	UUUUUAGACACCUUACCUCC	1975	1935-1953	
AV03427-19-1.µm	AGUUACACACAUUUGAUUA	1513	UACAUGCAAUUGUGUAACU	1976	1953-1971	
AV03428-19-1.µm	UUCACACAUAUGAUUAUA	1514	UAUACAUUGCAAUUGUGAA	1977	1955-1973	
AV03429-19-1.µm	CACAUAUGCAUUAUUCUUGA	1515	UCAAGAUACAUUGCAAUUGG	1978	1959-1977	
AV03430-19-1.µm	GC AUUGUAUUCUUGUAAAA	1516	UUUUUACACAAGAUUACAUGC	1979	1965-1983	
AV03431-19-1.µm	CAUGUAUUCUUGUAAAAACA	1517	UGUUUACACAAGAUUACAUG	1980	1966-1984	
AV03432-19-1.µm	UGUAUUCUUGUAAAAACA	1518	UGUGUUUACACAAGAUUACA	1981	1968-1986	
AV03433-19-1.µm	UAUCUUUGUUAACACUUA	1519	UUAGUUUUUACACAAGAUUA	1982	1970-1988	
AV03434-19-1.µm	UCAGACACUUGAUCAUUA	1520	UGAAUUGAUCAAGUGUCUGA	1983	2032-2050	
AV03435-19-1.µm	CAGACACUUGAUCAUUA	1521	UAGAUAUGAUCAAGUGUCUG	1984	2033-2051	
AV03436-19-1.µm	AAAUUUGCCUUUCUUA	1522	UGAAAGAGAAAGGCAUUAUUU	1985	2053-2071	

AV03437-19-1.µm	AAUUAUGCCUUCUCUUCUA	1523	UAGAAAGAGAGGCAUAAU	1986	2054-2072	
AV03438-19-1.µm	UGCCUUCUCUUCUUAUGA	1524	UCAUAAGAAAAGAGAGCA	1987	2058-2076	
AV03439-19-1.µm	GCCUUCUCUUCUUAUGCA	1525	UGCAUAAGAAAAGAGAGGC	1988	2059-2077	
AV03440-19-1.µm	UUCUUAUGCUGAUUUGACA	1526	UGUCAAUVCAGCAUAAGAA	1989	2068-2086	
AV03441-19-1.µm	AUGCUGAUUUGACAGAACCA	1527	UGUUCUGUCAAAUVCAGCAU	1990	2073-2091	
AV03442-19-1.µm	UUGACAGAACCUUGCAUUA	1528	UAAAUGCAGGUAUCUGCAA	1991	2081-2099	
AV03443-19-1.µm	GAAACUAGCAUUGCUUAUA	1529	UAUAAGCAAAUVCAGGUC	1992	2087-2105	
AV03444-19-1.µm	AACCUAGCAUUGCUUAUCA	1530	UGAUAAAGCAAAUVCAGGUU	1993	2088-2106	
AV03445-19-1.µm	GCAUUUUGCUUAUCUUCAAA	1531	UUUGAAGAUAAAGCAAAUVC	1994	2093-2111	
AV03446-19-1.µm	UCUUAACAAAUAVUGGUAVA	1532	UAUACCCAUAAUUUGAAGA	1995	2104-2122	
AV03447-19-1.µm	UUCAAAUAUUGGUUAUCAA	1533	UUUGAUACCCAUAAUUUGAA	1996	2106-2124	
AV03448-19-1.µm	AGAUUUUUGUUUCAUUAUA	1534	UAGUAAUGAAACAAAUUCU	1997	2157-2175	
AV03449-19-1.µm	ACUUUAAAGGUAAUUAUAGA	1535	UCAUAUAUUAACCUUAAAAGU	1998	2172-2190	
AV03450-19-1.µm	AAGGUAAUAUAUGAUUUAUA	1536	UGUAUUAUAUAUUAUACCUU	1999	2177-2195	
AV03451-19-1.µm	GGUAAUAUAUGAUUUAUAUA	1537	UAGGUAAUAUAUAUUAUACC	2000	2179-2197	
AV03452-19-1.µm	CAUAAGUAAUAUACAUUUGACA	1538	UGUCAUUGUAUUAUUAUUG	2001	2529-2547	
AV03453-19-1.µm	UUGACAUUGAUACAAAUUUA	1539	UGAAUUUUGUAUUAUUGUCAA	2002	2542-2560	
AV03454-19-1.µm	UACAAAUUUCUGUAAAUUAUA	1540	UGUAUUUAACAGAAUUUUGUA	2003	2551-2569	
AV03455-19-1.µm	UUCUGUAAUUAACAAAAGGA	1541	UCCUUUUUGUAUUUAACAGAA	2004	2557-2575	
AV03456-19-1.µm	UCCUUCUAGUUAACCUAAUA	1542	UAGUUAGGUACUCAGAGGA	2005	2607-2625	
AV03457-19-1.µm	CUGAGUUAACCUAAAUUUAUA	1543	UACAAAGUUAGGUUAUUAUA	2006	2611-2629	
AV03458-19-1.µm	CAUGUAUCCUUGCCAGAUUA	1544	UUUAUUCUGGAGGAUUAUAUG	2007	2658-2676	
AV03459-19-1.µm	UGUUCAUAUUGUAAGAUUA	1545	UUUAUUCUUAACAAUAUUAUA	2008	2681-2699	
AV03460-19-1.µm	UUCAUUAUUUAAGAUUAAGAA	1546	UUUAUUCUUAACAAUAUUAUA	2009	2683-2701	
AV03461-19-1.µm	AAGAUUAUAUUUAAAAUUGCA	1547	UAGAUUUUUAUUUAUUAUUA	2010	2693-2711	
AV03462-19-1.µm	GAUUGUAUUCUACAUUUGUA	1548	UACAAUUGUAGAGAUUAUAUC	2011	2760-2778	
AV03463-19-1.µm	UUAGCAUUGCUUCUAAAAUUA	1549	UUAUUUUAAGAGCAUUGCUAA	2012	3061-3079	
AV03464-19-1.µm	AGCAUUGCUUCUAAAAUUAUA	1550	UUUUAUUUAAGAGCAUUGCU	2013	3063-3081	

AV03465-19-1.µm	GAAAUCAACUCGCAUUAAGGA	1551	UCCUAAUGCAGUUGAUUUUC	2014	3073-3091	
AV03466-19-1.µm	UCAACUGCAUUAAGGUUUAA	1552	UUAAACCUAAUUGCAGUUUA	2015	3077-3095	
AV03467-19-1.µm	CAACUGCAUUAAGGUUUUAUA	1553	UAUAAACCUAAUUGCAGUUUG	2016	3078-3096	
AV03468-19-1.µm	UGUCCCGAGAUUGGC AUUUUA	1554	UAAAUGCCAUUCUGGGACAC	2017	1651-1669	
AV03469-19-1.µm	GCAUUAUGGUAAAGAAUAUCU	1555	AGAUUAUUCUUAACCAAAUUGC	2018	1662-1680	
AV03470-19-1.µm	UUUCAUUUAAGUUCAUUGAA	1556	UUCAUGAACUAAAUGAAAU	2019	1070-1088	
AV03471-19-1.µm	CCGCUCCCUACAUUGGGUA	1557	UACCCAAGUGAGGGAGCGG	2020	597-615	
AV03472-19-1.µm	CUCUUCUACAUAUUGCAA	1558	UUGACAUAUGUAGGAAGAGC	2021	1048-1066	
AV03473-19-1.µm	AGGGGAGGCAGAGCCUUGA	1559	UCAAGGCUUCGCCUCCCU	2022	634-652	
AV03474-19-1.µm	UGCCACUUCUCCUUCUA	1560	UAGAAGAGGGAAGUGGCAC	2023	824-842	
AV04179-19-1.µm	AACUUAACGUGGUGAUUAAA	1561	UUUAUUCACCACGUAAGUU	2024	1197-1215	
AV04180-19-1.µm	ACUUAACGUGGUGAUUAAUA	1562	UAUUAAUCACCACGUAAGU	2025	1198-1216	
AV04181-19-1.µm	UUACGUGGUGAUUAAUGAA	1563	UUCAUUAUUCACCACGUA	2026	1200-1218	
AV04182-19-1.µm	UACGUGGUGAUUAAUGAAA	1564	UUUCAUUAAUUCACCACGUA	2027	1201-1219	
AV04183-19-1.µm	GGUGAUUUAUUGAAAUUAUA	1565	UAUAAUUAUUAUUAUUAUUA	2028	1206-1224	
AV04184-19-1.µm	UCUUAUUAUUAAGGAAGAA	1566	UUUUUUUUAAUUAUUAAGA	2029	1223-1241	
AV04185-19-1.µm	AUUAUUAAGGAAGAUUGAUA	1567	UAUCAACUUCUUCUAAUAU	2030	1229-1247	
AV04186-19-1.µm	UUAGGAAGAUUGAUUGAA	1568	UUCAUUAUUAUUAUUAUUA	2031	1232-1250	
AV04187-19-1.µm	GGAAAGAUUGAUUGAAGUA	1569	UACUUAUUAUUAUUAUUA	2032	1235-1253	
AV04188-19-1.µm	GAAAGAUUGAUUGAAGUA	1570	UAACUUAUUAUUAUUAUUA	2033	1236-1254	
AV04189-19-1.µm	AAGAGUUGAUUGAAGUUA	1571	UAAACUUAUUAUUAUUAUUA	2034	1237-1255	
AV04190-19-1.µm	GAUUAAGAUUUUUUGCCUA	1572	UAGGCAAAAAACUUAUUAUUA	2035	1244-1262	
AV04191-19-1.µm	UACAUUUUAUUAUUAUUAUUA	1573	UGAAUUAUUAUUAUUAUUA	2036	1330-1348	
AV04192-19-1.µm	ACAUAUUUAUUAUUAUUAUUA	1574	UGGAUUAUUAUUAUUAUUA	2037	1331-1349	
AV04193-19-1.µm	CUCAGAUUGUGCCAUGUAAA	1575	UUUUAUUAUUAUUAUUAUUA	2038	1395-1413	
AV04194-19-1.µm	UCAGAUUGUGCCAUGUAAAA	1576	UUUUUAUUAUUAUUAUUAUUA	2039	1396-1414	
AV04195-19-1.µm	CAGUGAAAGGUGUUUCUGUA	1577	UACAGAAACCUUUUAUUAUUA	2040	1406-1424	
AV04196-19-1.µm	AGUGAAAGGUGUUUCUGUA	1578	UAACAGAAACCUUUUAUUAUUA	2041	1407-1425	

AV04197-19-1.µm	GAAAGGGUUCUGUUUGCA	1579	UGCAACAGAAACCCTUUC	2042	1410-1428	
AV04198-19-1.µm	AGGGSUUUCGUUUUGCUUCA	1580	UGAAGCAAAACAGAAACCCTU	2043	1413-1431	
AV04199-19-1.µm	UUCUGUUUGCUUUCAUUUGCA	1581	UGCAAUGAAGCAAAACAGAA	2044	1418-1436	
AV04200-19-1.µm	UCAUUGCUGACAGCUCUUGA	1582	UACAAGCUGUCAGCAAUUGA	2045	1429-1447	
AV04201-19-1.µm	CAUUGCUGACAGCUCUUGUA	1583	UACAAGCUGUCAGCAAUUG	2046	1430-1448	
AV04202-19-1.µm	AUUGCUGACAGCUCUUGUAA	1584	UUAACAAGCUGUCAGCAAU	2047	1431-1449	
AV04203-19-1.µm	GCUGACAGCUCUUGUACUUA	1585	UAAGUAAACAAGCUGUCAGC	2048	1434-1452	
AV04204-19-1.µm	CAGCUGUUAACUUUUUGGA	1586	UCCAAAAAGUAAACAAGCUG	2049	1439-1457	
AV04205-19-1.µm	AGCUGUUAACUUUUUGGAA	1587	UUCCAAAAAGUAAACAAGCU	2050	1440-1458	
AV04206-19-1.µm	UUACUUUUUGGAAAGCUAGA	1588	UCUAGCUUCCAAAAAGUAA	2051	1446-1464	
AV04207-19-1.µm	UCUCGUUCUCCAAGUUUAA	1589	UUAAACUUUGAAGACGAGA	2052	1743-1761	
AV04208-19-1.µm	AUUAGAAAAUGAUUCCGGAA	1590	UUCCGAAUCAUUUUUCUAU	2053	1761-1779	
AV04209-19-1.µm	UUCGAGAGCAGUGUUAGA	1591	UCUAAACACUGCUCUCCGAA	2054	1773-1791	
AV04210-19-1.µm	GGAGAGCAGUGUUAGCUUA	1592	UAAAGCUAACACUGCUCUCC	2055	1776-1794	
AV04211-19-1.µm	AGAGCAGUGUUAGCUUAUA	1593	UAUAAGCUAACACUGCUCU	2056	1778-1796	
AV04212-19-1.µm	GAGCAGUGUUAGCUUAUA	1594	UAAUAAAGCUAACACUGCUC	2057	1779-1797	
AV04213-19-1.µm	GCAUGUGUAGCUUAUUUGA	1595	UCAAAUAAAGCUAACACUGC	2058	1781-1799	
AV04214-19-1.µm	CAGUGUUAGCUUAUUUGUA	1596	UACAAAUAAAGCUAACACUG	2059	1782-1800	
AV04215-19-1.µm	UGUUAGCUUAUUUGUUGA	1597	UCCAACAUAUAAAGCUAACA	2060	1785-1803	
AV04216-19-1.µm	GCUUAUUUGUUGGAAUAAA	1598	UUUAUUUCCAACAUAUAAAGC	2061	1790-1808	
AV04217-19-1.µm	UUGGAAUAAAAUUVUAGGAA	1599	UUCCUAAAAUUVUUVCCAA	2062	1799-1817	
AV04218-19-1.µm	GGAUUAAAAUUVUAGGAUUA	1600	UAUUCCUAAAUUVUUAUUC	2063	1801-1819	
AV04219-19-1.µm	UAUUUUAAAAAGAUUGAAAAA	1601	UUUUCCAUCUUVUAGAAUA	2064	1823-1841	
AV04220-19-1.µm	AUUUUAAAAAGAUUGAAAAA	1602	UUUUUCCAUCUUVUAGAAU	2065	1824-1842	
AV04221-19-1.µm	GAUGGAAAAAACUUUUUGGA	1603	UCCAAAAAGUUUUUCCAUUC	2066	1833-1851	
AV04222-19-1.µm	GGAAAAAACUUUUUGGAUUA	1604	UUAUCCAAAAAAGUUUUUCC	2067	1836-1854	
AV04223-19-1.µm	AACUUUUUGGAUUAUUUGGA	1605	UCCAUAUUAUCCAAAAAAGUU	2068	1841-1859	
AV04224-19-1.µm	UUGGAUAUUUGGAGAAAUUA	1606	UAUUUCCUCCAUAUAUCCAA	2069	1847-1865	

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AD03507.µm	GUUCACAGAUUGGCCAGUGAAA	3507	UUUCACUUGGCACAUUCUGAGAC	3548	1393-1413	
AD03508.µm	CCCAUGUGAAAGGGUUCUGUA	3508	UACAGAAACCCTUUCACUGGG	3549	1404-1424	
AD03509.µm	GCAGUGAAAGGGUUCUGUA	3509	UACAGAAACCCTUUCACUGC	3550	1405-1425	
AD03510.µm	CUGAAAGGGUUCUGUUGCA	3510	UGCAACAGAAACCCTUUCAG	3551	1408-1428	
AD03511.µm	GUUCAUUGCUGACAGCUGUA	3511	UACAAGCUGUCAGCAAUUGAAC	3552	1427-1447	
AD03512.µm	GUCAUUGCUGACAGCUGUA	3512	UAACAAGCUGUCAGCAAUUGAC	3553	1428-1448	
AD03513.µm	GCAUUGCUGACAGCUGUAA	3513	UUACAAGCUGUCAGCAAUUGC	3554	1429-1449	
AD03514.µm	CACAGCUGUUAUUCUUUGA	3514	UCCAAAAAGUAAACAAGCUGUG	3555	1437-1457	
AD03515.µm	GGUUAUUUUUGGAAAGCUAGA	3515	UCUAGCUUCCAAAAAGUUAACC	3556	1444-1464	
AD03516.µm	GUGGCAUUGGUAAGAUAUA	3516	UAUAUUUCUUAACCAAUUGCCAC	3557	1660-1680	
AD03517.µm	GAAUUAAGAAAUUGAUUCGGAA	3517	UUCCGAUUCAUUUUCUAUUC	3558	1759-1779	
AD03518.µm	GCGGAGAGCAGUGUUAUCUUA	3518	UAAGCUAACACUGCUCUCCGC	3559	1774-1794	
AD03519.µm	GGCAGUGUUAUCUUAUUGUA	3519	UACAAAUAAAGCUAACACUGCC	3560	1780-1800	
AD03520.µm	GGUGUUAUCUUAUUGUUGGA	3520	UCCAACAUAUAAAGCUAACACCC	3561	1783-1803	
AD03521.µm	GAGCUUAUUGUUGGAUUAUA	3521	UUUAUUCCAACAAAUUAAGCUC	3562	1788-1808	
AD03522.µm	GGUUGGAUUAUUAUUGAGAA	3522	UUCCUAAAUUUUAUUCCAACC	3563	1797-1817	
AD03523.µm	GUGGAUUAUUAUUGGAUUA	3523	UAUUCUUAUUAUUAUUCAC	3564	1799-1819	
AD03524.µm	GUUAUUCUAAAGGAUUGAAAA	3524	UUUUCCAUCCUUAUAGAUUAAC	3565	1821-1841	
AD03525.µm	GGGAUUGGAUAAACUUUUUGA	3525	UCCAAAAAGUUUUUCCAUCC	3566	1831-1851	
AD03526.µm	GUGGAAAAACUUUUUGAUAA	3526	UUAUCCAAAAAGUUUUUCCAC	3567	1834-1854	
AD03527.µm	GUUUGGAUUAUUGGAGAAUA	3527	UAUUUCUCCAAAUUAUCCAAAC	3568	1845-1865	
AD03528.µm	GUUUAAAAACAUUUUGCUUAA	3528	UUAAGCCAAAUUGUUUUUAAC	3569	1864-1884	
AD03529.µm	GUUAAAAACAUUUUGCUUAUA	3529	UAUAAGCCAAAUUGUUUUUAAC	3570	1865-1885	
AD03530.µm	GUUCUUAUUUGACAGAAACCUA	3530	UAGGUUUCUGUCAAUAUCCAGCAC	3571	2073-2093	
AD03531.µm	CAUUUGACAGAAACCUUGAUUA	3531	UAAUUGCAGGUUCUGUCAAUUG	3572	2078-2098	
AD03532.µm	GUAGACAGAAACCUUGAUUUUGCA	3532	UGCAAAUUGCAGGUUCUGUCCAC	3573	2081-2101	
AD03533.µm	GGACAGAAACCUUGAUUUUGCUA	3533	UAGCAAAUUGCAGGUUCUGUCC	3574	2082-2102	
AD03534.µm	GCAGAAACCUUGAUUUUGCUUAA	3534	UUAAAGCAAAUUGCAGGUUCUGC	3575	2084-2104	

AD03535. um	CAACCGCAUUUGCUUAUCUA	3535	UAGAUAAAGCAAUUGCAGGUUG	3576	2087-2107	
AD03536. um	GACCGCAUUUGCUUAUCUUA	3536	UAAGAUAAAGCAAUUGCAGGUC	3577	2088-2108	
AD03537. um	GCCUGCAUUUGCUUAUCUUA	3537	UGAAGAUAAAGCAAUUGCAGGC	3578	2089-2109	
AD03538. um	GCUGCAUUUGCUUAUCUCAA	3538	UUGAAGAUAAAGCAAUUGCAGC	3579	2090-2110	
AD03539. um	GGCAUUUGCUUAUCUUAUCAA	3539	UUUUGAAGAUAAAGCAAUUGCC	3580	2092-2112	
AD03540. um	GUUGCUUAUCUUAUAAAUUA	3540	UAUAUUUUGAAGAUAAAGCAAC	3581	2096-2116	
AD03541. um	GUUCUUAUCUUAUAAAUUA	3541	UCAUAUUUUGAAGAUAAAGCAC	3582	2097-2117	

Table 2 and Table 2A shows certain chemically modified HTT RNAi agent antisense strand and sense strand sequences of the invention. In some embodiments of methods of the invention, an RNAi agent with a polynucleotide sequence shown in Table 2 and Table 2A is administered to a cell and/or subject. In some embodiments of methods of the invention, a RNAi agent with a polynucleotide sequence shown in Table 2 and Table 2A is administered to a subject. In some embodiments of the invention an RNAi agent administered to a subject comprises a duplex identified in a row in Table 2 and Table 2A, column one and includes the sequence modifications show in the sense and antisense strand sequences in the same row in Table 2 and Table 2A, columns three and six, respectively. In some embodiments of methods of the invention, a sequence shown in Table 2 and Table 2A may be attached to (also referred to herein as “conjugated to”) a compound capable of delivering the RNAi agent to a cell and/or tissue in a subject. A non-limiting example of a delivery compound that may be used in certain embodiments of the invention is a GalNAc-containing compound or a GLS-15*-containing compound. In Table 2, the first column indicates the Duplex AV# of the base sequences as shown in Table 1, In Table 2A, the first column indicates the Duplex AV# of the base sequences as shown in Table 1A. Table 2 and Table 2A discloses Duplex AV# and also shows chemical modifications included in sense and antisense sequence of the duplexes. For example, Table 1A shows base single-strand sequences SEQ ID NO: 1233 (sense) and SEQ ID NO: 1696 (antisense), which together are the double-stranded duplex identified as: Duplex AV# AV03373. um and Table 2A lists Duplex AV# AV03373, which indicates that the duplex of SEQ ID NO: 2747 and SEQ ID NO: 2986 includes base sequences of SEQ ID NO: 1233 and SEQ ID NO: 1696, respectively, but with the chemical modifications shown in the sense and antisense sequences shown in columns three and six, respectively. The “Sense strand SS#” in Table 2 column two is the assigned identifier

for the Sense Sequence (including modifications) shown column 3 in the same row. The “Antisense strand AS#” in Table 2 column five is the assigned identifier for the Antisense sequence (including modifications) shown in column six.

Table 2: provides chemically modified HTT RNAi agent antisense strand and sense strand sequences. All sequences shown 5' to 3'. These sequences were used in certain in vitro testing studies described herein.

Duplex AV#	Sense strand SS#	Sense Sequence	SEQ ID NO.	Antisense strand AS#	Antisense Sequence	SEQ ID NO.
AV02731	AV02731-SS	u*c*auaacAfcAfuUfcguuuu*g*u*a	2089	AV02731-AS	u*Af*caaaCfgaauGfuGfaUfuau*g*a	2382
AV02732	AV02732-SS	g*c*ugguuGaAfuCfcGfauuccu*g*a	2090	AV02732-AS	u*CF*aggaAfuccgAfuUfcAfeca*g*c	2383
AV02734	AV02734-SS	u*u*uccuacAfcAfaAfcucuaa*a*a	2091	AV02734-AS	u*Uf*auagAfguuuCfcUfgAfaga*a*a	2384
AV02736	AV02736-SS	c*g*guaccgAfcAfaCfcagaua*u*a	2092	AV02736-AS	u*Af*auacUfgguuCfcUfgAfagg*c*g	2385
AV02737	AV02737-SS	a*a*ccuucAfaGfaGfuuaug*c*a	2093	AV02737-AS	u*GF*caauAfacucUfuGfaAfagg*u*u	2386
AV02738	AV02738-SS	c*a*guuacCfuCfaGfuuaug*a*g	2094	AV02738-AS	u*CF*uucaAfacugAfgUfaCfagc*u*g	2387
AV02740	AV02740-SS	u*c*c*ugaaucGfaGfaUfcggaug*u*u	2095	AV02740-AS	a*Af*caucCfgaucUfcGfaUfua*g*a	2388
AV02741	AV02741-SS	a*c*agcaguGfuUfgAfaaaau*u*g	2096	AV02741-AS	c*Af*aaauUfaucaAfcAfcUfgcu*g*u	2389
AV02742	AV02742-SS	c*u*guuagUfcCfaUfgcuuaa*g*a	2097	AV02742-AS	u*CF*uuagGfcaugGfaCfcUfagc*a*g	2390
AV02804	AV02804-SS	g*u*gcacgcAfcCfaAfaagaag*a*a	2098	AV02804-AS	u*Uf*culUfu(cUNA)uuugGfuCfGfugc*a*c	2391
AV02805	AV02805-SS	g*g*gcacgcAfcAfaAfaagaag*a*a	2099	AV02805-AS	u*Uf*ucUfu(aUNA)cuuugGfuCfGfugc*c*c	2392
AV02806	AV02806-SS	c*c*ccgaaCfaAfaGfaagaag*c*a	2100	AV02806-AS	u*GF*uuCfu(aUNA)uauUfgGfuCfGfu*g*g	2393
AV02807	AV02807-SS	g*a*ccgaaCfaAfaAfaagaag*c*a	2101	AV02807-AS	u*Af*guUfc(aUNA)uuuUfuGfuUfcggu*u*c	2394
AV02808	AV02808-SS	g*c*c*gaaccaAfaGfaAfaagaag*c*a	2102	AV02808-AS	u*Af*aguuCfuucUfuUfgGfuCfGfu*g*c	2395
AV02809	AV02809-SS	g*c*c*gaaccaAfaAfaAfaagaag*c*a	2103	AV02809-AS	u*Af*aguuUfcuuCfuUfuGfuCfGfu*g*c	2396
AV02810	AV02810-SS	g*g*gaaccaAfaAfaAfaagaag*c*a	2104	AV02810-AS	u*Gf*aaagUfuuuUfcUfuUfggu*c*c	2397
AV02811	AV02811-SS	c*a*ccaagAfaAfaAfaagaag*c*a	2105	AV02811-AS	u*Uf*gaagGfuuuUfuCfuUfuug*u*g	2398
AV02812	AV02812-SS	g*c*c*caagAfaGfaAfaagaag*c*a	2106	AV02812-AS	u*CF*ugaaAfguucUfuUfcUfuug*g*c	2399
AV02813	AV02813-SS	g*a*aaagaAfaAfaAfaagaag*c*a	2107	AV02813-AS	u*Af*guuAfaaguUfcUfuUfcuu*u*c	2400
AV02814	AV02814-SS	g*a*aaagaAfaCfuUfucagau*a*a	2108	AV02814-AS	u*Uf*agcuGfaagUfuCfuUfuu*u*c	2401
AV02815	AV02815-SS	g*g*aaauuCfaGfcUfaccagau*a*a	2109	AV02815-AS	u*Uf*cuugGfuagcUfgAfaAfguu*c*c	2402
AV02816	AV02816-SS	g*a*gaagaCfcGfuGfuagaag*c*a	2110	AV02816-AS	u*Uf*gaauCfacaCfGfuUfcUfuuc*u*c	2403
AV02817	AV02817-SS	c*a*agaccGfuGfuGfaaua*u*a	2111	AV02817-AS	u*Af*augaUfuacAfcCfGfuUfcuu*u*g	2404

AV02818	AV02818-SS	c*a*cceguuGfAfuCfaumugc*u*a	2112	AV02818-AS	u*A*fgacaAfugauUfcAfcAfcgg*u*g	2405
AV02819	AV02819-SS	g*g*ugugauUfcAfuUfgucugc*a*a	2113	AV02819-AS	u*G*fucAfgu(UNA)caanGfaUfuCfaca*c*c	2406
AV02820	AV02820-SS	c*u*ugugauCfaUfuCficucgac*a*a	2114	AV02820-AS	u*U*fugacGfacaUfgAfufUfcaac*a*g	2407
AV02821	AV02821-SS	c*u*gtaucaUfuGfuCfugacaa*u*a	2115	AV02821-AS	u*A*fugcCfagacAfaUfgAfucuc*a*g	2408
AV02822	AV02822-SS	c*a*aucauuGfuCfuCfacaana*u*a	2116	AV02822-AS	u*A*fuuuuGfucagAfcAfaUfgau*u*g	2409
AV02823	AV02823-SS	g*u*ugucugCfaAfuAfugugaa*a*a	2117	AV02823-AS	u*U*fuucaCfauauUfgUfcAfagac*a*c	2410
AV02824	AV02824-SS	c*u*ugacaaAfuaAfufugaaana*c*a	2118	AV02824-AS	u*G*fuuuuCfcauuAfuUfgUfcagc*a*g	2411
AV02825	AV02825-SS	g*u*ugacagAfaUfuCfucacag*a*a	2119	AV02825-AS	u*U*fucugGfagaaUfuUfcUfgac*a*a*c	2412
AV02826	AV02826-SS	g*u*ucuccaGfaAfuUfucagaa*a*a	2120	AV02826-AS	u*U*fuuucGfcauuUfcUfgGfagc*a*c	2413
AV02827	AV02827-SS	g*u*ucuccaGfaUfuUfucagaa*c*a	2121	AV02827-AS	u*G*fuuucUfgaaUfuCfuGfagc*a*c	2414
AV02828	AV02828-SS	c*c*uauggaAfcUfuUfucugc*u*a	2122	AV02828-AS	u*A*fugacAfacaGfuUfcCfana*g*g	2415
AV02829	AV02829-SS	g*c*ucacaaAfagGfuUfcaaca*g*a	2123	AV02829-AS	u*C*fuuugAfuaacUfuUfgUfugag*g*c	2416
AV02830	AV02830-SS	c*u*uaucaaAfgcCfuUfugaugc*a*a	2124	AV02830-AS	u*U*fuccauCfaagCfuUfuCfana*a*g	2417
AV02831	AV02831-SS	g*a*ucaagCfuUfuCfauugau*u*a	2125	AV02831-AS	u*A*fauccAficaaAfgcCfuUfuga*u*c	2418
AV02832	AV02832-SS	g*a*aaugauUfgAfuGfgauuc*a*a	2126	AV02832-AS	u*U*fugaaUfccauCfaAfaCfeu*u*c	2419
AV02833	AV02833-SS	g*g*cuuugUfgGfaUfucuauc*c*a	2127	AV02833-AS	u*G*fauuaGfauucCfaUfcAfagc*c*c	2420
AV02834	AV02834-SS	c*c*uuugauGfgAfuUfcauanc*u*a	2128	AV02834-AS	u*A*fugauAfagauCfcAfuCfana*g*g	2421
AV02835	AV02835-SS	g*u*uuugaugGfaUfuCfuaucuc*u*a	2129	AV02835-AS	u*A*fugauUfgaaUfcCfaUfcaaa*c*c	2422
AV02836	AV02836-SS	c*a*ugugauCfuAfaUfcauucca*a*a	2130	AV02836-AS	u*U*fuggaAfugauAfgaAfaUfcca*u*g	2423
AV02837	AV02837-SS	c*a*uuucaUfcUfuCfcaaggu*u*a	2131	AV02837-AS	u*A*faccuUfggaGfaUfuAfagaa*u*g	2424
AV02838	AV02838-SS	g*u*ucuaaCfuUfcCfagguu*a*a	2132	AV02838-AS	u*U*fauacUfuggaAfgaAfuUfaga*a*c	2425
AV02839	AV02839-SS	g*c*uaucuuUfcCfaAfugguac*a*a	2133	AV02839-AS	u*U*fugaaCfcuugCfaAfgaAfuaa*g*c	2426
AV02840	AV02840-SS	g*g*uuuccaAfaAfuUfauugcu*u*a	2134	AV02840-AS	u*A*fagccAfuaauUfuUfgGfaga*c*c	2427
AV02841	AV02841-SS	c*u*uccaaAfaUfuAfugguuc*c*a	2135	AV02841-AS	u*G*faaGfc(cUN)AuaauUfuUfuGfuga*a*g	2428
AV02842	AV02842-SS	g*c*ccaaauAfuAfuGfgguuc*u*a	2136	AV02842-AS	u*A*fagaaGfcauAfaUfuUfugc*g*c	2429
AV02843	AV02843-SS	g*u*auugcuUfcUfuUfugcaca*u*a	2137	AV02843-AS	u*A*fuuugCfcaagGfaAfgcCfcau*a*c	2430
AV02844	AV02844-SS	g*u*uuugcaAfuUfuUfgcaau*u*a	2138	AV02844-AS	u*C*fauuuGfcaaaAfuUfgCfcaaa*a*c	2431
AV02845	AV02845-SS	g*u*uguuuaAfgCfcCfuaucana*g*a	2139	AV02845-AS	u*C*fuaugAfagcCfuUfuAfaca*a*c	2432
AV02846	AV02846-SS	g*a*uauggaAfcCfuCfagguca*a*a	2140	AV02846-AS	u*U*fugacUfucagCfuUfcGfcau*u*c	2433
AV02847	AV02847-SS	c*a*caaggaAfagGfaAfauugaa*g*a	2141	AV02847-AS	u*C*fuucaAfuaucUfuUfcCfugc*u*g	2434
AV02848	AV02848-SS	g*c*aaaggaAfgaAfaUfugagc*u*a	2142	AV02848-AS	u*A*fucucCfauuuCfuUfuCfeu*u*g*c	2435

AV02849	AV02849-SS	g*u*uguccaGfgUfuUfaugaac*u*a	2143	AV02849-AS	u*Af*guucAfuaaaCfcUfgGfaca*a*c	2436
AV02850	AV02850-SS	g*a*gguuuaUfgAfafCfugacgu*u*a	2144	AV02850-AS	u*Af*acguCfaguuCfaUfaAfacc*u*c	2437
AV02851	AV02851-SS	c*g*uuuaugAfafCfuGfacaagua*c*a	2145	AV02851-AS	u*G*f*uaacGfucagUfuCfaUfaaa*c*g	2438
AV02852	AV02852-SS	g*u*ugaacugAfafCfuUfacaaca*a*a	2146	AV02852-AS	u*Af*ugauGfuaacGfuCfaGfhuac*a*c	2439
AV02853	AV02853-SS	g*g*aaacugaCfguUfuAfcaucaa*a*a	2147	AV02853-AS	u*U*f*augauUfguaaCfgeUfcAfguu*c*c	2440
AV02854	AV02854-SS	g*u*ugacguuAfafCfuCfaaacac*a*a	2148	AV02854-AS	u*U*f*ugguAfugauGfuAfafCfugc*a*c	2441
AV02855	AV02855-SS	g*g*ggaaaguaUfuGfuGfagaacuu*a*a	2149	AV02855-AS	u*U*f*aaquUfecaacAfafUfaCfucc*c*c	2442
AV02856	AV02856-SS	c*a*guauuugUfgGfafaCfuuaaa*g*a	2150	AV02856-AS	u*C*f*uaaaAfguucCfaCfaAfuaac*u*g	2443
AV02857	AV02857-SS	g*a*aaagccaAfafGfuGfucuuu*a*a	2151	AV02857-AS	u*C*f*uaagAfgeaacUfuUfgCfcuu*u*c	2444
AV02858	AV02858-SS	g*c*c*ucugaaUfcGfafaGfauagga*u*a	2152	AV02858-AS	u*Af*ucecgAfhuacGfaUfuCfaga*g*c	2445
AV02859	AV02859-SS	g*u*ugaacugAfguUfuCfugaauu*a*a	2153	AV02859-AS	u*Af*auuuCfagaacCfuGfuCfuga*a*c	2446
AV02860	AV02860-SS	g*a*guucugAfafAfuUfuguuaa*g*a	2154	AV02860-AS	u*C*f*uaacAfcaauUfuCfafaGfaac*u*c	2447
AV02861	AV02861-SS	g*g*uuucugaAfafAfuUfuGfuguuaa*g*a	2155	AV02861-AS	u*U*f*cuaaCfacaauUfuUfaAfgaac*c*c	2448
AV02862	AV02862-SS	g*u*cuugaauUfuGfuGfuaagac*g*a	2156	AV02862-AS	u*C*f*guccAfacaacAfafUfuUfag*a*c	2449
AV02863	AV02863-SS	c*u*ugaaauAfuUfuGfuguuag*g*a	2157	AV02863-AS	u*C*f*ucaaaCfacaacAfuUfuUfag*a*c	2450
AV02864	AV02864-SS	g*g*ccuuuuAfufCfuGfucuuu*u*a	2158	AV02864-AS	u*Af*acgaAfgeaacAfuUfuUfag*c*c	2451
AV02865	AV02865-SS	g*u*uuuauuGfcUfuCfuguuuu*u*a	2159	AV02865-AS	u*C*f*aaaaAfgegaGfcAfgaAfuaa*a*c	2452
AV02866	AV02866-SS	g*u*ucuguuCfguUfuUfuuuguaa*a*a	2160	AV02866-AS	u*U*f*uaagAfuaaaCfgaAfafGfag*a*c	2453
AV02867	AV02867-SS	g*u*uguuugUfuUfuUfuguuaac*a*a	2161	AV02867-AS	u*U*f*guuaGfcaaaAfafCfgaAfagc*a*c	2454
AV02868	AV02868-SS	g*g*gcuuugUfuUfuGfcauaac*g*a	2162	AV02868-AS	u*C*f*uguuAfgecaaAfafAfefGfagc*c*c	2455
AV02869	AV02869-SS	g*g*gaauuuUfuCfuUfcaugca*a*a	2163	AV02869-AS	u*U*f*uuugUfgaaagAfafAfafAfuaac*c*c	2456
AV02870	AV02870-SS	c*g*gaauuuUfuCfuCfagaacaa*c*a	2164	AV02870-AS	u*G*f*uuugCfugaacGfaAfafGfauu*c*g	2457
AV02871	AV02871-SS	g*u*ucagccaAfafCfuCfuaaaag*g*a	2165	AV02871-AS	u*C*f*uuuaUfagagUfuUfgCfuga*a*c	2458
AV02872	AV02872-SS	g*c*c*agcaaaCfuCfuAfuaaagu*u*a	2166	AV02872-AS	u*Af*acuuUfaugagAfguUfuUfgeu*g*c	2459
AV02873	AV02873-SS	g*g*gaacuuCfuAfuAfagaucac*u*a	2167	AV02873-AS	u*G*f*gaacUfuuaaUfgAfguUfuug*c*c	2460
AV02874	AV02874-SS	g*u*ucuaaaAfguUfuCfucuuug*a*a	2168	AV02874-AS	u*U*f*caagAfgegaacCfuUfuAfuaag*a*c	2461
AV02875	AV02875-SS	g*u*ucagcaUfcUfuGfacaac*c*a	2169	AV02875-AS	u*U*f*guagUfucaacGfaUfuUfegu*a*c	2462
AV02876	AV02876-SS	g*c*auuuuAfafCfuAfcaugca*u*a	2170	AV02876-AS	u*Af*ucgaUfguagUfuCfaAfgaug*g*c	2463
AV02877	AV02877-SS	g*u*ucuuuugCfuAfafAfucgauc*a*a	2171	AV02877-AS	u*U*f*gaucGfauguAfguUfuCfagaag*a*c	2464
AV02878	AV02878-SS	g*u*ugaacuuAfafCfuCfagaucuu*g*a	2172	AV02878-AS	u*C*f*augauUfcaugGfuAfguUfuaa*a*c	2465
AV02879	AV02879-SS	g*c*c*cucaacaGfgAfafAfuaaauu*u*a	2173	AV02879-AS	u*Af*aaugUfauuuCfufUfgUfgag*g*c	2466

AV02880	AV02880-SS	g* ^a a* ^u uuccuUf ^g CfuCf ^g cgzaa* ^a * ^a	2174	AV02880-AS	u*U ^f * ^u uuccCf ^g ca ^g CfaAfa ^g fzaa* ^u * ^c	2467
AV02881	AV02881-SS	c* ^a a* ^u uccuucUf ^g UfuAfcuugca* ^a * ^a	2175	AV02881-AS	u*U ^f * ^u gcaAfguaaCfaGfaAfgac* ^u * ^g	2468
AV02882	AV02882-SS	g* ^c * ^u uccuugUfaCfuUf ^g caagu* ^u * ^a	2176	AV02882-AS	u*Af* ^a acuUGfca ^g UfaAfcAf ^g zaa* ^g * ^c	2469
AV02883	AV02883-SS	c* ^a * ^a * ^g gaucGfuGfuCfaugagu* ^g * ^a	2177	AV02883-AS	u*G ^f * ^a cucAf ^u gacAfcAfgUfucc* ^u * ^g	2470
AV02884	AV02884-SS	g* ^g * ^g * ^c agcaCfaGfuGf ^g guuag* ^g * ^a	2178	AV02884-AS	u*C ^f * ^a uaaCf ^u cacUf ^g UfaGfcug* ^c * ^c	2471
AV02885	AV02885-SS	g* ^u * ^u * ^g aggaCfaGfuUf ^g ccuanu* ^g * ^a	2179	AV02885-AS	u*C ^f * ^a auaGf ^g zacUf ^g UfuCf ^u c* ^a * ^c	2472
AV02886	AV02886-SS	g* ^a * ^g * ^c cazaAfaCfuUf ^g acaca* ^g * ^a	2180	AV02886-AS	u*U ^f * ^u cugGfuagUfuUfuCfu ^g * ^u * ^c	2473
AV02887	AV02887-SS	g* ^u * ^u * ^a uacagGf ^g CfuUf ^u uaaaz* ^c * ^a	2181	AV02887-AS	u*G ^f * ^u uuuAfaagCfcCfuGfuau* ^a * ^c	2474
AV02888	AV02888-SS	g* ^g * ^g * ^u gcauAfuAfaUf ^g uuugc* ^a * ^a	2182	AV02888-AS	u*U ^f * ^g acaAfcuuAfuUf ^g Afgca* ^c * ^c	2475
AV02889	AV02889-SS	g* ^a * ^a * ^a uaauUfuGfuCfauccau* ^u * ^a	2183	AV02889-AS	u*Af* ^a augAf ^u gacAfaCfaUfuau* ^u * ^c	2476
AV02890	AV02890-SS	g* ^a * ^a * ^u auugUfcAfuCfcauuug* ^c * ^a	2184	AV02890-AS	u*G ^f * ^a caaaUf ^g gaugGfaCfaAfcuu* ^u * ^c	2477
AV02891	AV02891-SS	g* ^c * ^c * ^a uuugCfuUf ^g Gfagaug* ^a * ^a	2185	AV02891-AS	u*U ^f * ^u cauChuccaAfcCfaAfaug* ^g * ^c	2478
AV02892	AV02892-SS	g* ^a * ^a * ^u uugcuUf ^g GfaCfaugag* ^a * ^a	2186	AV02892-AS	u*U ^f * ^u cucAf ^u cucCfaAfgCfaa* ^u * ^c	2479
AV02893	AV02893-SS	c* ^a * ^a * ^u caagCfaGfuGfuuuac* ^u * ^a	2187	AV02893-AS	u*Af* ^g guAfaaacUf ^g CfuUfu ^g za* ^u * ^g	2480
AV02894	AV02894-SS	g* ^a * ^a * ^a agcagUf ^g UfuUf ^g accug* ^a * ^a	2188	AV02894-AS	u*U ^f * ^u ucagGfuaaCfaCfuGfcu* ^u * ^c	2481
AV02895	AV02895-SS	g* ^a * ^a * ^u agugCfuAfuAfacuac* ^u * ^a	2189	AV02895-AS	u*Af* ^g uagGfuauAfgCfcUfcua* ^u * ^c	2482
AV02896	AV02896-SS	c* ^g * ^g * ^a aaauaAfcCfuUf ^g caagz* ^g * ^a	2190	AV02896-AS	u*C ^f * ^a ucuuGfzaagGfuUfaUfuuu* ^c * ^g	2483
AV02897	AV02897-SS	g* ^u * ^u * ^u gacgaGfuUfuChicauag* ^a * ^a	2191	AV02897-AS	u*U ^f * ^u cauGfagaAfcUf ^g Cfu ^g * ^a * ^c	2484
AV02898	AV02898-SS	g* ^g * ^g * ^a gcaucCfaCfaUfuugau* ^g * ^a	2192	AV02898-AS	u*C ^f * ^a uacAf ^u raugUf ^g AfgUf ^g cu* ^c * ^c	2485
AV02899	AV02899-SS	g* ^c * ^c * ^a cauuuGf ^g AfuGfcu ^g ugz* ^a * ^a	2193	AV02899-AS	u*U ^f * ^u caacAf ^g cauCfcAfaAfu ^g * ^g * ^c	2486
AV02900	AV02900-SS	g* ^g * ^g * ^c cuugzAfgCfuUfu ^g uguc* ^u * ^a	2194	AV02900-AS	u*Af* ^g acaCfaagCfuUfcafcag* ^c * ^c	2487
AV02901	AV02901-SS	c* ^c * ^c * ^u gugzaGfcUfuUf ^g uguc* ^u * ^a	2195	AV02901-AS	u*Af* ^a gucAfcaagGfcUfuCfaca* ^g * ^g	2488
AV02902	AV02902-SS	c* ^u * ^u * ^g aaagUfuGfuGfucuuu* ^u * ^a	2196	AV02902-AS	u*Af* ^a gaaGfacacAf ^u AfgCfuuc* ^a * ^g	2489
AV02903	AV02903-SS	c* ^a * ^a * ^g cuuuGfuGfuChuccuu* ^c * ^a	2197	AV02903-AS	u*G ^f * ^a aaagAf ^u gacAfcAfaAfgcu* ^u * ^g	2490
AV02904	AV02904-SS	g* ^c * ^c * ^a aguuGfcAfuUf ^g ugzag* ^u * ^a	2198	AV02904-AS	u*Af* ^a cucCfaauGfcAfaAfcug* ^g * ^c	2491
AV02905	AV02905-SS	g* ^c * ^c * ^a guugCfaUfuUf ^g ugaguu* ^u * ^a	2199	AV02905-AS	u*Af* ^a acuCfcaaaUf ^g CfaAfacu* ^g * ^c	2492
AV02906	AV02906-SS	g* ^a * ^a * ^u uugcAfuUfuGf ^g uguuu* ^a * ^a	2200	AV02906-AS	u*U ^f * ^u aaacUfccaAfuGfcAfaac* ^u * ^c	2493
AV02907	AV02907-SS	g* ^c * ^c * ^u caauGfaGfuChagagz* ^g * ^a	2201	AV02907-AS	u*C ^f * ^a uuccUfagacUfcafuCfu ^g * ^g * ^c	2494
AV02908	AV02908-SS	c* ^c * ^c * ^a ucaAfgAfuGf ^u cuuuz* ^u * ^a	2202	AV02908-AS	u*Af* ^u caAfgcauChUf ^g Afu ^g * ^g * ^g	2495
AV02909	AV02909-SS	g* ^u * ^u * ^u icuagCfaAfuCh ^g gauc* ^c * ^a	2203	AV02909-AS	u*G ^f * ^g uaaCfagaUf ^g UfcUfaga* ^a * ^c	2496
AV02910	AV02910-SS	g* ^u * ^u * ^a gucgCfuGfuUf ^g acaaaz* ^a * ^a	2204	AV02910-AS	u*U ^f * ^u guuGfuaacAfgGfaCfcug* ^a * ^c	2497

AV02911	AV02911-SS	g*a*caacaGfuAfaAfuccua*u*a	2205	AV02911-AS	u*Af*ugagGfaunuAfcUfuGfuug*u*c	2498
AV02912	AV02912-SS	g*a*acaaguAfaAfucucca*c*a*a	2206	AV02912-AS	u*Uf*gaugAfgeguUfuAfcUfhuu*u*c	2499
AV02913	AV02913-SS	g*c*c*acuggeGfaGfuUfhuuanc*a*a	2207	AV02913-AS	u*Uf*gaugAfaancUfcCfcCfagu*u*c	2500
AV02914	AV02914-SS	g*a*cuuggeAfGfuUfuUfcuauca*u*a	2208	AV02914-AS	u*Af*ugauAfgaaGfuCfcCfcag*u*c	2501
AV02915	AV02915-SS	g*u*ucuaaAfuCfuUfccuua*u*a	2209	AV02915-AS	u*Af*ugaaGfgaagAfuGfuUfaga*u*c	2502
AV02916	AV02916-SS	g*u*cuuacaUfcUfuCfcuuaa*u*a	2210	AV02916-AS	u*Uf*ugaAfggaGfuUfgAfuag*u*c	2503
AV02917	AV02917-SS	g*u*cuuccUfcAfuAfcucaa*a*a	2211	AV02917-AS	u*Uf*ugaGfgauGfaAfgGfaag*a*c	2504
AV02918	AV02918-SS	g*u*acucaAfaCfuGfcaugau*u*a	2212	AV02918-AS	u*CF*aucaUfgeagUfuUfgAfgu*u*a*c	2505
AV02919	AV02919-SS	g*a*acugaUfgAfuGfucuga*a*a	2213	AV02919-AS	u*Uf*ucagGfcauGfuUfgCfagu*u*c	2506
AV02920	AV02920-SS	g*g*aaauceUfgCfuUfhuagug*a*a	2214	AV02920-AS	u*Uf*cgaUfaagCfaGfgAfuuu*c*c	2507
AV02921	AV02921-SS	c*a*uggecaGfuGfuUfhuuguu*u*c*a	2215	AV02921-AS	u*Gf*aaCaFaancAfGfuGfcca*u*g	2508
AV02922	AV02922-SS	g*g*gcacuuGfuUfuGfuguuca*a*a	2216	AV02922-AS	u*Uf*ugaaCfaacaAfcAfGfuUfug*c*c	2509
AV02923	AV02923-SS	g*a*acuguuUfgUfgUfucaca*a*a	2217	AV02923-AS	u*Uf*uguuGfaacaCfaAfcCfagu*u*c	2510
AV02924	AV02924-SS	g*a*cuuuuuGfuGfuUfcaaca*u*a	2218	AV02924-AS	u*Af*uuuuUfgaacAfcAfaAfcag*u*c	2511
AV02925	AV02925-SS	g*u*caacaUfuGfuUfcaaguc*u*a	2219	AV02925-AS	u*Af*guuuUfcaacAfaUfuGfuug*a*c	2512
AV02926	AV02926-SS	g*c*c*aaacuUfgUfuGfaagacu*c*a	2220	AV02926-AS	u*Gf*agucUfcaacCfaAfuUfguu*u*c	2513
AV02927	AV02927-SS	g*u*guuugaGfaCfuChicuuu*g*a	2221	AV02927-AS	u*CF*caaaGfagagUfcUfuChaac*a*c	2514
AV02928	AV02928-SS	g*c*c*aaagaCfcGfuGfcaagaa*a*a	2222	AV02928-AS	u*Uf*uaucUfgaacGfgUfuChuuu*g*c	2515
AV02929	AV02929-SS	g*a*ccguuAfGfuAfaagaug*c*a	2223	AV02929-AS	u*Gf*cauuChuuuChuCfcAfcegg*u*c	2516
AV02930	AV02930-SS	c*c*agauaaGfaAfuGfcauu*a*a	2224	AV02930-AS	u*Uf*gaauAfgcauUfcUfuAfuuu*g*g	2517
AV02931	AV02931-SS	c*a*uaagaUfgCfuAfuuaa*a*a	2225	AV02931-AS	u*Uf*uaugAfaaagCfaUfuChuaa*u*g	2518
AV02932	AV02932-SS	g*a*agaauGfuAfuUfcauaa*c*a	2226	AV02932-AS	u*Gf*auuaUfgaaUfGfuAfuUfuUfu*c	2519
AV02933	AV02933-SS	c*c*uaaucaUfaAfuCfaauu*c*a	2227	AV02933-AS	u*CF*gaauGfuauUfaUfgAfuaa*g*g	2520
AV02934	AV02934-SS	g*c*c*aaauCfcAfuUfcauuu*g*u*a	2228	AV02934-AS	u*Af*caaaCfgaauGfuGfaUfuuaa*g*c	2521
AV02935	AV02935-SS	g*a*ucacauUfcGfuUfhuuuu*g*a*a	2229	AV02935-AS	u*Uf*caaaCfaaacGfaAfuGfuga*u*c	2522
AV02936	AV02936-SS	g*c*acauucGfuUfuGfuuuuga*c*a	2230	AV02936-AS	u*Gf*uaaAfaaaAfcGfaAfuuu*g*c	2523
AV02937	AV02937-SS	g*c*c*auucuuUfuGfuUfugaac*u*a	2231	AV02937-AS	u*Af*guuuCfaaaAfaAfcGfaa*u*c	2524
AV02938	AV02938-SS	g*u*ucguuuGfuUfuGfcauc*u*a	2232	AV02938-AS	u*Af*gaagUfuaaAfaAfcGfaa*a*c	2525
AV02939	AV02939-SS	g*u*guuugAfcCfuCfuuuuaa*u*a	2233	AV02939-AS	u*Af*uaacAfaagagGfuUfcAfaa*c*c	2526
AV02940	AV02940-SS	c*u*uuugaCfuCfuUfhuuaa*a*a	2234	AV02940-AS	u*Uf*uaaaAfaagAfGfuUfcaaa*a*g	2527
AV02941	AV02941-SS	g*u*ugaacUfcUfuGfuuaa*a*a	2235	AV02941-AS	u*Uf*uaauAfaaaGfaGfgUfuaa*a*c	2528

AV02942	AV02942-SS	g* ^g g* ^a aaccucUfhuGfhuUfaaaaa ^g * ^a	2236	AV02942-AS	u* ^C f* ^u uuuAfuaacAfaGfaGfguu* ^c * ^c	2529
AV02943	AV02943-SS	c* ^a * ^a ccuccUf ^g UfhuAfuaaa ^g * ^c * ^a	2237	AV02943-AS	u* ^G f* ^c uuuUfauaaCfaAfgAf ^g u ^g * ^u * ^g	2530
AV02944	AV02944-SS	g* ^g * ^g * ^c uuuaaAfaCfaGfiacac ^g * ^a * ^a	2238	AV02944-AS	u* ^U f* ^c gugUf ^{ac} ugUfhuUfhuAfaga* ^c * ^c	2531
AV02945	AV02945-SS	g* ^c * ^c * ^g aagcAf ^g GfhuUfhuagau* ^u * ^a	2239	AV02945-AS	u* ^A f* ^a uccuAfuaacCfuGfcUf ^u cu ^g * ^g * ^c	2532
AV02946	AV02946-SS	c* ^a * ^a g ^c agguUfhuUfhuAf ^g auuug* ^c * ^a	2240	AV02946-AS	u* ^G f* ^c aaauUf ^u uaaAfaCfcUf ^g cu* ^u * ^g	2533
AV02947	AV02947-SS	g* ^u * ^u * ^c aguuaCf ^g Gf ^g Ufhuaua* ^c * ^a	2241	AV02947-AS	u* ^G f* ^u auuUf ^{ac} ccCf ^g Uf ^u faAf ^c ug ^g * ^a * ^c	2534
AV02948	AV02948-SS	g* ^c * ^c * ^g uuaaCf ^g GfhuUf ^u faaac* ^u * ^a	2242	AV02948-AS	u* ^A f* ^g uaaUf ^{ua} acCfcGfuAf ^u cu ^g * ^c	2535
AV02949	AV02949-SS	c* ^g * ^g * ^g uuauUfaCfuGf ^u cuu ^g * ^g * ^a	2243	AV02949-AS	u* ^C f* ^a g ^a aaGf ^{ac} agUfaAf ^u Uf ^u faac* ^c * ^g	2536
AV02950	AV02950-SS	g* ^a * ^a * ^u uaucGfuCfuUf ^u cu ^g auu* ^u * ^a	2244	AV02950-AS	u* ^A f* ^a u ^{cc} Af ^{ga} agAfcAf ^g Ufaa* ^u * ^c	2537
AV02951	AV02951-SS	g* ^g * ^g * ^u cuccuGf ^g AfuUf ^u ca ^g au ^c * ^a * ^a	2245	AV02951-AS	u* ^U f* ^g au ^c Uf ^{ga} auCfcAf ^g Afaga* ^c * ^c	2538
AV02952	AV02952-SS	c* ^a * ^a * ^u caagguGfuUfhuAf ^u ug ^g cu* ^u * ^a	2246	AV02952-AS	u* ^A f* ^a ag ^{cc} Af ^{ua} aaAfcAf ^c Cfuga* ^u * ^g	2539
AV02953	AV02953-SS	g* ^a * ^a * ^g uguuUfaUfhuGf ^u cuuug* ^u * ^a	2247	AV02953-AS	u* ^A f* ^c aaatGf ^u ccaaUfaAfaCf ^{ac} * ^u * ^c	2540
AV02954	AV02954-SS	g* ^g * ^g * ^u uuauGf ^g CfuUfhu ^g auu* ^g * ^a	2248	AV02954-AS	u* ^C f* ^a auaCf ^{aa} agCfcAfaUf ^u faa* ^c * ^c	2541
AV02955	AV02955-SS	g* ^a * ^a * ^u ugcuUfhuGfuAf ^u ga ^a * ^c * ^a	2249	AV02955-AS	u* ^G f* ^u uuuAf ^{ua} acAfaAf ^g Cfca* ^u * ^c	2542
AV02956	AV02956-SS	g* ^u * ^u * ^g ccuuGfuAf ^u Uf ^g aa ^a * ^g * ^a	2250	AV02956-AS	u* ^C f* ^g u ^{gu} Uf ^{ca} auAfcAfaAf ^g cc* ^a * ^c	2543
AV02957	AV02957-SS	g* ^c * ^c * ^a uccuuUfhuCfuUf ^u cu ^g gu* ^u * ^a	2251	AV02957-AS	u* ^U f* ^a accaAf ^{ga} agAfaAfaAf ^g au* ^g * ^c	2544
AV02958	AV02958-SS	g* ^a * ^a * ^u ccuuUf ^u UfhuCfu ^u g ^u ua* ^u * ^a	2252	AV02958-AS	u* ^A f* ^a u ^{ac} Af ^{aga} aaGfaAfaAfa ^g * ^u * ^c	2545
AV02959	AV02959-SS	g* ^u * ^u * ^u uuuuUf ^u UfhuGf ^u guua* ^c * ^a	2253	AV02959-AS	u* ^G f* ^u aaauAf ^u ccaaGfaAfgAf ^u aa* ^a * ^c	2546
AV02960	AV02960-SS	g* ^u * ^u * ^a cuuacUfhuAfhuCf ^u aa ^g cu* ^a * ^a	2254	AV02960-AS	u* ^U f* ^a g ^{cg} Uf ^u cauAfaCfaUf ^{ag} * ^a * ^c	2547
AV02961	AV02961-SS	g* ^a * ^a * ^c uaucUfaUf ^g Af ^u ag ^u * ^u * ^a	2255	AV02961-AS	u* ^A f* ^u ag ^c Gf ^u ucaUfaAf ^g Af ^u ag* ^u * ^c	2548
AV02962	AV02962-SS	g* ^u * ^u * ^a uccuaUf ^g AfaCf ^g cuac* ^a * ^a	2256	AV02962-AS	u* ^U f* ^g uaaGf ^u cguuCfuAfaAf ^g au* ^a * ^c	2549
AV02963	AV02963-SS	g* ^a * ^a * ^u ccuaaGfaAf ^c Gf ^u cauca* ^u * ^a	2257	AV02963-AS	u* ^A f* ^u g ^{au} Af ^g cuUf ^u CaFuAf ^{ag} * ^u * ^c	2550
AV02964	AV02964-SS	g* ^c * ^c * ^u uaugaAf ^c Gf ^u Uf ^u cauu* ^c * ^a	2258	AV02964-AS	u* ^G f* ^a au ^g Af ^u agCfuUf ^u CaFuaa* ^g * ^c	2551
AV02965	AV02965-SS	g* ^u * ^u * ^a uaugaCf ^g CfuAfu ^u cau ^c * ^a * ^a	2259	AV02965-AS	u* ^U f* ^g aaUGfaugaCf ^g UfhuCfaua* ^a * ^c	2552
AV02966	AV02966-SS	g* ^a * ^a * ^u gaucGfuAfuCfa ^u uca* ^a * ^a	2260	AV02966-AS	u* ^U f* ^u ugaAfu ^{ga} auAf ^g Cf ^g Uf ^u ca* ^u * ^c	2553
AV02967	AV02967-SS	g* ^a * ^a * ^c gaucAfuUfhuCfaa ^a * ^g * ^a	2261	AV02967-AS	u* ^C f* ^u guuUf ^u gaalUf ^g AfuAf ^g c ^g * ^u * ^c	2554
AV02968	AV02968-SS	g* ^c * ^c * ^a uuccAfaCfaGf ^u cau ^c * ^g * ^a	2262	AV02968-AS	u* ^C f* ^a au ^g Afu ^{cu} gUfhuUfhuGfaa* ^g * ^c	2555
AV02969	AV02969-SS	g* ^u * ^u * ^a caaacAf ^g AfuCfa ^u ug ^g * ^a * ^a	2263	AV02969-AS	u* ^U f* ^u uccaAf ^u gaauCfuGfuUf ^u ug* ^a * ^c	2556
AV02970	AV02970-SS	g* ^a * ^a * ^a acgaUf ^u CaFuUf ^g gaau* ^c * ^a	2264	AV02970-AS	u* ^G f* ^a auuCf ^u cauGfaUf ^u cf ^u guu* ^u * ^c	2557
AV02971	AV02971-SS	g* ^a * ^a * ^a ccagaCfaUfhuGf ^u gaau ^c * ^c * ^a	2265	AV02971-AS	u* ^G f* ^g aaUf ^u ccaaUf ^g AfuCfu ^g * ^u * ^c	2558
AV02972	AV02972-SS	g* ^u * ^u * ^u ggaauUf ^u CaFuAfaa ^u * ^a * ^a	2266	AV02972-AS	u* ^A f* ^u gaauUf ^u uagGfaAfuUf ^u cca* ^a * ^c	2559

AV02973	AV02973-SS	g*a*uucaaaAfaAfuCfaaucaug*c*a	2267	AV02973-AS	u*G*f*cuagAfuagauUfuUfaGfcaaa*u*c	2560
AV02974	AV02974-SS	g*u*ucuaaaAfaUfcAfucaugc*u*a	2268	AV02974-AS	u*Af*geugAfauagauUfuUfaAfgeaa*a*c	2561
AV02975	AV02975-SS	g*c*cuuuuuGfuAfuUfagaagug*a*a	2269	AV02975-AS	u*U*f*cuucUfuauuAfcAfaAfagug*c*c	2562
AV02976	AV02976-SS	g*g*aggaacAfaAfuAfaagucug*c*a	2270	AV02976-AS	u*U*f*cagcUfuauuUfuGfuUfcu*c*c	2563
AV02977	AV02977-SS	g*g*guuguaAfuGfuUfacugug*a*a	2271	AV02977-AS	u*U*f*cucaGfuaacAfuUfgAfcaac*c*c	2564
AV02978	AV02978-SS	g*c*aucaugUfgUfuCfagaugug*u*a	2272	AV02978-AS	u*Af*caucUfcaaaCfaCfcUfgau*g*c	2565
AV02979	AV02979-SS	c*g*uuugugAfgAfuGfuauau*c*a	2273	AV02979-AS	u*G*f*auugAfacaauCfuCfcAfaca*c*g	2566
AV02980	AV02980-SS	g*g*acaucaUfcCfuCfcaauu*c*a	2274	AV02980-AS	u*Af*cauuGfagaugGfaUfgAfuuu*c*c	2567
AV02981	AV02981-SS	g*a*gaugcaCfaUfuGfacuuc*a*a	2275	AV02981-AS	u*U*f*gaagGfucauUfgUfgCfauc*u*c	2568
AV02982	AV02982-SS	g*g*cauuuGfaCfuCfucaug*a*a	2276	AV02982-AS	u*U*f*ucauGfagaugUfcAfaUfgug*c*c	2569
AV02983	AV02983-SS	g*a*cauuuGfuCfuCfaugaaug*c*a	2277	AV02983-AS	u*G*f*cuucAfuagugAfgUfcAfauug*u*c	2570
AV02984	AV02984-SS	g*c*cuugugGfuGfuUfaauac*a*a	2278	AV02984-AS	u*U*f*guuuUfuaacAfcUfcCfaagug*c*c	2571
AV02985	AV02985-SS	g*c*uuugugUfgUfuAfaauaca*u*a	2279	AV02985-AS	u*Af*uguaUfuuaaCfaCfuCfcaaa*g*c	2572
AV02986	AV02986-SS	g*u*uaaggaGfuAfuGfuucugc*a*a	2280	AV02986-AS	u*U*f*gaugAfacaauAfcUfcCfuuaa*a*c	2573
AV02987	AV02987-SS	g*g*ugaagcaCfuGfuUfcacugc*u*a	2281	AV02987-AS	u*Af*cauuUfgaaacAfgUfgCfuca*c*c	2574
AV02988	AV02988-SS	g*u*uuuugugGfuUfuCfuugauu*c*a	2282	AV02988-AS	u*G*f*aaauCfagaagCfcCfuCfaaa*a*c	2575
AV02989	AV02989-SS	g*g*auuuuGfaGfuCfaacug*a*a	2283	AV02989-AS	u*U*f*ucagUfugaugUfgGfgAfauu*c*c	2576
AV02990	AV02990-SS	g*c*aacugAfgAfuAfuuguc*u*a	2284	AV02990-AS	u*Af*gaacAfauauCfuUfcAfguu*g*c	2577
AV02991	AV02991-SS	g*c*ugaagUfaUfuCfuucuu*c*a	2285	AV02991-AS	u*G*f*aaugAfacaauUfaUfcUfcaug*c*c	2578
AV02992	AV02992-SS	g*g*auuuuGfuCfuUfucugug*a*a	2286	AV02992-AS	u*U*f*aggaGfaagAfaCfaAfuau*c*c	2579
AV02993	AV02993-SS	g*u*uuuuuGfuCfuCfuuauc*a*a	2287	AV02993-AS	u*U*f*gaauAfcgaagAfaAfgAfaca*a*c	2580
AV02994	AV02994-SS	g*a*gaauuuGfcCfaGfaagaa*c*a	2288	AV02994-AS	u*G*f*uuucUfucugGfcAfaAfuuc*u*c	2581
AV02995	AV02995-SS	g*a*gaagaaAfcAfuUfuucaug*c*a	2289	AV02995-AS	u*C*f*cuugAfauauGfuUfuCfuuc*u*c	2582
AV02996	AV02996-SS	g*g*agaagaaCfaUfuUfcaagug*u*a	2290	AV02996-AS	u*Af*ccuuGfaaaauUfgUfuUfcuu*c*c	2583
AV02997	AV02997-SS	g*u*uuucaagGfuUfuUfcuauua*c*a	2291	AV02997-AS	u*G*f*uaauAfgaaacCfcUfuGfaaa*a*c	2584
AV02998	AV02998-SS	g*a*agguuuCfuAfuUfacaacug*a	2292	AV02998-AS	u*C*f*aguuGfuauuAfgAfaAfccu*u*c	2585
AV02999	AV02999-SS	c*g*uuuguaUfuCfuUfuaagaa*g*a	2293	AV02999-AS	u*C*f*uuuuAfagaagAfaUfaCfcaaa*c*g	2586
AV03000	AV03000-SS	g*u*guuuuGfuUfuUfagaagaa*c*a	2294	AV03000-AS	u*G*f*uuuuCfuuaaAfgAfaUfaca*c*c	2587
AV03001	AV03001-SS	g*g*guuuuGfuUfuUfagaagaa*c*a	2295	AV03001-AS	u*U*f*guuuUfcaaaAfaGfaAfuac*c*c	2588
AV03002	AV03002-SS	g*u*agaagaaCfaUfuGfuuaaca*a*a	2296	AV03002-AS	u*U*f*uuuuAfacaauUfgUfcUfuu*a*c	2589
AV03003	AV03003-SS	g*a*gaauuGfuUfaCfaaaaca*g*a	2297	AV03003-AS	u*C*f*uuuuUfuguaAfcAfaUfguc*u*c	2590

AV03004	AV03004-SS	c*a*gcagcaAfcAfuAfcuucuc*a*a	2298	AV03004-AS	u*Uf*a*gzaAfcuaGfuUfgCfugc*u*g	2591
AV03005	AV03005-SS	g*g*caacuAfcUfuUfcuauug*c*a	2299	AV03005-AS	u*Gf*caauAfcraaGfuAfuGfuug*c*c	2592
AV03006	AV03006-SS	c*c*aacauAfuUfuCfauugc*c*a	2300	AV03006-AS	u*Gf*gcaAUFagaAfgUfaUfguu*g*g	2593
AV03007	AV03007-SS	g*a*acugcUfaAfuGfugucg*a*a	2301	AV03007-AS	u*Uf*cagcAfcacuUfaGfcAfgug*u*c	2594
AV03008	AV03008-SS	g*u*gcuaaGfuGfuCfugauc*a*a	2302	AV03008-AS	u*Uf*ggaUCfagacAfcAfuUfagc*a*c	2595
AV03009	AV03009-SS	g*c*agcaAfcAfuUfauug*u*a	2303	AV03009-AS	u*Af*cuagfuacUfuUfgUfgcu*g*c	2596
AV03010	AV03010-SS	g*a*gcacaAfgUfuAfcuauug*c*a	2304	AV03010-AS	u*Gf*acuaAfguaAfuUfuGfugc*u*c	2597
AV03011	AV03011-SS	c*c*agccaaAfcUfuGfagaug*u*a	2305	AV03011-AS	u*Cf*acauUfcraaGfuUfuGfugc*u*g	2598
AV03012	AV03012-SS	g*a*cuugcaAfuGfuCfcauug*a*a	2306	AV03012-AS	u*Uf*cuauUfecaAfuUfcCfag*u*c	2599
AV03013	AV03013-SS	c*u*gcacuaAfcAfuAfaugua*c*a	2307	AV03013-AS	u*Gf*uaauAfuucUfcUfaUfugc*a*g	2600
AV03014	AV03014-SS	g*u*cucauuCfuCfuUfcugug*a*a	2308	AV03014-AS	u*Af*ucacAfgaagAfgAfaUfgag*a*c	2601
AV03015	AV03015-SS	g*a*uuucucUfcUfgUfgauuug*a*a	2309	AV03015-AS	u*Cf*auaaUfcraaAfgAfgAfga*u*c	2602
AV03016	AV03016-SS	g*u*ucucuuCfuGfuCfauuug*u*a	2310	AV03016-AS	u*Af*cauaAfuacAfgAfaCfag*a*c	2603
AV03017	AV03017-SS	g*c*uuucugAfuUfuAfuuguc*u*a	2311	AV03017-AS	u*Af*cagaCfaaaUfcAfcAfga*g*c	2604
AV03018	AV03018-SS	g*u*cuugcaUfuAfuGfucugc*a*a	2312	AV03018-AS	u*Uf*gacaGfcauAfuUfcAfcag*a*c	2605
AV03019	AV03019-SS	g*u*gucauuAfuGfuCfugucg*a*a	2313	AV03019-AS	u*Uf*cuagCfagacAfuAfaUfcac*a*c	2606
AV03020	AV03020-SS	c*u*gaauuAfuCfuCfugagaa*c*a	2314	AV03020-AS	u*Gf*uuuAfuacAfcAfuAfauc*a*g	2607
AV03021	AV03021-SS	g*u*gucaAfcCfuCfcaugac*a*a	2315	AV03021-AS	u*Af*gucaUfgagGfuUfcUfgac*a*c	2608
AV03022	AV03022-SS	g*u*uaacguGfgCfuCfauugua*a*a	2316	AV03022-AS	u*Uf*uaaAfuagCfcAfcGfuua*a*c	2609
AV03023	AV03023-SS	g*a*cgugcUfcAfuUfguaau*c*a	2317	AV03023-AS	u*Gf*auuuAfcuuAfuCfagCfagc*u*c	2610
AV03024	AV03024-SS	c*u*ggucaUfuGfuAfaucg*a*a	2318	AV03024-AS	u*Uf*guagUfuuaAfuUfgAfgcc*a*g	2611
AV03025	AV03025-SS	g*u*cauuuAfuAfuCfcauuc*a*a	2319	AV03025-AS	u*Uf*gaauGfugauUfuAfcAfaug*a*c	2612
AV03026	AV03026-SS	g*g*uaaauAfcAfuUfcaagau*c*a	2320	AV03026-AS	u*Gf*auucUfcauGfuGfaUfuua*c*c	2613
AV03027	AV03027-SS	g*u*cauucUfgUfuCfugaaaa*c*a	2321	AV03027-AS	u*Gf*uuuuCfacaCfagAfgAfcug*a*c	2614
AV03028	AV03028-SS	g*u*gaagaaAfaCfuCfuucgu*a*a	2322	AV03028-AS	u*Cf*acugAfgagUfuUfuCfuuc*a*c	2615
AV03029	AV03029-SS	g*u*ggugcAfaAfuUfuacaga*g*a	2323	AV03029-AS	u*Cf*ucugUfaauUfuCfcAfgcc*a*c	2616
AV03030	AV03030-SS	c*g*cuagcaAfuUfuAfcagagc*a*a	2324	AV03030-AS	u*Uf*gcUfc(uNA)guaaAfuUfuGfcaug*c*g	2617
AV03031	AV03031-SS	g*c*uaacaAfaAfuCfcaagaa*u*a	2325	AV03031-AS	u*Af*uuucUfgauUfcUfgUfuuga*g*c	2618
AV03032	AV03032-SS	g*g*acaccaAfaGfgCfuaauu*c*a	2326	AV03032-AS	u*Gf*aaauAfgagcUfuUfgGfugu*c*c	2619
AV03033	AV03033-SS	g*c*auagcaAfaCfuCfcauug*u*a	2327	AV03033-AS	u*Af*cuagGfugagUfcUfuGfcau*g*c	2620
AV03034	AV03034-SS	g*a*cuuacUfcUfuGfuaaa*c*a	2328	AV03034-AS	u*Gf*auuuGfacaAfgaUfgAfgag*u*c	2621

AV03035	AV03035-SS	c*u* ^u ggaucAfgGfuCfagauc* ^u a	2329	AV03035-AS	u* ^A fgaauCfugaCfuGfgUfeca* ^a g	2622
AV03036	AV03036-SS	g*a* ^u ccggaufcCfuGfcuga* ^a a	2330	AV03036-AS	u* ^U f* ^u cuucAfgcagGfaAfuCfega* ^u c	2623
AV03037	AV03037-SS	g* ^u u* ^u ccggaufcAfaGfauga* ^a a	2331	AV03037-AS	u* ^U f* ^u ucauAfuauCfaGfcAfga* ^a c	2624
AV03038	AV03038-SS	g* ^u u* ^u gggaugGfaGfuCfagaauu* ^c a	2332	AV03038-AS	u* ^G f* ^a aaauUfcaucUfcAfuCfcu* ^a c	2625
AV03039	AV03039-SS	g* ^g g* ^g gaugaGfuGfaAfauuu* ^g a	2333	AV03039-AS	u* ^C f* ^a gaAfauuuAfcUfcAfucc* ^c c	2626
AV03040	AV03040-SS	g* ^u u* ^u gggaugAfgUfuCfagaug* ^c a	2334	AV03040-AS	u* ^G f* ^a ucaUfucaCfuUfgcFucc* ^a c	2627
AV03041	AV03041-SS	c*a* ^u gggaugAfgAfuCfcaaca* ^c a	2335	AV03041-AS	u* ^G f* ^u guuUffgauCfuAfcUfucc* ^u g	2628
AV03042	AV03042-SS	g* ^u u* ^u gggaugUfgcGfuGfcaga* ^a a	2336	AV03042-AS	u* ^U f* ^u uucGfccacCfaUfcUfca* ^a c	2629
AV03043	AV03043-SS	c*c* ^c uuggcUfcAfuAfaaga* ^a a	2337	AV03043-AS	u* ^U f* ^u uucUfuauGfaCfcCfaag* ^g g	2630
AV03044	AV03044-SS	g*a* ^u gggaugUfcUfuUfagaag* ^u a	2338	AV03044-AS	u* ^A f* ^c uucUfuauGfaCfuUfcu* ^u c	2631
AV03045	AV03045-SS	g*a* ^u gggaugCfuUfuAfaagga* ^u a	2339	AV03045-AS	u* ^A f* ^a acucCfuuaAfgAfcUfucc* ^u c	2632
AV03046	AV03046-SS	c*a* ^u agucuuUfaAfgCfagauc* ^u a	2340	AV03046-AS	u* ^A f* ^u gaacCfuucUfaAfaGfauc* ^u g	2633
AV03047	AV03047-SS	c* ^u u* ^c uuaaGfgAfgUfucauc* ^a a	2341	AV03047-AS	u* ^U f* ^u gaugGfaucCfcUfuAfaag* ^a g	2634
AV03048	AV03048-SS	c* ^u u* ^c guacuCfaGfuUfugaag* ^a a	2342	AV03048-AS	u* ^U f* ^u ucuuCfaacUfgAfgUfag* ^a g	2635
AV03049	AV03049-SS	g*c* ^g gaucAfgUfuUfagaag* ^a a	2343	AV03049-AS	u* ^U f* ^u uucUfcaacCfuGfaGfuac* ^g c	2636
AV03050	AV03050-SS	g* ^g g* ^u uacucaGfuUfuGfagaac* ^c a	2344	AV03050-AS	u* ^G f* ^u uucUfucaAfcUfgAfgua* ^c c	2637
AV03051	AV03051-SS	c* ^g g* ^u agcaagAfgAfuUfcaagca* ^a a	2345	AV03051-AS	u* ^U f* ^u ugcuUfgauCfuCfuUfgeu* ^c g	2638
AV03052	AV03052-SS	c*a* ^u gcaagGfaUfuCfaagca* ^u a	2346	AV03052-AS	u* ^A f* ^u uugcUfugaUfcUfcUfugc* ^u g	2639
AV03053	AV03053-SS	c*a* ^g gaucAfgCfaAfuuguu* ^c a	2347	AV03053-AS	u* ^G f* ^a aacCfaugCfuUfgAfauc* ^u g	2640
AV03054	AV03054-SS	g* ^g g* ^u aucaGfcAfaUfuguuc* ^a a	2348	AV03054-AS	u* ^U f* ^u gaacCfaucGfcUfuGfaau* ^c c	2641
AV03055	AV03055-SS	c*a* ^u ucaaGcfaAfuGfuuuca* ^a a	2349	AV03055-AS	u* ^U f* ^u ugaAfcacuUfgcUfuUfgaa* ^u g	2642
AV03056	AV03056-SS	g*c* ^a agcaUfgGfuUfucaga* ^g a	2350	AV03056-AS	u* ^U f* ^c uuuGfacaCfaUfuGfcu* ^g c	2643
AV03057	AV03057-SS	g* ^u u* ^c caucCfuGfuUfgcagu* ^u a	2351	AV03057-AS	u* ^A f* ^a cuGcFgaacAfgCfaGfuug* ^a c	2644
AV03058	AV03058-SS	g*a* ^u gaucaAfuAfaUfaccagu* ^g a	2352	AV03058-AS	u* ^C f* ^a uucGfuauAfuUfgAfuuc* ^u c	2645
AV03059	AV03059-SS	g* ^g g* ^u caucaUfaAfuAfcagau* ^a a	2353	AV03059-AS	u* ^A f* ^c aucUfgauUfaUfuGfaug* ^c c	2646
AV03060	AV03060-SS	g*a* ^u ccccuCfcAfuCfauuac* ^c a	2354	AV03060-AS	u* ^G f* ^u gaAfuauGfgAfgGfgg* ^u c	2647
AV03061	AV03061-SS	c* ^u u* ^u aucuUfcUfuUfugaau* ^g a	2355	AV03061-AS	u* ^C f* ^u aucAfaaaGfaAfcAfgau* ^a g	2648
AV03062	AV03062-SS	g*c* ^u ugmuUfuUfuGfagaag* ^u a	2356	AV03062-AS	u* ^A f* ^u ucUfucaAfaAfgAfaa* ^g c	2649
AV03063	AV03063-SS	g*c* ^a ggcaUfcAfuGfacaac* ^g a	2357	AV03063-AS	u* ^C f* ^u uugUfucaUfuUfgUfcu* ^g c	2650
AV03064	AV03064-SS	c* ^g g* ^u guauAfgGfuCfuuuacg* ^a a	2358	AV03064-AS	u* ^U f* ^c ugaAfaacCfuUfaUfaca* ^c g	2651
AV03065	AV03065-SS	c* ^g g* ^a cguuAfcCfuUfuucugc* ^c a	2359	AV03065-AS	u* ^G f* ^u gcagAfaagGfuUfcAfcgu* ^c g	2652

AV03066	AV03066-SS	g* ^g *ccacagAfcUfhuCfhuacga* ^c * ^a	2360	AV03066-AS	u* ^G *ucugUfagaaGfhuCfhuGfhu ^g * ^c * ^c	2653
AV03067	AV03067-SS	c* ^g * ^c ugcugAfcUfhuGfhuuag* ^a * ^a	2361	AV03067-AS	u* ^U * ^c guuaAfacaGfhuCfhuGfag* ^c * ^g	2654
AV03068	AV03068-SS	g* ^u * ^u gucagUfhuGfhuUfhuacga* ^a * ^a	2362	AV03068-AS	u* ^U * ^u uegUfhuacAfhuGfhuCfagc* ^a * ^c	2655
AV03069	AV03069-SS	g* ^g * ^g * ^c ugacugUfhuUfhuUfhuacga* ^a * ^a	2363	AV03069-AS	u* ^A * ^f * ^u uueGfhuaaCfhuAfhuUfhuag* ^c * ^c	2656
AV03070	AV03070-SS	c* ^c * ^u gacugGfhuAfhuAfegaa* ^g * ^a	2364	AV03070-AS	u* ^C * ^f * ^u uuuUfhuaaAfcAfhuGfhuca* ^g * ^g	2657
AV03071	AV03071-SS	g* ^g * ^u uuuagAfhuAfhuGfhuca* ^a * ^a	2365	AV03071-AS	u* ^U * ^f * ^u gugGfhuauUfhuCfhuUfhuaa* ^c * ^c	2658
AV03072	AV03072-SS	g* ^c * ^c * ^c auuueCfcCfhuUfhuuuc* ^u * ^a	2366	AV03072-AS	u* ^A * ^f * ^g agagAfagagGfhuAfhuAfau* ^g * ^c	2659
AV03073	AV03073-SS	g* ^u * ^u * ^u cuuuUfhuCfhuacga* ^u * ^a	2367	AV03073-AS	u* ^A * ^f * ^u uecuGfagaaGfhuAfhuAfag* ^a * ^c	2660
AV03074	AV03074-SS	g* ^c * ^c * ^u auuueUfhuAfhuCfhuauuc* ^g * ^a	2368	AV03074-AS	u* ^C * ^f * ^g aaugfhuauUfhuUfhuAfhuafu* ^g * ^c	2661
AV03077	AV03077-SS	c* ^c * ^c * ^g ucagGfhuUfhuUfhuuuu* ^a * ^a	2369	AV03077-AS	u* ^U * ^f * ^u aaagGfhuagafhuCfhuCfhuac* ^g * ^g	2662
AV03078	AV03078-SS	a* ^g * ^g * ^g * ^u uueAfhuAfhuCfhuagcu* ^g * ^a	2370	AV03078-AS	u* ^C * ^f * ^g agguUfhuuAfhuGfhuAfhuagc* ^c * ^u	2663
AV03079	AV03079-SS	g* ^c * ^c * ^u acaaagAfcCfhuCfhuauuu* ^g * ^a	2371	AV03079-AS	u* ^C * ^f * ^g aaacaUfhuuGfhuCfhuUfhuu* ^g * ^c	2664
AV03080	AV03080-SS	c* ^a * ^a * ^g uuuaUfhuAfhuCfhuagcu* ^u * ^a	2372	AV03080-AS	u* ^A * ^f * ^g agcuCfhuuuCfhuUfhuAfhuafacc* ^u * ^g	2665
AV03081	AV03081-SS	u* ^u * ^u * ^u * ^u agagUfhuUfhuUfhuagca* ^c * ^a	2373	AV03081-AS	u* ^G * ^f * ^u gacGfhuacUfhuCfhuCfhu* ^a * ^a	2666
AV03082	AV03082-SS	a* ^u * ^u * ^u * ^u * ^u cauuCfhuUfhuUfhuuuu* ^a * ^a	2374	AV03082-AS	u* ^U * ^f * ^u ucaAfhuacafhuCfhuCfhu* ^g * ^a	2667
AV03083	AV03083-SS	u* ^c * ^c * ^u gauuCfhuCfhuGfhuacau* ^g * ^a	2375	AV03083-AS	u* ^C * ^f * ^g aguuGfhuagGfhuAfhuafu* ^g * ^a	2668
AV03084	AV03084-SS	g* ^c * ^c * ^u auuueGfhuCfhuCfhuuuu* ^g * ^a	2376	AV03084-AS	u* ^U * ^f * ^u caacaAfhuagAfcUfhuAfhuu* ^g * ^c	2669
AV03085	AV03085-SS	g* ^u * ^u * ^g acauCfhuUfhuGfhuuugc* ^g * ^a	2377	AV03085-AS	u* ^C * ^f * ^g acaaAfhucaGfhuGfhuag* ^a * ^c	2670
AV03086	AV03086-SS	c* ^u * ^u * ^g ucugUfhuCfhuUfhuuuu* ^g * ^a	2378	AV03086-AS	u* ^C * ^f * ^u uaaGfhuagGfhuCfhuUfhuagc* ^a * ^g	2671
AV03087	AV03087-SS	c* ^u * ^u * ^g acuuUfhuUfhuCfhuuuu* ^g * ^a	2379	AV03087-AS	u* ^A * ^f * ^u cauuUfhuuaAfhuCfhuAfhuagc* ^a * ^g	2672
AV03088	AV03088-SS	u* ^c * ^c * ^u gaagAfhuAfhuUfhuuagc* ^g * ^a	2380	AV03088-AS	u* ^U * ^f * ^u ccgaUfhuuUfhuGfhuUfhuau* ^g * ^a	2673
AV03089	AV03089-SS	a* ^g * ^g * ^u aaucAfhuAfhuCfhuauuc* ^c * ^a	2381	AV03089-AS	u* ^G * ^f * ^g aauuAfhuuuCfhuGfhuAfhuu* ^c * ^u	2674

Table 2A: provides chemically modified HTT RNAi agent antisense strand and sense strand sequences. All sequences shown 5' to 3'. These sequences were used in certain *in vitro* testing studies described herein.

Duplex AV#	Sense strand SS#	Sense Sequence	SEQ ID NO.	Antisense strand AS#	Antisense Sequence	SEQ ID NO.
AV02733	AV02733-SS	g* ^c * ^c gucuaGfhuCfhuCfhuuuu* ^u * ^a	2675	AV02733-AS	u* ^A * ^f * ^u aaagCfhuagCfhuUfhuAfhuagc* ^g * ^c	2914
AV02735	AV02735-SS	g* ^g * ^g * ^a agggccGfhuUfhuAfhuuuu* ^g * ^a	2676	AV02735-AS	u* ^C * ^f * ^g aaCfhuagGfhuGfhuCfhuagc* ^c * ^c	2915
AV02739	AV02739-SS	g* ^g * ^g * ^u uucugUfhuUfhuAfhuuagc* ^g * ^a	2677	AV02739-AS	u* ^C * ^f * ^g gaaCfhuuaAfhuGfhuAfhuagc* ^c * ^c	2916

AV02743	AV02743-SS	c*c*c*gggagGfGChuCfcaagau*g*a	2678	AV02743-AS	u*Gf*auChU(uUNA)ggagcCfcGfuCfccc*g*g	2917
AV02744	AV02744-SS	g*g*gguecaAfGAtuGfagggc*c*a	2679	AV02744-AS	u*Gf*gcCfG(uUNA)ccauChUfGcfac*c*c	2918
AV02745	AV02745-SS	g*g*gaagggcCfGChuCfagguuc*u*a	2680	AV02745-AS	u*Af*gaAf(cUNA)ugagCfGfcCfgu*c*c	2919
AV02746	AV02746-SS	c*c*c*gguecaGfGChUcFugcuu*u*a	2681	AV02746-AS	u*Af*aaagCfaggaCfcUfG Afggg*g*g	2920
AV02747	AV02747-SS	g*g*gcueagUfGChUcFcuuuu*c*a	2682	AV02747-AS	u*Gf*uaaaAfgcagAfAcCfcUfga*g*c	2921
AV02748	AV02748-SS	c*c*c*ucagguUfGcFcuuuuac*c*a	2683	AV02748-AS	u*Gf*guAf(aUNA)ggcaGfaAfCcfuga*g*g	2922
AV02749	AV02749-SS	g*u*u*c*ggguuChUcFcuuuacc*u*a	2684	AV02749-AS	u*Af*gguaAfagcAfG AfAcCfcu*g*c	2923
AV02750	AV02750-SS	g*c*agguuUfGChUfhuacu*g*a	2685	AV02750-AS	u*Gf*gguaAfagcAfG AfAcCfcu*g*c	2924
AV02751	AV02751-SS	g*a*ggguuUfGChUfhuacu*c*a	2686	AV02751-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2925
AV02752	AV02752-SS	g*g*guuUfGChUfhuacu*c*a	2687	AV02752-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2926
AV02753	AV02753-SS	c*g*uuUfGChUfhuAfccu*c*a	2688	AV02753-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2927
AV02754	AV02754-SS	g*u*gguuuAfCChUcFggcc*c*a	2689	AV02754-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2928
AV02755	AV02755-SS	g*c*agagccCfcAtuUfcau*c*a	2690	AV02755-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2929
AV02756	AV02756-SS	g*g*cccauUfCAtuUfcccgg*g*a	2691	AV02756-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2930
AV02757	AV02757-SS	c*c*c*cccauUfCAtuUfcccgg*g*a	2692	AV02757-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2931
AV02758	AV02758-SS	g*g*ccccUfGChUcFggggg*c*a	2693	AV02758-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2932
AV02759	AV02759-SS	c*g*ugcuUfGChUcFggggg*c*a	2694	AV02759-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2933
AV02760	AV02760-SS	c*g*ggggGfGChUcFggggg*c*a	2695	AV02760-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2934
AV02761	AV02761-SS	g*g*ccggGfGChUcFggggg*c*a	2696	AV02761-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2935
AV02762	AV02762-SS	g*g*ggggGfGChUcFggggg*c*a	2697	AV02762-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2936
AV02763	AV02763-SS	c*c*ccggGfGChUcFggggg*c*a	2698	AV02763-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2937
AV02764	AV02764-SS	g*g*ggggGfGChUcFggggg*c*a	2699	AV02764-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2938
AV02765	AV02765-SS	g*c*uccggGfGChUcFggggg*c*a	2700	AV02765-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2939
AV02766	AV02766-SS	g*c*c*ggggGfGChUcFggggg*c*a	2701	AV02766-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2940
AV02767	AV02767-SS	g*g*ugcuUfGChUcFggggg*c*a	2702	AV02767-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2941
AV02768	AV02768-SS	c*g*ggggGfGChUcFggggg*c*a	2703	AV02768-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2942
AV02769	AV02769-SS	c*c*ggggGfGChUcFggggg*c*a	2704	AV02769-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2943
AV02770	AV02770-SS	c*c*agggGfGChUcFggggg*c*a	2705	AV02770-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2944
AV02771	AV02771-SS	c*a*ccggGfGChUcFggggg*c*a	2706	AV02771-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2945
AV02772	AV02772-SS	g*a*ugggGfGChUcFggggg*c*a	2707	AV02772-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2946
AV02773	AV02773-SS	g*g*agggGfGChUcFggggg*c*a	2708	AV02773-AS	u*Gf*agguAfagcAfG AfAcCfcu*g*c	2947

AV02774	AV02774-SS	c*a*ccuugAfiaAfiaCfiauug*a*a	2709	AV02774-AS	u*Uf*caUf(aUNA)gcuUfuCfcafgg*u*g	2948
AV02775	AV02775-SS	g*c*ccuugAfiaAfiaCfiauug*a*a	2710	AV02775-AS	u*Uf*ucAfia(cUNA)agcuUfuUfCfagg*c*c	2949
AV02776	AV02776-SS	g*c*cuugAfiaGf(cUfgauug*a*a	2711	AV02776-AS	u*Cf*ucaUfcaugUfuUfuCfag*c*c	2950
AV02777	AV02777-SS	g*u*ugAfiaAfiaCfiauug*a*a	2712	AV02777-AS	u*Cf*cuuAfiaugCfuUfuUfca*a*c	2951
AV02778	AV02778-SS	g*u*ugAfiaAfiaCfiauug*c*a	2713	AV02778-AS	u*Gf*cuUfu(cUNA)ucaGf(cUfuUfuc*a*c	2952
AV02779	AV02779-SS	c*g*aaugUf(aUNA)Cfiauug*c*a	2714	AV02779-AS	u*Af*ggCf(cUNA)ucaCfagUfuuu*c*c	2953
AV02780	AV02780-SS	c*a*aaugAfiaUf(aCfiauug*c*a	2715	AV02780-AS	u*Af*agGf(cUNA)ucaUf(aCfiauug*c*c	2954
AV02781	AV02781-SS	g*a*agcuUf(aCfiauug*c*a	2716	AV02781-AS	u*Cf*gaAfia(cUNA)ccuUf(aCfiauug*c*c	2955
AV02782	AV02782-SS	g*c*cuugAfiaAfiaCfiauug*a*a	2717	AV02782-AS	u*Uf*cgaAfia(cUNA)gcuUf(aCfiauug*c*c	2956
AV02783	AV02783-SS	c*c*ugauAfiaGf(cUfgauug*a*a	2718	AV02783-AS	u*Af*cuCf(aUNA)agcuUf(aCfiauug*c*c	2957
AV02784	AV02784-SS	g*u*auugAfiaCfiauug*c*a	2719	AV02784-AS	u*Gf*gaCf(cUNA)gaugGf(cUfuUfcau*c*c	2958
AV02785	AV02785-SS	c*a*agcuUf(aCfiauug*c*a	2720	AV02785-AS	u*Uf*gaGf(cUNA)ucaGf(aCfiauug*c*c	2959
AV02786	AV02786-SS	g*u*ucgcuUf(aCfiauug*c*a	2721	AV02786-AS	u*Af*ggcuUf(aCfiauug*c*c	2960
AV02787	AV02787-SS	c*a*guugAfiaAfiaCfiauug*c*a	2722	AV02787-AS	u*Uf*gaAfia(cUNA)gcuUf(aCfiauug*c*c	2961
AV02788	AV02788-SS	g*c*ucguAfiaGf(cUfgauug*c*a	2723	AV02788-AS	u*Cf*ugAfia(cUNA)gcuUf(aCfiauug*c*c	2962
AV02789	AV02789-SS	c*u*ccuAfiaGf(cUfgauug*c*a	2724	AV02789-AS	u*Gf*cuGf(cUNA)agcuUf(aCfiauug*c*c	2963
AV02790	AV02790-SS	g*c*cuugAfiaCfiauug*c*a	2725	AV02790-AS	u*Uf*gcUf(aUNA)agcuUf(aCfiauug*c*c	2964
AV02791	AV02791-SS	g*c*cuugAfiaCfiauug*c*a	2726	AV02791-AS	u*Cf*ugCf(cUNA)gaugGf(cUfuUfcau*c*c	2965
AV02792	AV02792-SS	g*c*cuugAfiaCfiauug*c*a	2727	AV02792-AS	u*Gf*cuGf(cUNA)gaugGf(aCfiauug*c*c	2966
AV02793	AV02793-SS	g*a*guugAfiaCfiauug*c*a	2728	AV02793-AS	u*Uf*gcUf(cUNA)gcuUf(aCfiauug*c*c	2967
AV02794	AV02794-SS	c*c*cuugAfiaCfiauug*c*a	2729	AV02794-AS	u*Gf*cuGf(cUNA)gaugGf(aCfiauug*c*c	2968
AV02795	AV02795-SS	g*c*ucguAfiaCfiauug*c*a	2730	AV02795-AS	u*Gf*gcUf(aUNA)gaugGf(aCfiauug*c*c	2969
AV02796	AV02796-SS	g*c*ccuAfiaCfiauug*c*a	2731	AV02796-AS	u*Af*gcGf(cUNA)gcuUf(aCfiauug*c*c	2970
AV02797	AV02797-SS	g*c*cuugAfiaCfiauug*c*a	2732	AV02797-AS	u*Cf*agCf(aUNA)gcuUf(aCfiauug*c*c	2971
AV02798	AV02798-SS	g*u*ugAfiaCfiauug*c*a	2733	AV02798-AS	u*Gf*gcAfia(cUNA)agcuUf(aCfiauug*c*c	2972
AV02799	AV02799-SS	c*g*aaugCfiauug*c*a	2734	AV02799-AS	u*Gf*agGf(cUNA)gaugGf(cUfuUfcau*c*c	2973
AV02800	AV02800-SS	g*c*ccuAfiaCfiauug*c*a	2735	AV02800-AS	u*Cf*cuCf(aUNA)ucaAfiaCfiauug*c*c	2974
AV02801	AV02801-SS	g*c*cuugAfiaCfiauug*c*a	2736	AV02801-AS	u*Gf*gcUf(cUNA)ucaAfiaCfiauug*c*c	2975
AV02802	AV02802-SS	c*u*ugcuGf(aCfiauug*c*a	2737	AV02802-AS	u*Uf*gcAfia(cUNA)gcuUf(aCfiauug*c*c	2976
AV02803	AV02803-SS	g*c*agcuGf(cUfuUfcauug*c*c	2738	AV02803-AS	u*Gf*ucGf(cUNA)gaugGf(cUfuUfcau*c*c	2977
AV03075	AV03075-SS	c*c*auugAfiaCfiauug*c*a	2739	AV03075-AS	u*Cf*uuuUf(aUNA)gaugGf(cUfuUfcau*c*c	2978

AV03076	AV03076-SS	g*c*guaccuGfGfAfaAfaagcu ^a *u ^a a	2740	AV03076-AS	u*Af ^u uca ^g CfuuuCfcAfGcfu ^g *c*c	2979
AV03090	AV03090-SS	c ^g *aaccUfGfGfaAfaagcu ^g *a ^a u	2741	AV03090-AS	a*Uf ^g *cagcUfuuuCfaGfGfu ^g *c ^g *g	2980
AV03091	AV03091-SS	g ^g *g ^g acGfGfUfcCfaagau ^g * ^g *a	2742	AV03091-AS	u*Cf ^g *caucUfugGfaCfcCfGfUfc ^g *c*c	2981
AV03092	AV03092-SS	u ^a *g ^g gaCfcCfuGfgaag ^g *c ^a u	2743	AV03092-AS	a*Gf ^g *cuuuUfccagGfGfUfcGfc ^g *c ^a a	2982
AV03093	AV03093-SS	g ^g *c ^g ggAfGfGfGfhucaag ^g *a ^a u	2744	AV03093-AS	a*Uf ^g *cu ^g GfaccGfuCfcCfG ^g * ^g *c	2983
AV03094	AV03094-SS	u ^g *ccccGfGfUfGfCfuagcu ^g *c*c	2745	AV03094-AS	g ^g *Cf ^g *cguCfagcaCfcGfGfG ^g *c ^a a	2984
AV03095	AV03095-SS	c ^g *u ^g ccGfGfGfGfGfag ^g *c ^g *g	2746	AV03095-AS	c*Gf ^g *guuCfcccGfcCfcGfGfCfa ^g *c ^g *g	2985
AV03373	AV03373-SS	u* ^u *uuaacuGfcCfuUfGfug ^g aa ^g *a ^a a	2747	AV03373-AS	u*Uf ^g *cuuCAfcaacGfcAfGfUfuaa ^g *a ^a a	2986
AV03374	AV03374-SS	g ^g *g ^g *aagacaUfaAfuGfuuuu ^g * ^g *a	2748	AV03374-AS	u*Cf ^g *uaaaAfgeauUfaUfGfUfcau ^g *c*c	2987
AV03375	AV03375-SS	a* ^u *g ^g acauaAfuGfcUfuuuag ^g *a ^a a	2749	AV03375-AS	u*Uf ^g *cuuAfaagcAfuUfaUfGuc ^g *a ^a u	2988
AV03376	AV03376-SS	u ^g * ^g *acauaaUfGfCfuUfuuag ^g aa ^g *c ^a a	2750	AV03376-AS	u*Gf ^g *uccuAfaagCfaUfuAfu ^g u ^g *c ^a a	2989
AV03377	AV03377-SS	a* ^u *g ^g ggagauUfuUfcUfuuccu ^g *a ^a a	2751	AV03377-AS	u*Uf ^g *aggaAfaagAfaUfcUfcc ^g *a ^a u	2990
AV03378	AV03378-SS	c ^g * ^u *uaugugCfaCfuUfuaaaca ^g * ^g *a	2752	AV03378-AS	u*Cf ^g *uguuUfuagUfGfCfcAfcau ^g * ^g *g	2991
AV03379	AV03379-SS	g ^g *a ^g *ggcuUfcCfuAfcuu ^g *c ^a a	2753	AV03379-AS	u*Gf ^g *acaUfGuaGfAfaAfGc ^g *u ^g *c	2992
AV03380	AV03380-SS	u* ^u * ^u *ccuacaUfuGfuCfaag ^g aa ^g *u ^a a	2754	AV03380-AS	u*Af ^g *u ^g ucCfugacAfaUfGfUfag ^g *a ^a a	2993
AV03381	AV03381-SS	u* ^u * ^u *uceuuuAfuUfuCfaug ^g aa ^g *a ^a a	2755	AV03381-AS	u*Uf ^g *gaucAfugaaCfuAfaAfu ^g aa ^g *a ^a a	2994
AV03382	AV03382-SS	c ^a *a ^g *u ^g aucaCfGfGfuGfua ^g ua ^g *a ^a a	2756	AV03382-AS	u*Uf ^g *ua ^g uAfccacCfGfUfGfAfuca ^g *u ^g *g	2995
AV03383	AV03383-SS	c ^a *a ^g *c ^g gu ^g UfGfGfuAfaac ^g aa ^g *u ^a a	2757	AV03383-AS	u*Af ^g *uc ^g uGfuuaCfAfcAfcc ^g *u ^g *g	2996
AV03384	AV03384-SS	u ^a *a ^g *guaaCaCfGfAfuUfuaa ^g aa ^g *a ^a a	2758	AV03384-AS	u*Uf ^g *gcuuAfaauCfGfUfGfUfuac ^g *u ^a a	2997
AV03385	AV03385-SS	c* ^u * ^u *aagagaUfcUfGfCfuac ^g u ^g *a ^a a	2759	AV03385-AS	u*Uf ^g *agauCfagcaGfaUfcUfcuu ^g *a ^a *g	2998
AV03386	AV03386-SS	a ^a *a ^g *g ^g gaucUfGfCfuCfaucua ^g * ^g *a	2760	AV03386-AS	u*Cf ^g *uuagAfugagCfaGfaUfcu ^g *u ^a u	2999
AV03387	AV03387-SS	u*c ^g *a ^g ucaaaGfcCfuAfa ^g uu ^g * ^g *a	2761	AV03387-AS	u*Af ^g *ccaCfuagGfcUfuAfu ^g au ^g * ^g *a	3000
AV03388	AV03388-SS	u ^g * ^g *aguu ^g UfGfUfuGfcca ^g uu ^g *a ^a a	2762	AV03388-AS	u*Uf ^g *acuUfGcaacCfcAfca ^g u ^g *c ^a a	3001
AV03389	AV03389-SS	g ^g * ^u * ^g aa ^g uAfcCfuGfug ^g auu ^g *a ^a a	2763	AV03389-AS	u*Uf ^g *a ^g u ^g AfccacCfuAfaGfu ^g u ^g *a ^a c	3002
AV03390	AV03390-SS	a ^a *a ^g *cuuagUfGfGfuGfauuu ^g * ^g *a	2764	AV03390-AS	u*Cf ^g *auuaAfuacCfaCfGfUfaag ^g *u ^a u	3003
AV03391	AV03391-SS	u* ^u * ^u *ac ^g uu ^g UfGfAfuUfaa ^g aa ^g *a ^a a	2765	AV03391-AS	u*Uf ^g *uucaUfuauCfaCfcAfca ^g u ^g *a ^a a	3004
AV03392	AV03392-SS	a* ^u * ^u *ag ^g aaGfaGfuUfGfauu ^g aa ^g *a ^a a	2766	AV03392-AS	u*Uf ^g *ucaUfcaacUfcUfuCfua ^g *a ^a u	3005
AV03393	AV03393-SS	u ^g * ^g *a ^g uuuuUfuUfGfCfauu ^g * ^g *a	2767	AV03393-AS	u*Cf ^g *acaUfGgcaAfaAfaAfcuu ^g *c ^a a	3006
AV03394	AV03394-SS	u* ^u * ^u *g ^g cuauGfuGfuGfu ^g ug ^g aa ^g *a ^a a	2768	AV03394-AS	u*Uf ^g *uccAfaacAfcaAfuAfu ^g cc ^g *a ^a a	3007
AV03395	AV03395-SS	g ^g *a ^g *u ^g gaugAfuGfuGfuacau ^g *u ^a a	2769	AV03395-AS	u*Af ^g *aaugUfacaCfuCfaUfuca ^g *u ^g *c	3008
AV03396	AV03396-SS	g ^g *a ^g *g ^g uu ^g uaCfaUfuUfuac ^g aa ^g *u ^a a	2770	AV03396-AS	u*Af ^g *cu ^g UfuaaUfGfUfaCfa ^g cc ^g *u ^g *c	3009

AV03397	AV03397-SS	g* _u *uguaCfFuUfuAfcecaua*u*a	2771	AV03397-AS	u*Af*uaCuCfuaaAfFuUfgUfaca*c*c	3010
AV03398	AV03398-SS	c* _a * _u gugaaGfgGfuUfucuu*u*a	2772	AV03398-AS	u*Af* _u aaCfuaaCfcUfuUfcaC*u* _g	3011
AV03399	AV03399-SS	a* _g * _u gaagGfgUfuUfucuu*u* _g *a	2773	AV03399-AS	u* _C * _u aaC AfgaagCfcCfuUfcaC*c* _u	3012
AV03400	AV03400-SS	c* _a * _g cuugUfCfuUfuugga*a*a	2774	AV03400-AS	u*Uf* _u ccaAfaaagUfaAfC AfagC*u* _g	3013
AV03401	AV03401-SS	a* _g * _u cuugAfCfuUfuugga*a* _g *a	2775	AV03401-AS	u* _C * _u ccAfaaagCfuAfACfaag*c* _u	3014
AV03402	AV03402-SS	g* _u * _u cuugUfGcFuUfgucuu*u* _g *a	2776	AV03402-AS	u* _C * _u agaAfcaagCfaAfC Afga*a*c	3015
AV03403	AV03403-SS	u* _u * _u cuugCfcUfuGfucuu* _g *a	2777	AV03403-AS	u* _C * _u caagAfcaagCfcAfACfaa*a*a	3016
AV03404	AV03404-SS	g* _g * _g gaagUfuUfuUfgaaca* _g *a	2778	AV03404-AS	u* _C * _u uuUfcaaaAfFuUfuCfucc*c*c	3017
AV03405	AV03405-SS	g* _a * _g ccauUfaAfAfcauca*a* _g *a	2779	AV03405-AS	u* _C * _u agaUfguuUfaAfFuGfucc*u*c	3018
AV03406	AV03406-SS	c* _a * _g cuuagCfcCfuUfucuu*a*a	2780	AV03406-AS	u*Uf* _u agaGfaagCfcCfuGfaac*u* _g	3019
AV03407	AV03407-SS	u* _u * _u cuuuAfCfuCfucagua*a*a	2781	AV03407-AS	u*Af* _u acuGfagagGfuAfAGfaga*a*a	3020
AV03408	AV03408-SS	u* _c * _u cuuacCfuCfuCfaaguu*c*a	2782	AV03408-AS	u* _C * _u aaCfuaagAfGgfuAfaga* _g *a	3021
AV03409	AV03409-SS	c* _c * _g auugCfaUfuUfguaag*a*a	2783	AV03409-AS	u*Uf* _u cuuCfcaauUfgCfcAfucuu* _g * _g	3022
AV03410	AV03410-SS	u* _u * _u uaguaUfaUfuUfcuuuu*c*a	2784	AV03410-AS	u* _C * _u aaC AfgaauUfaUfuAfcau*a*a	3023
AV03411	AV03411-SS	u* _u * _u cguuaUfgAfUfcuuguc*u*a	2785	AV03411-AS	u*Af* _g acaAfgaagCfaUfaAfcaag*a*a	3024
AV03412	AV03412-SS	u* _a * _g uagucUfuGfuCfucuu*a*a	2786	AV03412-AS	u*Af* _g agacGfagacAfAGfAfcau*a*a	3025
AV03413	AV03413-SS	u*c* _u cuugUfcGfuCfucuaa*a* _g *a	2787	AV03413-AS	u* _C * _u uuG AfagacGfaGfaCfaag* _g *a	3026
AV03414	AV03414-SS	c* _u * _u ugucGfuCfuUfcaaguu*u*a	2788	AV03414-AS	u*Af* _u acuUfgaagAfCfAGfaca*a* _g	3027
AV03415	AV03415-SS	u* _u * _g ucucUfcUfuCfaaguu*u*a	2789	AV03415-AS	u*Af* _u acuUfgaagAfCfAGfaca*a*a	3028
AV03416	AV03416-SS	g* _u * _u guagCfuAfUfuUfguuu* _g *a	2790	AV03416-AS	u*Uf* _u ccaCfaauAfAGfcUfcaC*a*c	3029
AV03417	AV03417-SS	u* _g * _u uagcuUfaUfuUfguuu* _g *a	2791	AV03417-AS	u*Uf* _u ccaAfcaauUfaAfGcFuua*c*a	3030
AV03418	AV03418-SS	g* _u * _u uagcuAfUfuGfuugaa*u*a	2792	AV03418-AS	u*Af* _u uccAfacaAfFuAfAGfcau*a*c	3031
AV03419	AV03419-SS	a* _u * _u cuuaaGfgAfUfGfaaaa*c*a	2793	AV03419-AS	u* _C * _u uuuUfcauCfcUfuUfaga*a* _u	3032
AV03420	AV03420-SS	a* _a * _a cauuuGfgCfuUfcaucuu*u*a	2794	AV03420-AS	u*Af* _g agAfuaagCfcAfAfuuu* _u * _u	3033
AV03421	AV03421-SS	u* _u * _u ugcuuAfUfuCfuucauu*a*a	2795	AV03421-AS	u*Uf* _u acuGfagagAfUfAGfcca*a*a	3034
AV03422	AV03422-SS	g* _c * _c uauuCuUfcAfuaagu*a*a	2796	AV03422-AS	u*Uf* _u acuAfcaagAfG AfG Afuaa* _g *c	3035
AV03423	AV03423-SS	u* _a * _u uucuCfaGfuAfagaau*u*a	2797	AV03423-AS	u*Af* _u uuuCuuaCfuuaCfUfAGfaga*u*a	3036
AV03424	AV03424-SS	g* _u * _u aauuUfcAfUfcfcaaaa*a*a	2798	AV03424-AS	u*Af* _u uuuUfgaagGfaGfaAfauu*a*c	3037
AV03425	AV03425-SS	a* _u * _u ccagaAfUfuAfcauuu* _u *a	2799	AV03425-AS	u*Af* _u cuacAfuaaAfUfuCfuga*a* _u	3038
AV03426	AV03426-SS	u* _a * _g gaagUfgGfuGfucuaa*a*a	2800	AV03426-AS	u*Uf* _u uuuGfacaCfuAfCfucc*u*a	3039
AV03427	AV03427-SS	a* _a * _g uuaCfaCfaUfugaau* _u *a	2801	AV03427-AS	u*Af* _u cauGfauuUfgUfgAfacu* _u * _u	3040

AV03428	AV03428-SS	a* ^g *uacacaCfaUfuCfcaugua* ^u *a	2802	AV03428-AS	u* ^A *uacaUfgecaUfgeUfgeUfgea* ^c *u	3041
AV03429	AV03429-SS	c* ^a *ceacauGfcAfuGfauuu* ^g *a	2803	AV03429-AS	u* ^{Cf} *aaagUfcauGfcAfaUfegu* ^u *g	3042
AV03430	AV03430-SS	u* ^u *gcauguAfuChuUfeguua* ^a *a	2804	AV03430-AS	u* ^{Uf} *uuacAfcagAfuAfcAfugc* ^a *a	3043
AV03431	AV03431-SS	u* ^a *caguuaUfcUfuGfuguaaa* ^c *a	2805	AV03431-AS	u* ^{Gf} *uuuacAfcacAfaUfaCfaug* ^c *a	3044
AV03432	AV03432-SS	c* ^a *uguaucUfuChuGfuaaca* ^c *a	2806	AV03432-AS	u* ^{Gf} *uguuUfcaacAfaGfaUfaca* ^u *g	3045
AV03433	AV03433-SS	u* ^g *uaucuuGfuChuAfaacau* ^a *a	2807	AV03433-AS	u* ^{Uf} *aguUfmuacAfcAfaGfaaa* ^c *a	3046
AV03434	AV03434-SS	c* ^u *ucazacAfcUfuGfaucauu* ^c *a	2808	AV03434-AS	u* ^{Gf} *aaugAfucaGfuChuCfuga* ^a *g	3047
AV03435	AV03435-SS	u* ^u *cegacaCfuUfgAficauc* ^u *a	2809	AV03435-AS	u* ^{Af} *gaaUGfaucAfgUfgeUfegu* ^a *a	3048
AV03436	AV03436-SS	a* ^a *aaauaGfcChuUfcauuu* ^c *a	2810	AV03436-AS	u* ^{Gf} *aaagAfgaaGfcAfuAfuuu* ^u *u	3049
AV03437	AV03437-SS	a* ^a *aaauaGfcUfuChuucuu* ^u *a	2811	AV03437-AS	u* ^{Af} *gaaGfagaGfgCfaUfauu* ^u *u	3050
AV03438	AV03438-SS	u* ^a *ugcauuChuChuUfucuuu* ^g *a	2812	AV03438-AS	u* ^{Cf} *auaaGfaaagAfgAfaGfgca* ^u *a	3051
AV03439	AV03439-SS	a* ^u *gcauuUfcUfuUfcauug* ^c *a	2813	AV03439-AS	u* ^{Gf} *cauaAfgaaGfaGfaAfgc* ^a *u	3052
AV03440	AV03440-SS	c* ^u *uucauUfgChuGfauuug* ^c *a	2814	AV03440-AS	u* ^{Gf} *ucaAfucaGfaUfaAfgaa* ^a *g	3053
AV03441	AV03441-SS	u* ^u *aaugcaAfuUfuGfacaagaa* ^c *a	2815	AV03441-AS	u* ^{Gf} *uuuUfcaAfuCfaGfcau* ^a *a	3054
AV03442	AV03442-SS	a* ^u *uagacaGfaAfcCfugaau* ^u *a	2816	AV03442-AS	u* ^{Af} *aaugCfaguUfcUfgeUfca* ^a *u	3055
AV03443	AV03443-SS	c* ^a *gaaucuGfcAfuUfgecuua* ^u *a	2817	AV03443-AS	u* ^{Af} *uaagCfaauGfcAfgGfuuc* ^u *g	3056
AV03444	AV03444-SS	a* ^g *aaucuGfaUfuUfgecuua* ^c *a	2818	AV03444-AS	u* ^{Gf} *auaaGfcaaaUfgCfaGfguu* ^c *u	3057
AV03445	AV03445-SS	c* ^u *gcauuGfcUfuAfuucua* ^a *a	2819	AV03445-AS	u* ^{Uf} *uagaaGfaaaGfcAfaAfuugc* ^a *g	3058
AV03446	AV03446-SS	u* ^a *uacuaAfaAfuAfuugguu* ^u *a	2820	AV03446-AS	u* ^{Af} *uaacCfaauUfuUfgeAfgaa* ^u *a	3059
AV03447	AV03447-SS	u* ^c *uacaaAfuAfuGfguauc* ^a *a	2821	AV03447-AS	u* ^{Uf} *gaucCfcauAfuUfuUfga* ^g *a	3060
AV03448	AV03448-SS	a* ^u *agauuuUfgUfuUfcauuac* ^u *a	2822	AV03448-AS	u* ^{Af} *guauUfgaaCfaAfaAfuuc* ^a *u	3061
AV03449	AV03449-SS	u* ^u *acuuaAfgGfuAfauaau* ^g *a	2823	AV03449-AS	u* ^{Cf} *auauAfuuaCfuUfaAfaugu* ^a *a	3062
AV03450	AV03450-SS	u* ^u *aaaguaAfuAfuAfuuguaa* ^c *a	2824	AV03450-AS	u* ^{Gf} *uaauCfaauAfuUfaCfcuu* ^a *a	3063
AV03451	AV03451-SS	a* ^a *gguauAfuAfuGfauuacc* ^u *a	2825	AV03451-AS	u* ^{Af} *gguAfucauAfuAfuUfacc* ^u *u	3064
AV03452	AV03452-SS	u* ^a *cuaaagUfaAfuAfcuuug* ^c *a	2826	AV03452-AS	u* ^{Gf} *ucauUfguauUfaChuUfaugc* ^a *a	3065
AV03453	AV03453-SS	c* ^a *uuagcaUfgAfuAfcuaau* ^c *a	2827	AV03453-AS	u* ^{Gf} *aauUfguauCfaUfgeUfca* ^u *g	3066
AV03454	AV03454-SS	g* ^a *uacaaUfuChuGfuaaua* ^c *a	2828	AV03454-AS	u* ^{Gf} *uaauUfcaagAfaUfuUfguu* ^u *c	3067
AV03455	AV03455-SS	a* ^a *uuuuguAfaUfuAfcuaag* ^g *a	2829	AV03455-AS	u* ^{Cf} *cauuUfguaUfuAfcAfgaa* ^u *u	3068
AV03456	AV03456-SS	u* ^u *uuccuGfaGfuAfcuaac* ^u *a	2830	AV03456-AS	u* ^{Af} *guuaGfuaucUfcAfgAfgaa* ^a *a	3069
AV03457	AV03457-SS	c* ^u *cuigaauAfcChuAfauuug* ^u *a	2831	AV03457-AS	u* ^{Af} *caagGfuagGfuAfcUfagc* ^a *g	3070
AV03458	AV03458-SS	c* ^u *cauguaUfcChuGfcaagaa* ^a *a	2832	AV03458-AS	u* ^{Uf} *auucGfcaagGfaUfaCfaug* ^a *g	3071

AV03459	AV03459-SS	c*c*ugnucaUfɪaUfɪuGfɪuaɣau*ɹ*a	2833	AV03459-AS	u*Uf*aucuUfɪacaUfɪaUfɪaGfɪaɸa*ɣ*ɣ	3072
AV03460	AV03460-SS	u*ɣ*unucauUfɪuGfɪuAɸaɣuaɣ*ɹ*a	2834	AV03460-AS	u*Uf*cuauCfɪuaCɸaUfɪaUfɪaɣa*c*ɹa	3073
AV03461	AV03461-SS	ɣ*ɹ*a*ɣaɣuaGfɪaUfɪuUfɪaaɣu*ɸ*a	2835	AV03461-AS	u*Gf*cauuUfɪaaUfɪaUfɪaUfɪcu-u*a*c	3074
AV03462	AV03462-SS	ɣ*ɹ*a*ɣaɣuaGfɪuCfɪuCfɪaauuɣ*U*a	2836	AV03462-AS	u*Af*cauGfɪuɣaɸɸɸUfɪaCfɪaue*c*U	3075
AV03463	AV03463-SS	u*c*unuaɣaUfɪɸCfɪuCfɪuɣaau*c*ɹa	2837	AV03463-AS	u*Gf*auuuCfɪaɣaɣCfɪaUfɪɸCfɪaa*ɣ*a	3076
AV03464	AV03464-SS	u*U*ɣaɣauGfɪuCfɪuGfɪaauca*ɹ*a	2838	AV03464-AS	u*Uf*ɣaɣuUfɪuɣaɸfɪuɣaCfɪaUfɪɸu*ɹ*a	3077
AV03465	AV03465-SS	c*U*ɣ*ɣaaucAɸɸCfɪuGfɪaauuɣ*ɣ*a	2839	AV03465-AS	u*Cf*cuauUfɪɸaɸUfɪuGfɪaUfɪuuc*ɹa*ɣ	3078
AV03466	AV03466-SS	ɹ*a*ɹ*a*ucaaucAɸɸUfɪaUfɪaɣuuu*ɹ*a	2840	AV03466-AS	u*Uf*ɣaaCfɪuaaCfɪaAɸɸUfɪuɣa*U*U	3079
AV03467	AV03467-SS	ɹ*a*U*cɸaauGfɪaUfɪaUfɪɣuuua*U*a	2841	AV03467-AS	u*Af*uaaaCfɪuaaUfɪɸCfɪaGfɪuɣ*ɹa*U	3080
AV03468	AV03468-SS	u*ɣ*U*ɣuucCfɪaGfɪaUfɪɸɣcauu*U*a	2842	AV03468-AS	u*Af*aaɣCfɪaueUfɪɸGfɪɸAɸa*c*ɹa	3081
AV03469	AV03469-SS	ɹ*a*ɣ*ɣcauuGfɪɸUfɪaAɸaauau*c*U	2843	AV03469-AS	ɹ*a*Gf*auauUfɪcuuaCfɪaAɸaAɸuɣ*c*U	3082
AV03470	AV03470-SS	c*ɹa*uuucaUfɪuUfɪaGfɪucauɣ*ɹ*a	2844	AV03470-AS	u*Uf*cauɣAɸaɸuaAɸaUfɪɸAɸaa*U*ɣ	3083
AV03471	AV03471-SS	ɹ*a*c*ccɣueCfɪeUfɪeAɸcuuɣɣ*U*a	2845	AV03471-AS	u*Af*ccaAɸuɣaɸGfɪuGfɪaGfɪɸɣ*ɣ*U	3084
AV03472	AV03472-SS	ɣ*ɣ*ɸcuauCfɪeUfɪaCfɪauuɣuc*ɹ*a	2846	AV03472-AS	u*Uf*ɣacaAɸuɣaaGfɪuAɸaGfɪaɣ*c*U	3085
AV03473	AV03473-SS	ɹ*a*ɣ*aaɣɣaGfɪuGfɪaGfɪaɣcuu*ɣ*ɹa	2847	AV03473-AS	u*Cf*aaɣɣCfɪuɣCfɪeUfɪeCfɪcu*c*U	3086
AV03474	AV03474-SS	ɹ*a*ɣ*ugccaCfɪuUfɪeCfɪeucuc*U*a	2848	AV03474-AS	u*Af*ɣaaɣAɸɣɣaAɸuUfɪɸGfɪa*c*U	3087
AV04179	AV04179-SS	ɣ*ɣ*aaucuaCfɪɸUfɪɸGfɪuɣaua*ɹ*a	2849	AV04179-AS	u*Uf*uaauCfɪaacCfɪuUfɪaAɸuɣu*c*U	3088
AV04180	AV04180-SS	c*ɹa*acuaucGfɪuGfɪuUfɪaauaa*U*a	2850	AV04180-AS	u*Af*uaauUfɪcaacAɸɸGfɪuAɸaɣu*U*ɣ	3089
AV04181	AV04181-SS	ɣ*ɸ*uuacɣuGfɪɸUfɪaAɸuaauɣ*ɹ*a	2851	AV04181-AS	u*Uf*cauuAɸaueaCfɪeAɸGfɪaa*ɣ*c	3090
AV04182	AV04182-SS	ɣ*U*uaɣuɣuGfɪuGfɪaUfɪuaauɣa*ɹ*a	2852	AV04182-AS	u*Uf*ucauUfɪaueaCfɪeCfɪaCfɪuɣa*ɹa*c	3091
AV04183	AV04183-SS	c*U*ɣɣuɣauUfɪaAɸuGfɪaauaa*U*a	2853	AV04183-AS	u*Af*uaauUfɪucauUfɪaAɸuCfɪac*ɹa*ɣ	3092
AV04184	AV04184-SS	ɣ*ɹ*a*ucuaaAɸuAɸuUfɪaɣɣaaɣ*ɹ*a	2854	AV04184-AS	u*Uf*cuucCfɪuaaAɸuUfɪuAɸaɣa*U*c	3093
AV04185	AV04185-SS	ɣ*ɹ*a*auaauaGfɪaAɸaGfɪaauuɣa*U*a	2855	AV04185-AS	u*Af*ucaacCfɪucucCfɪeUfɪaAɸua-u*c	3094
AV04186	AV04186-SS	ɣ*ɹ*a*uaaɣuAɸaAɸuUfɪuɣauuɣ*ɹ*a	2856	AV04186-AS	u*Uf*caauCfɪaauCfɪuUfɪeCfɪuaa*U*c	3095
AV04187	AV04187-SS	ɣ*ɹ*a*ɣɣaaɣuGfɪuUfɪaAɸuaaɣ*U*a	2857	AV04187-AS	u*Af*cuucAɸaueaAɸɸUfɪeUfɪuc*U*c	3096
AV04188	AV04188-SS	ɣ*ɣ*ɣaaɣuɸuGfɪuGfɪuɣaau*U*a	2858	AV04188-AS	u*Af*acuuCfɪaueaAɸaCfɪuCfɪuc*c*c	3097
AV04189	AV04189-SS	c*ɣ*aaɣuɣuUfɪaAɸuUfɪaɣauu*U*a	2859	AV04189-AS	u*Af*aaauUfɪcauUfɪaCfɪeUfɪeui*c*ɣ	3098
AV04190	AV04190-SS	ɣ*U*ɣaaauAɸuUfɪuUfɪuuɣc*U*a	2860	AV04190-AS	u*Af*ɣɣcaAɸaaacCfɪuUfɪeAɸuc*ɹa*c	3099
AV04191	AV04191-SS	ɣ*ɣ*uaauuUfɪuAɸCfɪaɣauu*c*ɹa	2861	AV04191-AS	u*Gf*aaauCfɪuɣuAɸaAɸaUfɪuɣaa*c*c	3100
AV04192	AV04192-SS	c*U*acauuuUfɪaCfɪaAɸuauc*c*ɹa	2862	AV04192-AS	u*Gf*ɣaaUaAɸeuɣuUfɪaAɸaAɸuɣu*ɹa*ɣ	3101
AV04193	AV04193-SS	ɣ*U*ucacɣaUfɪuUfɪɸCfɪaɣuɣa*ɹ*a	2863	AV04193-AS	u*Uf*ucauUfɪɣɣcaCfɪaUfɪeUfɪaɣa*ɹa*c	3102

AV04194	AV04194-SS	g*c*ucagauGfuGfcCfaugaa*a*a	2864	AV04194-AS	u*Uf*unecaChugcAfcAfucHuga*g*c	3103
AV04195	AV04195-SS	c*c*ceugaaAfaGfgGfuuncu*g*u*a	2865	AV04195-AS	u*Af*cagaAfaceUfuUfcAfcu*g*g*g	3104
AV04196	AV04196-SS	g*c*agugaaAfaGfgUfucugu*u*a	2866	AV04196-AS	u*Af*acagAfaaccChuUfuCfaeu*g*c	3105
AV04197	AV04197-SS	c*u*gaagugGfuUfuCfuuguuu*g*c*a	2867	AV04197-AS	u*Gf*canaCfagaaAfcCfcUfhuc*a*g	3106
AV04198	AV04198-SS	g*g*aguguuUfcUfgUfhugcu*u*c*a	2868	AV04198-AS	u*Gf*agcAfaacaGfaAfaCfcu*u*c	3107
AV04199	AV04199-SS	c*u*uuucuUfuGfcUfhucuuu*g*c*a	2869	AV04199-AS	u*Gf*cauGfaagcAfaAfcAfgaa*a*g	3108
AV04200	AV04200-SS	g*u*ucauugChuGfaCfaugcu*g*u*a	2870	AV04200-AS	u*Af*cagChuucAfgCfaAfauga*a*c	3109
AV04201	AV04201-SS	g*u*cauugUfgAfcAfcuuguu*u*a	2871	AV04201-AS	u*Af*acagCfcugCfaGfcAfaug*a*c	3110
AV04202	AV04202-SS	g*c*auugcuGfaCfaGcuuuu*a*a	2872	AV04202-AS	u*Uf*aaacAfcuugUfcAfgCfaau*g*c	3111
AV04203	AV04203-SS	g*u*gcugacAfgChuUfhuaau*u*a	2873	AV04203-AS	u*Af*aguaAfaagChuGfuCfauc*a*c	3112
AV04204	AV04204-SS	c*a*agcuuGfuUfaCfuuuuug*g*a	2874	AV04204-AS	u*Cf*canaAfaugaAfcAfaGfcu*u*g	3113
AV04205	AV04205-SS	g*g*agcuugUfuAfcUfhuuug*g*a	2875	AV04205-AS	u*Uf*ccaaAfaaguAfaCfaAfgcu*g*c	3114
AV04206	AV04206-SS	g*g*uaauuUfuUfgGfaagaa*g*a	2876	AV04206-AS	u*Cf*agcUfhuccaAfaAfaGfuaa*g*c	3115
AV04207	AV04207-SS	g*g*ucucuChuUfcAfaaguu*a*a	2877	AV04207-AS	u*Uf*aaacUfhugaAfgAfcGfauga*g*c	3116
AV04208	AV04208-SS	g*a*auuagAfaAfuGfaucg*a*a	2878	AV04208-AS	u*Uf*ccgaAfucauUfuUfcUfaau*u*c	3117
AV04209	AV04209-SS	c*a*uuugcuGfaGfcAfcuugaa*g*a	2879	AV04209-AS	u*Cf*uaacAfcuugUfcUfcCfaaa*u*g	3118
AV04210	AV04210-SS	g*c*ggagugCfaGfuGfuagcu*u*a	2880	AV04210-AS	u*Af*agcuAfaacUfgChuChuc*g*c	3119
AV04211	AV04211-SS	c*g*agagcaGfuGfuUfaucua*u*a	2881	AV04211-AS	u*Af*uaagChuaacAfcUfgChucu*g*g	3120
AV04212	AV04212-SS	c*a*ggagcuUfgUfuAfcuuaa*u*a	2882	AV04212-AS	u*Af*uaagCfuuaacCfaChuGfcu*u*g	3121
AV04213	AV04213-SS	c*a*ggagcuUfuAfcCfuuaauu*g*a	2883	AV04213-AS	u*Cf*aaauAfauguAfaCfaCfuug*u*g	3122
AV04214	AV04214-SS	g*g*caugcuUfaGfcUfhauuu*g*a	2884	AV04214-AS	u*Af*caauUfaagcUfaAfcAfcu*g*c	3123
AV04215	AV04215-SS	g*g*uguuagChuUfaUfhuguuu*g*a	2885	AV04215-AS	u*Cf*caacAfaauaAfgChuAfaaa*c*c	3124
AV04216	AV04216-SS	g*a*gcuaauUfuGfuUfgaaua*a*a	2886	AV04216-AS	u*Uf*uaauCfaaacAfaAfuAfauc*u*c	3125
AV04217	AV04217-SS	g*g*uuugaaUfaAfaAfuuaag*g*a	2887	AV04217-AS	u*Uf*ccuaAfaauuUfaUfuCfaaa*c*c	3126
AV04218	AV04218-SS	g*u*ggaaauAfaAfuUfhagaa*u*a	2888	AV04218-AS	u*Af*uuccUfaauUfuUfaUfhuc*a*c	3127
AV04219	AV04219-SS	g*u*uaauuAfaAfgGfaugaa*a*a	2889	AV04219-AS	u*Uf*uucaAfucauUfuAfgAfaaa*a*c	3128
AV04220	AV04220-SS	g*u*auucaaAfaGfgAfhugaa*a*a	2890	AV04220-AS	u*Uf*uucaAfucauUfuUfaGfaau*a*c	3129
AV04221	AV04221-SS	g*g*gaugaaAfaAfaCfuuuuug*g*a	2891	AV04221-AS	u*Cf*caaaAfaaguuUfuUfcCfauc*c*c	3130
AV04222	AV04222-SS	g*u*ggaaauAfcUfuUfhugaa*u*a	2892	AV04222-AS	u*Uf*aucaAfaaaGfuUfuUfhuc*a*c	3131
AV04223	AV04223-SS	g*a*aaauuuUfuGfgAfhauuu*g*a	2893	AV04223-AS	u*Cf*caaaUfauceAfaAfaAfguu*u*c	3132
AV04224	AV04224-SS	g*u*uuugaaAfuUfuGfagaa*u*a	2894	AV04224-AS	u*Af*uuucUfhuccaAfaAfuCfaaa*a*c	3133

AV04225	AV04225-SS	g* ^u *uuaaaCfaAfuUfugcuu* ^a * ^a	2895	AV04225-AS	u* ^U * ^f * ^a agcCfaauUfgUfuUfuua* ^a * ^c	3134
AV04226	AV04226-SS	g* ^u * ^u aaacAfUfuUfgcuu* ^u * ^a	2896	AV04226-AS	u* ^A * ^f * ^u aaGfcaaaUfuGfuUfuua* ^a * ^c	3135
AV04227	AV04227-SS	g* ^u * ^a aaacAfUfuGfgcuuau* ^c * ^a	2897	AV04227-AS	u* ^G * ^f * ^a aaGfccaAfUfuUfuu* ^a * ^c	3136
AV04228	AV04228-SS	g* ^u * ^a aaacAUfuGfgCfuuauc* ^c * ^a	2898	AV04228-AS	u* ^G * ^f * ^u gaUAfagccAfAfuUfguu* ^u * ^c	3137
AV04229	AV04229-SS	g* ^u * ^g cu gauUfuGfaCfagaacc* ^u * ^a	2899	AV04229-AS	u* ^A * ^f * ^g guCfugucAfAfuCfagc* ^a * ^c	3138
AV04230	AV04230-SS	c* ^a * ^u uugacAf ^a CfCfugcau* ^u * ^a	2900	AV04230-AS	u* ^A * ^f * ^u agcAf ^g guuCfuGfuCfaa* ^u * ^g	3139
AV04231	AV04231-SS	g* ^u * ^u * ^g acagAfCfuGfcauuug* ^c * ^a	2901	AV04231-AS	u* ^G * ^f * ^c aaUf ^g caGfuUfuUf ^u cu* ^a * ^c	3140
AV04232	AV04232-SS	g* ^g * ^g * ^a agaaCfCfuGfcauuug* ^u * ^a	2902	AV04232-AS	u* ^A * ^f * ^g caaAf ^u gcaGfuUfuCfu ^g u* ^c * ^c	3141
AV04233	AV04233-SS	g* ^c * ^u * ^a gaacUf ^g CfaUf ^u gcuu* ^a * ^a	2903	AV04233-AS	u* ^U * ^f * ^a agcAf ^{au} gCfaGfuUfu ^u * ^g * ^c	3142
AV04234	AV04234-SS	c* ^a * ^a * ^a acugcAfUfuGfcauuu* ^u * ^a	2904	AV04234-AS	u* ^A * ^f * ^g auAf ^g caaAf ^u GfCf ^u g ^u * ^u * ^g	3143
AV04235	AV04235-SS	g* ^u * ^g * ^c cu gcaUfuUf ^g Cfuuauc* ^u * ^a	2905	AV04235-AS	u* ^A * ^f * ^g gaUAf ^g caAfAfuUf ^g Cf ^u g ^u * ^u * ^c	3144
AV04236	AV04236-SS	g* ^c * ^c * ^u gcgaUfuGfCfuuauc* ^c * ^a	2906	AV04236-AS	u* ^G * ^f * ^a agaUf ^u gaagAfAfuGf ^u g ^u * ^g * ^c	3145
AV04237	AV04237-SS	g* ^c * ^u gcgaUf ^g CfuUf ^u cauc* ^a * ^a	2907	AV04237-AS	u* ^U * ^f * ^g aaAf ^u gaagCfaAfAfuUf ^g ca* ^g * ^c	3146
AV04238	AV04238-SS	g* ^g * ^g * ^c cauuGfuUfuUf ^u cauc* ^a * ^a	2908	AV04238-AS	u* ^U * ^f * ^u gaaAf ^g auAf ^g CfaAf ^u g ^u * ^c * ^c	3147
AV04239	AV04239-SS	g* ^u * ^u * ^u gcuuAf ^u CfuUf ^u caau* ^a * ^a	2909	AV04239-AS	u* ^U * ^f * ^a uuUf ^g gaAf ^u Af ^u Gfca* ^a * ^c	3148
AV04240	AV04240-SS	g* ^u * ^u * ^u gcuaUf ^u CfuCfaaau* ^u * ^a	2910	AV04240-AS	u* ^A * ^f * ^u auUf ^u gaGfaUfaAf ^g ca* ^a * ^c	3149
AV04241	AV04241-SS	g* ^u * ^u * ^g cuauCfuUf ^u Cf ^u Afaauu* ^g * ^a	2911	AV04241-AS	u* ^C * ^f * ^g auuUf ^u gaAf ^g AfuAf ^u g ^u * ^a * ^c	3150
AV03075	AV03075-SS	c* ^c * ^c * ^a uggcgAf ^u CfCfuUf ^g gaau* ^g * ^a	2912	AV03075-AS	u* ^C * ^f * ^u uuCf ^u gagGfuCf ^u gCf ^u cau* ^g * ^g	3151
AV03076	AV03076-SS	g* ^c * ^g * ^g accuGf ^u CfaAf ^u g ^u g ^u * ^u * ^a	2913	AV03076-AS	u* ^A * ^f * ^u caagCfuuuCf ^u Cf ^u Af ^g Gf ^u g ^u * ^g * ^c	3152

Table 3 and Table 3A shows certain chemically modified HTT RNAi agent antisense strand and sense strand sequences of the invention. In some embodiments of methods of the invention, RNAi agents shown in Table 3 and Table 3A are administered to a cell and/or subject. In some embodiments of methods of the invention, a RNAi agent with a polynucleotide sequence shown in Table 3 and Table 3A is administered to a subject. In some embodiments of the invention an RNAi agent administered to a subject comprises is a duplex identified in a row in Table 3 and Table 3A, column one and includes the sequence modifications and/or delivery compound show in the sense and antisense strand sequences in the same row in Table 3 and Table 3A, columns three and six, respectively. The sequences were used in certain in vivo testing studies described elsewhere herein. In some embodiments of methods of the invention, a sequence shown in Table 3 and Table 3A may be attached to (also referred to herein as

“conjugated to”) a compound for delivery, a non-limiting example of which is a GalNAc-containing compound, with a delivery compound identified in Table 3 as “GLX-n” on sense strands in column three. As used herein, “GLX-n” is used to represent either a “GLS-n*” or a GLO-n” delivery compound (“X” can be either “S” or “O”) and GLX-0 can be any of the “GLS-n*” and “GLO-n” delivery compounds that can be attached to 3'-end of oligonucleotide during synthesis. As used herein and shown in Table 3, “GLX-n” is used to indicate the attached GalNAc-containing compound is any one of compounds GLS-1*, GLS-2*, GLS-3*, GLS-4*, GLS-5*, GLS-6*, GLS-7*, GLS-8*, GLS-9*, GLS-10*, GLS-11*, GLS-12*, GLS-13*, GLS-14*, GLS-15*, GLS-16*, GLO-1, GLO-2, GLO-3, GLO-4, GLO-5, GLO-6, GLO-7, GLO-8, GLO-9, GLO-10, GLO-11, GLO-12, GLO-13, GLO-14, GLO-15, and GLO-16, the structure of each of which is provided elsewhere herein. One skilled in the art will be able to prepare and use a dsRNA compound of the invention in which the attached delivery compound is one of GLS-1*, GLS-2*, GLS-3*, GLS-4*, GLS-5*, GLS-6*, GLS-7*, GLS-8*, GLS-9*, GLS-10*, GLS-11*, GLS-12*, GLS-13*, GLS-14*, GLS-15*, GLS-16*, GLO-1, GLO-2, GLO-3, GLO-4, GLO-5, GLO-6, GLO-7, GLO-8, GLO-9, GLO-10, GLO-11, GLO-12, GLO-13, GLO-14, GLO-15, and GLO-16. Column one of Table 3 and Table 3A provides a Duplex AD# assigned to the duplex of the sense and antisense sequences in that row of the table. For example, Duplex AD# AD01638 is the duplex of sense strand SEQ ID NO: 3291 and antisense strand SEQ ID NO: 3327. Each line in Table 3 and Table 3A provides a sense strand and an antisense strand, and discloses the duplex of the sense and antisense strands shown. The “Sense strand SS#” in Table 3 and Table 3A column two is the assigned identifier for the Sense Sequence (including modifications) shown column 3 in the same row. The “Antisense strand AS#” in Table 3 and Table 3A column five is the assigned identifier for the Antisense sequence (including modifications) shown in column six. An identifier for certain attached GalNAc-containing “GLO-n” or “GLS-n*” compounds is shown as GLS-5*, GLS-15* or GLX-0, and it will be understood that another of the “GLO-n” or “GLS-n*” compounds may be substituted for the compound shown as GLO-0, with the resulting compound included in an embodiment of a method and/or a composition of the invention.

Table 3 provides chemically modified HTT RNAi agent antisense strand and sense strand sequences. All sequences shown 5' to 3'. The sequences were used in certain in vivo testing studies described elsewhere herein. A delivery molecule used in the in vivo studies is indicated as “GLO-n” or “GLS-n*” at the 3'-end or 5'-end of each sense strand.

Duplex AD#	Sense strand SS#	Sense Sequence	SEQ ID NO	Antisense strand AS#	Antisense Sequence	SEQ ID NO
AD01240	AD01240-SS	g [*] c [*] uau(Uhd)CfaUfaAfAfcacauuc [*] g [*] a	3153	AD01240-AS	(V)Pu [*])Cf [*] gaUfIgUfGfaumaUfIgAfataugc [*] a [*] u	3219
AD01245	AD01245-SS	(GL-S-15 [*])(imann [*])cugaacauUfncfncCfngacaau [*] a [*] (imann)	3154	AD01245-AS	u [*] A [*] uugcCfagacAfiaUfIgAfimuc [*] a [*] g	3220
AD01246	AD01246-SS	(GL-S-15 [*])(imann [*])ggaagcuUfIgAfuCfngauucua [*] a [*] (imann)	3155	AD01246-AS	u [*] U [*] f [*] agaUfCcauChafafCfciu [*] u [*] c	3221
AD01247	AD01247-SS	(GL-S-15 [*])(imann [*])gguuggcAfuUfuUfCcaaug [*] a [*] (imann)	3156	AD01247-AS	u [*] C [*] auuuGfcaaaAfuUfCfcaat [*] a [*] c	3222
AD01248	AD01248-SS	(GL-S-15 [*])(imann [*])gucuuaaAfIgUfncCfucuuuga [*] a [*] (imann)	3157	AD01248-AS	u [*] U [*] f [*] caagAfIgaacChUfuAfhug [*] a [*] c	3223
AD01249	AD01249-SS	(GL-S-15 [*])(imann [*])gucagacUfCfuGfiacuaca [*] a [*] (imann)	3158	AD01249-AS	u [*] U [*] f [*] guagUfucacGfaUfIgUfCfug [*] a [*] c	3224
AD01250	AD01250-SS	(GL-S-15 [*])(imann [*])gucacauUfCfuCfncCfucuaa [*] a [*] (imann)	3159	AD01250-AS	u [*] U [*] f [*] augafIggaaGfaUfIgAfhuag [*] a [*] c	3225
AD01251	AD01251-SS	(GL-S-15 [*])(imann [*])gaucacauUfCfhuUfnguuga [*] a [*] (imann)	3160	AD01251-AS	u [*] U [*] f [*] caacCfcaacGfaAfuGfhga [*] u [*] c	3226
AD01252	AD01252-SS	(GL-S-15 [*])(imann [*])gcaucuuUfncfhuUfCuuugua [*] a [*] (imann)	3161	AD01252-AS	u [*] U [*] f [*] accaAfIgaagAfiaAfiaAfiau [*] g [*] c	3227
AD01253	AD01253-SS	(GL-S-15 [*])(imann [*])gaaacagaUfCfuUfCfngauuc [*] a [*] (imann)	3162	AD01253-AS	u [*] Gf [*] auuucfcauGfiauUfCfIgum [*] u [*] c	3228
AD01254	AD01254-SS	(GL-S-15 [*])(imann [*])gunguucUfncfhuCfngauuca [*] a [*] (imann)	3163	AD01254-AS	u [*] U [*] f [*] gaauAfCgagAfiaAfIga [*] a [*] c	3229
AD01255	AD01255-SS	(GL-S-15 [*])(imann [*])ggaaagaaCfaUfuUfCcaaggu [*] a [*] (imann)	3164	AD01255-AS	u [*] A [*] ccuuGfuaaUfIgUfuUfCuu [*] c [*] c	3230
AD01256	AD01256-SS	(GL-S-15 [*])(imann [*])gaaaguuucfhuAfuUfCcaacug [*] a [*] (imann)	3165	AD01256-AS	u [*] Cf [*] aguuGfuaaAfIgaAfiaAficu [*] u [*] c	3231
AD01257	AD01257-SS	(GL-S-15 [*])(imann [*])cagcagcaAfCfuAfuAfcuuuca [*] a [*] (imann)	3166	AD01257-AS	u [*] U [*] f [*] agaaAfIguauGfuUfCfCfuc [*] u [*] g	3232
AD01258	AD01258-SS	(GL-S-15 [*])(imann [*])gucugugafUfuAfuGfucugua [*] a [*] (imann)	3167	AD01258-AS	u [*] U [*] f [*] gacaGfcauAfiaUfCfCag [*] a [*] c	3233
AD01259	AD01259-SS	(GL-S-15 [*])(imann [*])gacguucaUfCfuGfucuauc [*] a [*] (imann)	3168	AD01259-AS	u [*] Gf [*] auuuGfcaacGfiauUfIgAfiaug [*] u [*] c	3234
AD01260	AD01260-SS	(GL-S-15 [*])(imann [*])gguacucaGfuUfncGfagaac [*] a [*] (imann)	3169	AD01260-AS	u [*] Gf [*] uuucUfucaaAfCfUfIgAfiau [*] c [*] c	3235
AD01471	AD01471-SS	(GL-S-15 [*])(imann [*])caccagcaCfCafCfAuuguuu [*] a [*] (imann)	3170	AD01471-AS	u [*] A [*] f [*] caacAfIuuuGfIgUfCfIuug [*] u [*] g	3236
AD01472	AD01472-SS	(GL-S-15 [*])(imann [*])ucauaucAfCfuUfCguuuu [*] a [*] (imann)	3171	AD01472-AS	u [*] A [*] f [*] caacCfgaucGfuGfiauUfuau [*] g [*] a	3237
AD01473	AD01473-SS	(GL-S-15 [*])(imann [*])gcuugugaAfuCfIgGfauucug [*] a [*] (imann)	3172	AD01473-AS	u [*] Cf [*] aggaAfucagAfuUfCafcca [*] g [*] c	3238
AD01474	AD01474-SS	(GL-S-15 [*])(imann [*])ugacuuuUfuAfuCfGfaaugu [*] a [*] (imann)	3173	AD01474-AS	u [*] Gf [*] acauUfucguAfiaAfCfiau [*] c [*] a	3239
AD01240-1-SS	AD01240-1-SS	(GL-S-15 [*])(imann [*])gcannucaUfaAfuCfcauucg [*] a [*] (imann)	3174	AD01240-1-AS	u [*] C [*] gaucGfugauUfaUfIgAfiana [*] g [*] c	3240
AD01919	AD01919-SS	(GL-S-15 [*])(imann [*])gggagggcCfIgCfncCfagguuc [*] a [*] (imann)	3175	AD01919-AS	u [*] A [*] f [*] gaAfC(cUNA)uagacCfIgCfCfuc [*] c [*] c	3241
AD01920	AD01920-SS	(GL-S-15 [*])(imann [*])ggcucggelUfncfhuGfciuuuac [*] a [*] (imann)	3176	AD01920-AS	u [*] Gf [*] uuaaAfIgcagAfafCfUfIgag [*] c [*] c	3242
AD01921	AD01921-SS	(GL-S-15 [*])(imann [*])cguuucgclUfuUfuAfcuuggg [*] a [*] (imann)	3177	AD01921-AS	u [*] C [*] cgCf(a(gUNA)guuaAfafGfCfAfgaat [*] c [*] g	3243
AD01922	AD01922-SS	(GL-S-15 [*])(imann [*])ggcccccUfCfuAfuUfIgccccgg [*] a [*] (imann)	3178	AD01922-AS	u [*] C [*] cgCfIg(gUNA)caauGfiaAfuCfIgag [*] c [*] c	3244
AD01923	AD01923-SS	(GL-S-15 [*])(imann [*])gaggggacCfCfuCfGfataag [*] a [*] (imann)	3179	AD01923-AS	u [*] Gf [*] cuuUfCagGfIgUfCfGfcca [*] u [*] c	3245

AD01924	AD01924-SS	(GL-S-1.5*)(imann*) <i>gcugaugAfcGfcChnucagu*</i> a*(imann)	3180	AD01924-AS	u* <i>At</i> [°] <i>cutCf</i> (aUNA) <i>agccCh</i> Uf <i>cAfuca*</i> g [°] g	3246
AD01925	AD01925-SS	(GL-S-1.5*)(imann*) <i>gaguccuCf</i> a <i>fCf</i> h <i>agcaga*</i> a*(imann)	3181	AD01925-AS	u* <i>U</i> [°] <i>gcUf</i> (cUNA) <i>uecuGf</i> gA <i>fA</i> G <i>f</i> gac [°] u [°] c	3247
AD01926	AD01926-SS	(GL-S-1.5*)(imann*) <i>ggacaaGf</i> a <i>fA</i> G <i>f</i> h <i>acuuu*</i> a*(imann)	3182	AD01926-AS	u* <i>G</i> [°] <i>aagUf</i> h <i>cuUf</i> cU <i>hUf</i> g [°] u [°] c [°] c	3248
AD01927	AD01927-SS	(GL-S-1.5*)(imann*) <i>gaaagaaGf</i> a <i>fC</i> Uf <i>hucagu*</i> a*(imann)	3183	AD01927-AS	u* <i>At</i> [°] <i>gcugAf</i> agauUf <i>cUf</i> hU <i>fcuu*</i> u [°] c	3249
AD01928	AD01928-SS	(GL-S-1.5*)(imann*) <i>gaaagaaGf</i> a <i>fCh</i> Uf <i>hucaga*</i> a*(imann)	3184	AD01928-AS	u* <i>U</i> [°] <i>gcugAf</i> agauUf <i>cUf</i> hU <i>fcu*</i> u [°] c	3250
AD01929	AD01929-SS	(GL-S-1.5*)(imann*) <i>ggaaauuCh</i> a <i>fCf</i> Uf <i>hacaga*</i> a*(imann)	3185	AD01929-AS	u* <i>U</i> [°] <i>gcugGh</i> agcUf <i>gAfa</i> A <i>fguu*</i> c [°] c	3251
AD01930	AD01930-SS	(GL-S-1.5*)(imann*) <i>gaaagaaGf</i> c <i>Gh</i> U <i>h</i> gaauc [°] a*(imann)	3186	AD01930-AS	u* <i>U</i> [°] <i>gaaUCh</i> acacG <i>fgUf</i> cUf <i>huc*</i> u [°] c	3252
AD01931	AD01931-SS	(GL-S-1.5*)(imann*) <i>cacccyguCh</i> a <i>fA</i> h <i>UCh</i> amug [°] u [°] a*(imann)	3187	AD01931-AS	u* <i>At</i> [°] <i>gcagAf</i> hgaUf <i>cAfcAfcg*</i> u [°] g	3253
AD01932	AD01932-SS	(GL-S-1.5*)(imann*) <i>ggugugauUf</i> cA <i>hUf</i> hucugac [°] a*(imann)	3188	AD01932-AS	u* <i>G</i> [°] <i>gcAcA</i> fg(aUNA) <i>caanGf</i> aU <i>hCh</i> fac [°] a [°] c [°] c	3254
AD01933	AD01933-SS	(GL-S-1.5*)(imann*) <i>cuugygaUCh</i> aUf <i>hCh</i> ucugac [°] a*(imann)	3189	AD01933-AS	u* <i>U</i> [°] <i>gcagGf</i> acauUf <i>gA</i> h <i>Uf</i> huc [°] a [°] g	3255
AD01934	AD01934-SS	(GL-S-1.5*)(imann*) <i>gyugucygaCh</i> a <i>hU</i> A <i>h</i> ugyga [°] a*(imann)	3190	AD01934-AS	u* <i>U</i> [°] <i>gcuncaCh</i> aanUf <i>gUf</i> cA <i>fgac*</i> a [°] c	3256
AD01935	AD01935-SS	(GL-S-1.5*)(imann*) <i>gyugycagaUf</i> h <i>UCh</i> ucaga [°] a*(imann)	3191	AD01935-AS	u* <i>U</i> [°] <i>gcugGf</i> agaaU <i>hUf</i> cUf <i>gcac*</i> a [°] c	3257
AD01936	AD01936-SS	(GL-S-1.5*)(imann*) <i>gyunuccaCh</i> a <i>hU</i> hucaga [°] a*(imann)	3192	AD01936-AS	u* <i>U</i> [°] <i>gcunccGf</i> aanUf <i>hUf</i> gGf <i>agaa*</i> a [°] c	3258
AD01937	AD01937-SS	(GL-S-1.5*)(imann*) <i>ccuauggaUf</i> hUf <i>hucygu*</i> a*(imann)	3193	AD01937-AS	u* <i>At</i> [°] <i>gcagAf</i> aaanChUf <i>cCh</i> aa [°] g [°] g	3259
AD01938	AD01938-SS	(GL-S-1.5*)(imann*) <i>cauggaUCh</i> a <i>hUf</i> hucucc [°] a*(imann)	3194	AD01938-AS	u* <i>U</i> [°] <i>gcugAf</i> gaauA <i>fgA</i> Uf <i>hccu*</i> u [°] g	3260
AD01939	AD01939-SS	(GL-S-1.5*)(imann*) <i>gagccagaA</i> f <i>acCh</i> Uf <i>hacacaga*</i> a*(imann)	3195	AD01939-AS	u* <i>U</i> [°] <i>gcugGh</i> aaUf <i>hUf</i> hChug [°] u [°] c	3261
AD01940	AD01940-SS	(GL-S-1.5*)(imann*) <i>gyunuccaA</i> h <i>UCh</i> Uf <i>hccuucac*</i> a*(imann)	3196	AD01940-AS	u* <i>At</i> [°] <i>ggaGf</i> gaagA <i>hCh</i> h <i>Uf</i> hag [°] a [°] c	3262
AD01941	AD01941-SS	(GL-S-1.5*)(imann*) <i>gyauccaA</i> f <i>acCh</i> Uf <i>h</i> gangaug [°] a*(imann)	3197	AD01941-AS	u* <i>C</i> [°] <i>gaucUf</i> gcaUf <i>hUf</i> gA <i>fguu*</i> a [°] c	3263
AD01942	AD01942-SS	(GL-S-1.5*)(imann*) <i>gaaucgaUf</i> gA <i>hCh</i> ucugaa [°] a*(imann)	3198	AD01942-AS	u* <i>U</i> [°] <i>gcugGf</i> acauCh <i>Uf</i> gCh <i>aguu*</i> u [°] c	3264
AD01943	AD01943-SS	(GL-S-1.5*)(imann*) <i>ggggcauCh</i> Uf <i>hCh</i> ugyucc [°] a*(imann)	3199	AD01943-AS	u* <i>U</i> [°] <i>gcugaaCh</i> acaaA <i>fcA</i> fgUf <i>hgc*</i> c [°] c	3265
AD01944	AD01944-SS	(GL-S-1.5*)(imann*) <i>gacuyuuCh</i> h <i>Uf</i> hcaacca [°] a*(imann)	3200	AD01944-AS	u* <i>At</i> [°] <i>gcunUf</i> gaacA <i>fcA</i> fgUf <i>hgc*</i> u [°] c	3266
AD01945	AD01945-SS	(GL-S-1.5*)(imann*) <i>cauaagaUf</i> gChU <i>A</i> fuuca [°] a*(imann)	3201	AD01945-AS	u* <i>U</i> [°] <i>gcuaugAf</i> aaugCh <i>Uf</i> hCh <i>ua*</i> u [°] g	3267
AD01946	AD01946-SS	(GL-S-1.5*)(imann*) <i>gaaagaaUCh</i> a <i>hUf</i> hcauauc [°] a*(imann)	3202	AD01946-AS	u* <i>G</i> [°] <i>gcannaUf</i> gaauA <i>fgCh</i> aUf <i>hcu*</i> u [°] c	3268
AD01947	AD01947-SS	(GL-S-1.5*)(imann*) <i>gyugyuugaA</i> f <i>cCh</i> Uf <i>h</i> guyuu [°] a [°] a*(imann)	3203	AD01947-AS	u* <i>At</i> [°] <i>gcuaacAf</i> agagChUf <i>hUf</i> hA <i>fiac*</i> a [°] c	3269
AD01948	AD01948-SS	(GL-S-1.5*)(imann*) <i>cuunygacCh</i> Uf <i>h</i> guyuu [°] a [°] a*(imann)	3204	AD01948-AS	u* <i>U</i> [°] <i>gcuaaAf</i> cgaaA <i>fgCh</i> Uf <i>h</i> gA <i>fiaca*</i> a [°] g	3270
AD01949	AD01949-SS	(GL-S-1.5*)(imann*) <i>gyuuuccaGf</i> Uf <i>hUf</i> hcauuac [°] a*(imann)	3205	AD01949-AS	u* <i>G</i> [°] <i>gcuaauAf</i> gaacC <i>fcUf</i> hChGf <i>aa*</i> a [°] c	3271
AD01950	AD01950-SS	(GL-S-1.5*)(imann*) <i>gyaagaaGf</i> aUf <i>hCh</i> fuuaacca [°] a*(imann)	3206	AD01950-AS	u* <i>U</i> [°] <i>gcunUf</i> gUf <i>gUf</i> cUf <i>hcu*</i> a [°] c	3272
AD01951	AD01951-SS	(GL-S-1.5*)(imann*) <i>gyuaacguGf</i> cChUf <i>h</i> augyaa [°] a*(imann)	3207	AD01951-AS	u* <i>U</i> [°] <i>gcuaaAf</i> hugagC <i>fcAfc</i> Gf <i>ua*</i> a [°] c	3273
AD01952	AD01952-SS	(GL-S-1.5*)(imann*) <i>gyuaaucaA</i> f <i>cA</i> hUf <i>h</i> caugac [°] a*(imann)	3208	AD01952-AS	u* <i>G</i> [°] <i>gcancUf</i> gaauChUf <i>h</i> Gf <i>Uf</i> ua [°] c [°] c	3274

AD01953	AD01953-SS	(GL-S-15*) ^g (imann*) ^g ucaugcufcUfhuCfhuagaac*a*(imann)	3209	AD01953-AS	u*Gf*unumCfacaCfcaAfcafcug*a*c	3275
AD01954	AD01954-SS	(GL-S-15*) ^g (imann*) ^g aucggauUfcChCfucaga*a*(imann)	3210	AD01954-AS	u*Uf*cuucAfccagGfcaAfuCfca*a*c	3276
AD01955	AD01955-SS	(GL-S-15*) ^g (imann*) ^g ugugagauUfgChCfucaga*a*(imann)	3211	AD01955-AS	u*Uf*uncuGfcaacChUfUfcac*a*c	3277
AD01956	AD01956-SS	(GL-S-15*) ^g (imann*) ^g ccuugggUfcAfuAtaaga*a*(imann)	3212	AD01956-AS	u*Uf*uncuUfhuauGfcaCfcaag* ^g * ^g	3278
AD01957	AD01957-SS	(GL-S-15*) ^g (imann*) ^g aaagagUfcUfhuCfhuagagu*a*(imann)	3213	AD01957-AS	u*Af*cuucUfhuauGfcaCfcaag* ^g * ^g	3279
AD01958	AD01958-SS	(GL-S-15*) ^g (imann*) ^g gaugagAfcaAfuUfcaagca*a*(imann)	3214	AD01958-AS	u*Uf*ugcuUfcauChCfuUfugc*c* ^g	3280
AD01959	AD01959-SS	(GL-S-15*) ^g (imann*) ^g cagcaagGfcaUfhuCfagaac*a*(imann)	3215	AD01959-AS	u*Af*ugcuUfugaUfcaUfUfcUfugc* ^g * ^g	3281
AD01960	AD01960-SS	(GL-S-15*) ^g (imann*) ^g cauucacAfcaUfhuCfhuagugc*a*(imann)	3216	AD01960-AS	u*Gf*aaacCfauugChUfUfcaAfauc* ^g * ^g	3282
AD01961	AD01961-SS	(GL-S-15*) ^g (imann*) ^g gaucacAfcaUfhuCfhuaguc*a*(imann)	3217	AD01961-AS	u*Uf*gaacCfcauugGfcaUfhuCfiau* ^g * ^g	3283
AD01962	AD01962-SS	(GL-S-15*) ^g (imann*) ^g cuuguaaAfcaUfhuCfhuaguc*a*(imann)	3218	AD01962-AS	u*Uf*cucaAfacaCfcaUfhuCfiau* ^g * ^g	3284
AD03542	AD03542-SS	(GL-S-15*) ^g * ^g ggucacAfcaUfhuCfhuaguc*c*(invab)	3583	AD03542-AS	u*Gf*ggcCfcaUfhuCfhuaguc*c*c	3635
AD03543	AD03543-SS	(GL-S-15*) ^g * ^g ccugacAfcaUfhuCfhuaguc*c*(invab)	3584	AD03543-AS	u*Cf*unacUfcaagUfhuCfhuCfcaag* ^g * ^g	3636
AD03544	AD03544-SS	(GL-S-15*) ^g * ^g aaagcuGfcaUfhuCfhuaguc*c*(invab)	3585	AD03544-AS	u*Af*agGfcaUfhuCfhuaguc*c*c	3637
AD03545	AD03545-SS	(GL-S-15*) ^g * ^g ggucugUfcaUfhuCfhuaguc*c*(invab)	3586	AD03545-AS	u*Gf*ggcUfcaUfhuCfhuaguc*c*c	3638
AD03546	AD03546-SS	(GL-S-15*) ^g * ^g ugacagAfcaUfhuCfhuaguc*c*(invab)	3587	AD03546-AS	u*Uf*cuucCfhuugGfcaUfhuCfhuaguc*c*c	3639
AD03547	AD03547-SS	(GL-S-15*) ^g * ^g ccgacacAfcaUfhuCfhuaguc*c*(invab)	3588	AD03547-AS	u*Af*agUfhuCfhuCfhuaguc*c*c	3640
AD03548	AD03548-SS	(GL-S-15*) ^g * ^g cagacacAfcaUfhuCfhuaguc*c*(invab)	3589	AD03548-AS	u*Af*aaChUfhuCfhuaguc*c*c	3641
AD03549	AD03549-SS	(GL-S-15*) ^g * ^g accaagAfcaUfhuCfhuaguc*c*(invab)	3590	AD03549-AS	u*Uf*gaAfcaUfhuCfhuaguc*c*c	3642
AD03550	AD03550-SS	(GL-S-15*) ^g * ^g ccaagAfcaUfhuCfhuaguc*c*(invab)	3591	AD03550-AS	u*Cf*ugAfcaUfhuCfhuaguc*c*c	3643
AD03551	AD03551-SS	(GL-S-15*) ^g * ^g aucauGfcaUfhuCfhuaguc*c*(invab)	3592	AD03551-AS	u*Af*uaugGfcaUfhuCfhuaguc*c*c	3644
AD03552	AD03552-SS	(GL-S-15*) ^g * ^g ucugacaAfuAfuCfhuagaac*c*(invab)	3593	AD03552-AS	u*Gf*unumCfcauAfuUfhuCfhuaguc*c*c	3645
AD03553	AD03553-SS	(GL-S-15*) ^g * ^g uugugGfcaUfhuCfhuaguc*c*(invab)	3594	AD03553-AS	u*Af*agauUfagaUfcaUfhuCfhuaguc*c*c	3646
AD03554	AD03554-SS	(GL-S-15*) ^g * ^g auucaUfcaUfhuCfhuaguc*c*(invab)	3595	AD03554-AS	u*Af*acauUfagaGfcaUfhuCfhuaguc*c*c	3647
AD03555	AD03555-SS	(GL-S-15*) ^g * ^g guucaAfcaUfhuCfhuaguc*c*(invab)	3596	AD03555-AS	u*Af*agccAfhuauUfhuCfhuaguc*c*c	3648
AD03556	AD03556-SS	(GL-S-15*) ^g * ^g uuguaaAfcaUfhuCfhuaguc*c*(invab)	3597	AD03556-AS	u*Cf*uaugAfcaUfhuCfhuaguc*c*c	3649
AD03557	AD03557-SS	(GL-S-15*) ^g * ^g aaugacAfcaUfhuCfhuaguc*c*(invab)	3598	AD03557-AS	u*Uf*ugacUfcaagGfcaUfhuCfhuaguc*c*c	3650
AD03558	AD03558-SS	(GL-S-15*) ^g * ^g uaugAfcaUfhuCfhuaguc*c*(invab)	3599	AD03558-AS	u*Af*ugAfuGfcaUfhuCfhuaguc*c*c	3651
AD03559	AD03559-SS	(GL-S-15*) ^g * ^g gaugacGfcaUfhuCfhuaguc*c*(invab)	3600	AD03559-AS	u*Uf*ugaUfgaUfcaUfhuCfhuaguc*c*c	3652
AD03560	AD03560-SS	(GL-S-15*) ^g * ^g ucugaaUfcaUfhuCfhuaguc*c*(invab)	3601	AD03560-AS	u*Cf*guucAfcaUfcaUfhuCfhuaguc*c*c	3653

[illegible]

AD03590	AD03590-SS	(GLS-15*)c*gcugcaAfuUfuAfcagagca*a*(invab)	3631	AD03590-AS	u*Uf*gcUfc(uNA)gnaaAfuUfuGfcag*c*g	3683
AD03591	AD03591-SS	(GLS-15*)g*caagcaUfGChUfUfcaaga*a*(invab)	3632	AD03591-AS	u*Uf*cuUfu(gUNA)naacCfaUfuGfcuu*u*g*c	3684
AD03592	AD03592-SS	(GLS-15*)c*uaucugUfCfuUfuUgugaug*a*(invab)	3633	AD03592-AS	u*Cf*uaucAfiaaafCfaAfcAfgau*a*g	3685
AD03593	AD03593-SS	(GLS-15*)g*cuugucUfuUfuGfaagga*a*(invab)	3634	AD03593-AS	u*Af*uccuAfuaaAfiaAfgaAfica*g*c	3686

Table 3A provides chemically modified HTT RNAi agent antisense strand and sense strand sequences. All sequences shown 5' to 3'. The sequences were used in certain in vivo testing studies described elsewhere herein. A delivery molecule used in the in vivo studies is indicated as “GL-O-η” or “GL-S-η*” at the 3'-end or 5'-end of each sense strand.

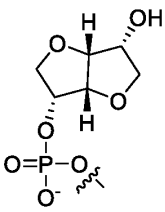
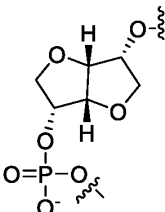
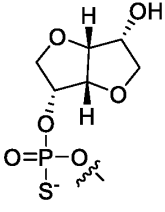
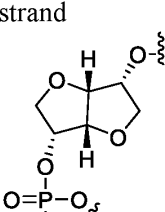
Duplex AD#	Sense strand SS#	Sense Sequence	SEQ ID NO	Antisense strand AS#	Antisense Sequence	SEQ ID NO
AD01241	AD01241-SS	(GLS-15*)(imann*)gcagguucUfGChUfUfuaacug*a*(imann)	3285	AD01241-AS	u*Cf*agguAfiaagCfaGfaAfcu*u*g*c	3321
AD01242	AD01242-SS	(GLS-15*)(imann*)gagguucUfCfuUfuUfuaacug*c*a*(imann)	3286	AD01242-AS	u*Gf*agguUfuaaGfcaAfcAfacu*u*c	3322
AD01243	AD01243-SS	(GLS-15*)(imann*)guucgagucUfCfuUfuaacug*c*a*(imann)	3287	AD01243-AS	u*Af*ggagUfugagGfGaUfcUfcga*a*c	3323
AD01244	AD01244-SS	(GLS-15*)(imann*)gcucucGfCfuUfCfucugcc*a*(imann)	3288	AD01244-AS	u*Gf*gcUfG(uNA)ggaaGfCufUfGfAfga*a*g*c	3324
AD01490	AD01490-SS	(GLS-15*)(imann*)cgaugcgAfCfCfuUfugaag*a*(imann)	3289	AD01490-AS	u*Cf*uuuucUfcagGfCfuGfCfcu*u*g	3325
AD01491	AD01491-SS	(GLS-15*)(imann*)acggccgUfCfAfGfuaucgu*a*(imann)	3290	AD01491-AS	u*Af*ggagAfuaacGfcaGfCfGfcu*u	3326
AD01638	AD01638-SS	(GLS-15*)(imann*)guuaacUfCfuUfugaag*a*(imann)	3291	AD01638-AS	u*Uf*cuucAfcaacGfcaAfcUfuaa*a*c	3327
AD01639	AD01639-SS	(GLS-15*)(imann*)ggacuaaUfGChUfUfuaagga*c*a*(imann)	3292	AD01639-AS	u*Gf*uccuAfiaagCfaUfuAfcu*u*c*c	3328
AD01640	AD01640-SS	(GLS-15*)(imann*)guugggagUfuUfCfuUfuaacua*a*(imann)	3293	AD01640-AS	u*Uf*aggaAfiaagAfafUfCfccc*a*c	3329
AD01641	AD01641-SS	(GLS-15*)(imann*)guucauuAfGfuUfuCfaugauca*a*(imann)	3294	AD01641-AS	u*Uf*gaucAfugaCfuAfafafuga*a*c	3330
AD01642	AD01642-SS	(GLS-15*)(imann*)guagaggaUfCfuUfGfuaacua*a*(imann)	3295	AD01642-AS	u*Uf*agauGfagcaGfaUfCfcau*a*c	3331
AD01643	AD01643-SS	(GLS-15*)(imann*)cugaauAfCfuUfGfugaaua*a*(imann)	3296	AD01643-AS	u*Uf*auucAfcaacGfuAfafGfmu*c*a*g	3332
AD01644	AD01644-SS	(GLS-15*)(imann*)guucgugUfGfuUfuUfuaugaa*a*(imann)	3297	AD01644-AS	u*Uf*uucaUfuaacGfcaAfcgu*a*c	3333
AD01645	AD01645-SS	(GLS-15*)(imann*)guuaggaGfaGfuUfugaag*a*(imann)	3298	AD01645-AS	u*Uf*uucaUfuaacGfcaAfcgu*a*c	3334
AD01646	AD01646-SS	(GLS-15*)(imann*)ggaguuuUfuUfGfCfaugug*a*(imann)	3299	AD01646-AS	u*Cf*acauAfggcaAfafafafcu*u*c*c	3335
AD01647	AD01647-SS	(GLS-15*)(imann*)cagaauAfGfuUfuUfuaugaa*a*(imann)	3300	AD01647-AS	u*Af*auuUfuaacGfuCfaUfuaa*u*g	3336
AD01648	AD01648-SS	(GLS-15*)(imann*)caguguaCfaUfuUfuaagau*a*(imann)	3301	AD01648-AS	u*Af*cuuUfuaaUfGfUfCfcau*u*g	3337
AD01649	AD01649-SS	(GLS-15*)(imann*)cguuacUfuUfuAfccagau*a*(imann)	3302	AD01649-AS	u*Af*uaucGfuaaAfafUfGfUfcau*c*g	3338

AD01650	AD01650-SS	(GL.S-15*)(imann*)jgagugacGfGhUfhucugunuu*a*(imann)	3303	AD01650-AS	u*Af*anacAfraacCfCfUfhUfcaac*u*c	3339
AD01651	AD01651-SS	(GL.S-15*)(imann*)jgacugugUfAfCfUfhUfugugaa*a*(imann)	3304	AD01651-AS	u*Uf*uccaAfraagUfAfAfCfAfCag*u*c	3340
AD01652	AD01652-SS	(GL.S-15*)(imann*)jggcugugUfCfUfhUfhungagug*a*(imann)	3305	AD01652-AS	u*Cr*unucAfraaagGfUfAfAfCfAgc*u*c	3341
AD01653	AD01653-SS	(GL.S-15*)(imann*)jguguguaUfAfUfhUfucuguc*a*(imann)	3306	AD01653-AS	u*Gf*anacAfjgaagUfAfUfhAfCuaa*a*c	3342
AD01654	AD01654-SS	(GL.S-15*)(imann*)jgucuguaUfjGfAfUfCfucuguc*u*a*(imann)	3307	AD01654-AS	u*Af*gacAfjgagCfAfUfAfCfag*u*a*c	3343
AD01655	AD01655-SS	(GL.S-15*)(imann*)jgucugucUfCfUfhCfAgaaguu*a*(imann)	3308	AD01655-AS	u*Af*aaCUfhgagGfAfCfjGfAfjgac*u*c	3344
AD01656	AD01656-SS	(GL.S-15*)(imann*)jggugagucUfAfUfhUfjgugagaa*a*(imann)	3309	AD01656-AS	u*Uf*uccAfCfaaUfAfAfjGfCfuaa*c*c	3345
AD01657	AD01657-SS	(GL.S-15*)(imann*)cunagucUfAfUfhUfhungagaa*a*(imann)	3310	AD01657-AS	u*Af*unucAfCfaaAfUfAfAfGfCuaa*a*g	3346
AD01658	AD01658-SS	(GL.S-15*)(imann*)jgucucuaaCfjGfAfUfhGfjgaaacaa*a*(imann)	3311	AD01658-AS	u*Gf*unnuUfccaCfCfUfhUfAgag*a*c	3347
AD01659	AD01659-SS	(GL.S-15*)(imann*)jgacannuGfjGfCfUfhfancucuu*a*(imann)	3312	AD01659-AS	u*Af*ggagAfhaagCfCfAfAfAfhuag*u*c	3348
AD01660	AD01660-SS	(GL.S-15*)(imann*)jggucacacCfAfUfhfCfcauguaa*a*(imann)	3313	AD01660-AS	u*Af*aaCUfjgcaUfjGfUfjGfUfjgaa*c*c	3349
AD01661	AD01661-SS	(GL.S-15*)(imann*)jguguaucUfGfGfUfAfafacuaa*a*(imann)	3314	AD01661-AS	u*Uf*agugUfhuaCfAfAfAfGfuaa*c*c	3350
AD01662	AD01662-SS	(GL.S-15*)(imann*)jguuugacAfAfAfCfjGcagannu*a*(imann)	3315	AD01662-AS	u*Af*aaugCfAgguUfCfUfjGfUfcaaa*a*c	3351
AD01663	AD01663-SS	(GL.S-15*)(imann*)jgagacucCfCfAfUfhUfhugcuaa*a*(imann)	3316	AD01663-AS	u*Af*haagCfhaaUfCfAfjGfGfuc*u*c	3352
AD01664	AD01664-SS	(GL.S-15*)(imann*)jgucaguuUfCfUfhAfufcuaa*a*(imann)	3317	AD01664-AS	u*Uf*jgagAfuaaGfCfAfAfAfugc*a*c	3353
AD01665	AD01665-SS	(GL.S-15*)(imann*)jgaaaguuUfjGfUfhUfcaucuu*a*(imann)	3318	AD01665-AS	u*Af*gaaUfjgaacCfAfAfAfAfucua*a*c	3354
AD01666	AD01666-SS	(GL.S-15*)(imann*)jgacuguaGfUfCfUfhCfcaaguu*a*(imann)	3319	AD01666-AS	u*Af*cauGfhuagAfCfUfAfCfCfaua*u*g	3355
AD01667	AD01667-SS	(GL.S-15*)(imann*)jgaucacUfCfAfUfhUfagaguuu*a*(imann)	3320	AD01667-AS	u*Uf*aaacCfuaaUfCfAfjGfUfhuga*u*c	3356
AD02260	AD02260-SS	(GL.S-15*)(imab*)jggacacUfCfUfjGfGfhgaauaa*a*(imab)	3357	AD02260-AS	u*Uf*aaacCfaccCfjGfUfAfAfjguu*c*c	3374
AD02261	AD02261-SS	(GL.S-15*)(imab*)jgucuaCfjGfUfjGfAfhuuaagaa*a*(imab)	3358	AD02261-AS	u*Uf*cauuAfuaaCfCfAfCfGfuaa*a*c	3375
AD02262	AD02262-SS	(GL.S-15*)(imab*)jcgugagUfAfAfUfhCfAaauuaa*a*(imab)	3359	AD02262-AS	u*Af*haaUfhcauUfAfAfUfhCfCfacc*a*g	3376
AD02263	AD02263-SS	(GL.S-15*)(imab*)jgaauuaaCfjGfAfAfCfjguguaa*a*(imab)	3360	AD02263-AS	u*Af*uccaCfucuuCfCfUfAfAfuaa*u*c	3377
AD02264	AD02264-SS	(GL.S-15*)(imab*)jgaauagaaAfjGfAfUfhugaagaa*a*(imab)	3361	AD02264-AS	u*Uf*cauCfcaucCfUfhUfCfCfuaa*h*c	3378
AD02265	AD02265-SS	(GL.S-15*)(imab*)jgaggaagGfUfjGfAfhuugaagaa*a*(imab)	3362	AD02265-AS	u*Af*cuuAfuaaAfCfUfCfUfhucc*u*c	3379
AD02266	AD02266-SS	(GL.S-15*)(imab*)jcgaaagagUfjGfAfUfhjgaaguuu*a*(imab)	3363	AD02266-AS	u*Af*aaCUfcauUfCfAfCfUfcauu*c*g	3380
AD02267	AD02267-SS	(GL.S-15*)(imab*)jgugaagaaAfjGfUfhUfhungcuaa*a*(imab)	3364	AD02267-AS	u*Af*ggcaAfhaaCfUfhUfAfuaa*a*c	3381
AD02268	AD02268-SS	(GL.S-15*)(imab*)jgaagagUfCfUfjGfUfhungcuaa*a*(imab)	3365	AD02268-AS	u*Gf*aaagAfraaCfAfAfCfCfcau*h*c	3382
AD02269	AD02269-SS	(GL.S-15*)(imab*)jgucugacAfCfCfUfhUfhugacuu*a*(imab)	3366	AD02269-AS	u*Af*agaaAfcaagCfUfhGfUfhCfAgc*a*c	3383
AD02270	AD02270-SS	(GL.S-15*)(imab*)jgugucugCfUfhUfhCfAgaaguuu*a*(imab)	3367	AD02270-AS	u*Uf*aaCUfhugAfjGfAfCfGfagaa*c*c	3384

AD02271	AD02271-SS	(GL.S.-1.5*) ^f cgagcagcaGfhuUfragcuuan* ^{a*} (invab)	3368	AD02271-AAS	u*Af*naagCfhaacAfcUfgCfhuc*c*g	3385
AD02272	AD02272-SS	(GL.S.-1.5*) ^f vcagagcagUfgUfruAfgcuuanu* ^{a*} (invab)	3369	AD02272-AAS	u*Af*anaaGfcuaaCfcaCfhuGfcuc*u*g	3386
AD02273	AD02273-SS	(GL.S.-1.5*) ^f gagcuuanUfnCfhuUfgagaaua* ^{a*} (invab)	3370	AD02273-AAS	u*Uf*nanuCfcaacAfiaAfuAfage*c*u*c	3387
AD02274	AD02274-SS	(GL.S.-1.5*) ^f (invab)*gutaacaAfhuUfuGfgcucuanc* ^{a*} (invab)	3371	AD02274-AAS	u*Gf*anaaGficcaaAfuUfgUfnuu* ^{a*} c	3388
AD02275	AD02275-SS	(GL.S.-1.5*) ^f (invab)*guunguafhuCfhuUfracaana* ^{a*} (invab)	3372	AD02275-AAS	u*Uf*annuUfgagAfhuAfiaGfcan* ^{a*} c	3389
AD02276	AD02276-SS	(GL.S.-1.5*) ^f (invab)*guugcuuaUfgUfruCfcaaanu* ^{a*} (invab)	3373	AD02276-AAS	u*Af*nanuUfrigaGfiaUfaAfica* ^{a*} c	3390
AD03501	AD03501-SS	(GL.S.-1.5*) ^f *ccaunucaUfnUfcafCfhuucauga* ^{a*} (invab)	3687	AD03501-AAS	u*Uf*caUfgaUNAJacuafafaUfgAfianu* ^{a*} c	3728
AD03502	AD03502-SS	(GL.S.-1.5*) ^f *uggugauUfaAfuCfhaanua* ^{a*} (invab)	3688	AD03502-AAS	u*Af*nanuUfnucaUfaAfafuCracc*a*g	3729
AD03503	AD03503-SS	(GL.S.-1.5*) ^f *taucunaAfuaFuUfragaaga* ^{a*} (invab)	3689	AD03503-AAS	u*Uf*cnucCfhaanAfhuUfruAfaga* ^{a*} u*c	3730
AD03504	AD03504-SS	(GL.S.-1.5*) ^f *ggagagagUfnGfiauUfgaguu* ^{a*} (invab)	3690	AD03504-AAS	u*Af*ncuucCfhaacAfiaCfhuCfinc*c*c	3731
AD03505	AD03505-SS	(GL.S.-1.5*) ^f *gnacanuUfnAfCcFaguauuc* ^{a*} (invab)	3691	AD03505-AAS	u*Gf*anaaCfugyuAfiaAfiaUfgua*c*c	3732
AD03506	AD03506-SS	(GL.S.-1.5*) ^f *uacanuUfCaCfAfeganucc* ^{a*} (invab)	3692	AD03506-AAS	u*Gf*gaauAfccuguUfaAfiaAfuhgu* ^{a*} g	3733
AD03507	AD03507-SS	(GL.S.-1.5*) ^f *nuceagauUfgUfgCfagauga* ^{a*} (invab)	3693	AD03507-AAS	u*Uf*ucaUfgagcaCfiaUficUfgag* ^{a*} c	3734
AD03508	AD03508-SS	(GL.S.-1.5*) ^f *cceagugafafCfgrCfhuucugu* ^{a*} (invab)	3694	AD03508-AAS	u*Af*cegaAfaccUfnUfcaFcug*f*g	3735
AD03509	AD03509-SS	(GL.S.-1.5*) ^f *gcagugaaafgCfgrUfnucugu* ^{a*} (invab)	3695	AD03509-AAS	u*Af*ncagAfiaaccCfhuUfnCfiacu* ^{a*} c	3736
AD03510	AD03510-SS	(GL.S.-1.5*) ^f *ugaaaggCfhuUfnCfhuugugc* ^{a*} (invab)	3696	AD03510-AAS	u*Gf*caaaCfagaafAcCfclUfnuc* ^{a*} g	3737
AD03511	AD03511-SS	(GL.S.-1.5*) ^f *uucanuGfhuGfcaCfagcugu* ^{a*} (invab)	3697	AD03511-AAS	u*Af*ceagCfugueAfccAfCfAfahga* ^{a*} c	3738
AD03512	AD03512-SS	(GL.S.-1.5*) ^f *nucanuGfUfgAfCcAfgcuuguu* ^{a*} (invab)	3698	AD03512-AAS	u*Af*caaaCfugucCfagfCfAfang* ^{a*} c	3739
AD03513	AD03513-SS	(GL.S.-1.5*) ^f *ccauygcCfcaCfCfcugugua* ^{a*} (invab)	3699	AD03513-AAS	u*Uf*ancaAfccugUfcaAfCfciacu* ^{a*} g*c	3740
AD03514	AD03514-SS	(GL.S.-1.5*) ^f *caacgmGfhuUfcaCfhuuuggc* ^{a*} (invab)	3700	AD03514-AAS	u*CF*caaaAfaguaAfCcAfiaGfgeu* ^{a*} u*g	3741
AD03515	AD03515-SS	(GL.S.-1.5*) ^f *gunaacUfnUfgGfagaagag* ^{a*} (invab)	3701	AD03515-AAS	u*CF*nagcUfnaccaAfiaAfagfinaa*c*c	3742
AD03516	AD03516-SS	(GL.S.-1.5*) ^f *ngcagcuUfgGfuaAfaaganu* ^{a*} (invab)	3702	AD03516-AAS	u*Af*naUfnUcUNA)nuaccFiaAfaiUfgcc* ^{a*} c	3743
AD03517	AD03517-SS	(GL.S.-1.5*) ^f *gaauuagafafafuGfianucgga* ^{a*} (invab)	3703	AD03517-AAS	u*Uf*ccgaAfucanUfnUfcaUfranu* ^{a*} u*c	3744
AD03518	AD03518-SS	(GL.S.-1.5*) ^f *ccgagagCfcaGfhuCfhuagcuu* ^{a*} (invab)	3704	AD03518-AAS	u*Af*agCfuaUNA)baacdUfgCfhuCfucc* ^{a*} g*c	3745
AD03519	AD03519-SS	(GL.S.-1.5*) ^f *gcaagcuUfcaGfclUfhaauugu* ^{a*} (invab)	3705	AD03519-AAS	u*Af*caadUfagcdUfaAfcaFcug*c*c	3746
AD03520	AD03520-SS	(GL.S.-1.5*) ^f *gugnuagCfhuUfaUfnuguyg* ^{a*} (invab)	3706	AD03520-AAS	u*CF*caacAfiaanaAfccCfuaAfaca*c*c	3747
AD03521	AD03521-SS	(GL.S.-1.5*) ^f *agcuauUfnGfhuUfggaanaa* ^{a*} (invab)	3707	AD03521-AAS	u*Uf*nanuCfcaacAfiaAfuAfage*c*u*c	3748
AD03522	AD03522-SS	(GL.S.-1.5*) ^f *guugagUfaAfafafumugag* ^{a*} (invab)	3708	AD03522-AAS	u*Uf*ccnaAfamuuUfaUfnCfcaac*c*c	3749
AD03523	AD03523-SS	(GL.S.-1.5*) ^f *uggaanaAfafafuUfragaau* ^{a*} (invab)	3709	AD03523-AAS	u*Af*nuccUfraauUfnUfaUfnucc* ^{a*} c	3750

AD03524	AD03524-SS	(GL-S-15%) _g [*] uuannucAfaAfcGfaungcaaa [*] _a (invab)	3710	AD03524-AS	u [*] U [†] puccAfhuccuUfhuAfcGfaanaa [*] _a c	3751
AD03525	AD03525-SS	(GL-S-15%) _g [*] ggauagcaAfaAfcCfuumung [*] _a (invab)	3711	AD03525-AS	u [*] C [†] caaaAfaagutUfhuUfcCfauc [*] _c c	3752
AD03526	AD03526-SS	(GL-S-15%) _g [*] gggaanaAfcUfhuUfhungcaaa [*] _a (invab)	3712	AD03526-AS	u [*] U [†] auccAfaanaCfhuUfhuUfucc [*] _a c	3753
AD03527	AD03527-SS	(GL-S-15%) _g [*] uuugcauAfuUfhuGfeggaana [*] _a (invab)	3713	AD03527-AS	u [*] A [†] muueUfccaAfuAfuCfcaaa [*] _a c	3754
AD03528	AD03528-SS	(GL-S-15%) _g [*] uuuaaaCfaAfuUfhugcuma [*] _a (invab)	3714	AD03528-AS	u [*] U [†] aaqcCfaauUfjUfhuUfnaa [*] _a c	3755
AD03529	AD03529-SS	(GL-S-15%) _g [*] uuuaaacAfaUfhuUfjgucuaa [*] _a (invab)	3715	AD03529-AS	u [*] A [†] uaagCfcaauUfhuCfuUfnaa [*] _a c	3756
AD03530	AD03530-SS	(GL-S-15%) _g [*] ugucguauUfhuCfhaCfaagaccu [*] _a (invab)	3716	AD03530-AS	u [*] A [†] gguncCfugucAfaAfuCfagcc [*] _a c	3757
AD03531	AD03531-SS	(GL-S-15%) _g [*] annugacAfaAfcCfugcauu [*] _a (invab)	3717	AD03531-AS	u [*] A [†] anGfc(aUNA)aggunCfhuCfnaa [*] _u g	3758
AD03532	AD03532-SS	(GL-S-15%) _g [*] ugacagcaAfcCfhuGfcaunugc [*] _a (invab)	3718	AD03532-AS	u [*] G [†] caauUfjgaagCfhuUfjguc [*] _c c	3759
AD03533	AD03533-SS	(GL-S-15%) _g [*] ggucgcauAfcUfjGfcaunugcu [*] _a (invab)	3719	AD03533-AS	u [*] A [†] ggCAfa(aUNA)ugcaCfjgUfhuCfugc [*] _c c	3760
AD03534	AD03534-SS	(GL-S-15%) _g [*] ccagaaCfUfjGfCfaUfhugcuaa [*] _a (invab)	3720	AD03534-AS	u [*] U [†] aaGfc(aUNA)aaugCfaGfjUfhuCf [*] _g c	3761
AD03535	AD03535-SS	(GL-S-15%) _g [*] aaacucgAfhuUfhGfcaunauc [*] _a (invab)	3721	AD03535-AS	u [*] A [†] gaf(aUNA)gcaaaufuGfcafcguc [*] _u g	3762
AD03536	AD03536-SS	(GL-S-15%) _g [*] aaacucgcaUfhuUfjGfCfuaucuu [*] _a (invab)	3722	AD03536-AS	u [*] A [†] ggAfu(aUNA)agcaAfaUfjGfCfagc [*] _u c	3763
AD03537	AD03537-SS	(GL-S-15%) _g [*] ccugcauUfhGfCfUfhauccuc [*] _a (invab)	3723	AD03537-AS	u [*] G [†] aaGfa(aUNA)aaagcaAfaAfuCfagc [*] _g c	3764
AD03538	AD03538-SS	(GL-S-15%) _g [*] ccugcauuUfjGfCfhuUfauccuca [*] _a (invab)	3724	AD03538-AS	u [*] U [†] gaaGfa(aUNA)uaagCfaAfaUfjgca [*] _g c	3765
AD03539	AD03539-SS	(GL-S-15%) _g [*] ggcaunugCfhuUfUfcaucaaa [*] _a (invab)	3725	AD03539-AS	u [*] U [†] uuugaAfgaanaAfgCfaAfaagc [*] _c c	3766
AD03540	AD03540-SS	(GL-S-15%) _g [*] uuugcauuUfjUfhuCfhaaanaa [*] _a (invab)	3726	AD03540-AS	u [*] A [†] tuauUfhugaaGfaUfUfaAfgca [*] _a c	3767
AD03541	AD03541-SS	(GL-S-15%) _g [*] ggcauuuCfhuUfUfaaanaug [*] _a (invab)	3727	AD03541-AS	u [*] C [†] aanuAfu(aUNA)uuugaAfgAfuAfaagc [*] _a c	3768

Table 4: Abbreviations of nucleotide monomers used in nucleic acid sequence representation. It will be understood that these monomers, when present in an oligonucleotide, are mutually linked by 5'-3'-phosphodiester bonds, and it is understood that when the nucleotide contains a 2'-fluoro modification, then the fluoro replaces the hydroxy at that position of the parent nucleotide (i.e., it is a 2'-deoxy-2'- fluoronucleotide). It will also be understood that the abbreviations correspond to nucleotides which omit the 3'-phosphate when found at the 3'-terminal position (i.e., they are 3'-OH). A skilled artisan will understand that these abbreviations are just identification symbols and are able to determine the linking modes of the nucleotide sequences containing these abbreviations.	
Abbreviations	Nucleotide(s)
A	adenosine-3'-phosphate
C	cytidine-3'-phosphate
G	guanosine-3'-phosphate
T	5-methyluridine-3'-phosphate
U	uridine-3'-phosphate
a	2'-O-methyladenosine-3'-phosphate
c	2'-O-methylcytidine-3'-phosphate
g	2'-O-methylguanosine-3'-phosphate
t	2'-O-methyl-5-methyluridine-3'-phosphate
u	2'-O-methyluridine-3'-phosphate
Af	2'-fluoroadenosine-3'-phosphate
Cf	2'-fluorocytidine-3'-phosphate
Gf	2'-fluoroguanosine-3'-phosphate
Tf	2'-fluoro-5-methyluridine-3'-phosphate
Uf	2'-fluorouridine-3'-phosphate
Af*	2'-fluoroadenosine-3'-phosphorothioate
Cf*	2'-fluorocytidine-3'-phosphorothioate
Gf*	2'-fluoroguanosine-3'-phosphorothioate
Tf*	2'-fluoro-5-methyluridine-3'-phosphorothioate
Uf*	2'-fluorouridine-3'-phosphorothioate
a*	2'-O-methyladenosine-3'-phosphorothioate
c*	2'-O-methylcytidine-3'-phosphorothioate
g*	2'-O-methylguanosine-3'-phosphorothioate
t*	2'-O-methyl-5-methyluridine-3'-phosphorothioate
u*	2'-O-methyluridine-3'-phosphorothioate
aUNA	2', 3'-seco-adenosine-3'-phosphate
cUNA	2', 3'-seco-cytidine-3'-phosphate
gUNA	2', 3'-seco-guanosine-3'-phosphate
tUNA	2', 3'-seco-5-methyluridine-3'-phosphate
uUNA	2', 3'-seco- uridine-3'-phosphate
Ahd	2'-O-hexadecyl-adenosine-3'-phosphate

Uhd	2'-O-hexadecyl-uridine-3'-phosphate	
Chd	2'-O-hexadecyl-cytidine-3'-phosphate	
Ghd	2'-O-hexadecyl-guanosine-3'-phosphate	
Tgn	Thymidine-glycol nucleic acid(GNA) S-Isomer	
dT	2'-deoxythymidine-3'-phosphate	
Vp	Vinyl-phosphate	
invab	inverted abasic-5'-phosphate. linked to adjacent nucleotide via a substituent at its 3' position (a 3'-3' linkage) when on the 3' end of a strand; linked to adjacent nucleotide via a substituent at its 5' position (a 5'-5' internucleotide linkage) when on the 5' end of a strand, It will also be understood that the abbreviations correspond to invab which omit the 5'-phosphate when found at the 3'-terminal position (i.e., they are 5'-OH)	
invab*	inverted abasic-5'-phosphorothioate. linked to adjacent nucleotide via a substituent at its 3' position (a 3'-3' linkage) when on the 3' end of a strand linked to adjacent nucleotide via a substituent at its 5' position (a 5'-5' internucleotide linkage) when on the 5' end of a strand, It will also be understood that the abbreviations correspond to invab* which omit the 5'-phosphorothioate when found at the 3'-terminal position (i.e., they are 5'-OH);	
imann	imann when at the end of each strand	imann when in the middle of each strand
		
imann*	isomannide residue- phosphorothioate	
	imann* when at the end of each strand	imann* when in the middle of each strand
		

In certain embodiments of the invention a dsRNA (also referred to herein as a “duplex”) is one disclosed in one of Tables 1-3, Tables 1A-3A. Each row in Tables 1-3, Tables 1A-3A discloses a duplex comprising the sequence of the sense strand and the sequence of the antisense strand in that table row. In addition to the duplexes disclosed in Tables 1-3, Tables 1A-3A, it will be understood that in some embodiments, a duplex of the invention may include sense and antisense sequences shown in Tables 1-3, Tables 1A-3A, that differ by zero, one, two, or three nucleotides shown in a sequence shown in Tables 1-3, Tables 1A-3A. Thus, as non-limiting examples, in some embodiments, an antisense strand in a duplex of the invention may be SEQ

ID NO: 3326, 3327, 3350, 3355, or 3356, with zero, one, two, or three different nucleotides than those in SEQ ID: 3326, 3327, 3350, 3355, or 3356.

It will be understood that the sequence of the sense strand and the sequence of the antisense strand in a duplex of the invention may be independently selected. Thus, a dsRNA of the invention may comprise a sense strand and an antisense strand of a duplex disclosed in a row in Tables 1-3 and Tables 1A-3A. Alternatively, in a dsRNA of the invention, one or both of the selected sense and antisense strand in the dsRNA may include sequences shown in Tables 1-3 and Tables 1A-3A, but with one or both of the sense and antisense sequences including 1, 2, 3, or more nucleobase substitutions from the parent sequence. The selected sequences may in some embodiments be longer or shorter than their parent sequence. Thus, dsRNA agents included in the invention can but need not include exact sequences of the sense and antisense pairs disclosed as duplexes in Tables 1-3 and Tables 1A-3A.

In some embodiments, a dsRNA agent comprises a sense strand and an antisense strand, nucleotide positions 2 to 18 in the antisense strand comprising a region of complementarity to a HTT RNA transcript, wherein the region of complementarity comprises at least 15 contiguous nucleotides that differ by 0, 1, 2, or 3 nucleotides from one of the antisense sequences listed in one of Tables 1-3, Tables 1A-3A, and optionally comprising a targeting ligand. In some instances, the region of complementarity to the HTT RNA transcript comprises at least 15, 16, 17, 18, or 19 contiguous nucleotides that differ by no more than 3 nucleotides from one of the antisense sequences listed in one of Tables 1-3, Tables 1A-3A. In some embodiments of a dsRNA agent of the invention, the antisense strand of the dsRNA is at least substantially complementary to any one of a target region of SEQ ID NO: 1 and is provided in any one of Tables 1-3. In some embodiments of a dsRNA agent of the invention, the antisense strand of the dsRNA is at least substantially complementary to any one of a target region of SEQ ID NO: 7 and is provided in any one of Tables 1A-3A. In some embodiments, an antisense strand of a dsRNA agent of the invention is fully complementary to any one of a target region of SEQ ID NO: 1 and is provided in any one of Tables 1-3. In some embodiments, an antisense strand of a dsRNA agent of the invention is fully complementary to any one of a target region of SEQ ID NO: 7 and is provided in any one of Tables 1A-3A. In some embodiments a dsRNA agent includes a sense strand sequence set forth in any one of Tables 1-3, and the sense strand sequence is at least substantially complementary to the antisense strand sequence in the dsRNA agent. In other embodiments, a dsRNA agent of the invention comprises a sense strand sequence set forth in any one of Tables 1-3, and the sense strand sequence is fully complementary to the antisense strand sequence in the dsRNA agent. In some embodiments a dsRNA agent includes a sense strand sequence set forth in any one of Tables 1A-3A, and the sense strand sequence is at least substantially complementary to the antisense strand sequence in the dsRNA agent. In other embodiments, a dsRNA agent of the invention comprises a sense strand sequence set forth in any one of Tables 1A-3A, and the sense strand sequence is fully complementary to the antisense strand sequence in the dsRNA agent. In some instances, a dsRNA agent of the invention comprises an antisense

strand sequence set forth in any one of Tables 1-3, Tables 1A-3A. Some embodiments of a dsRNA agent of the invention comprises the sense and antisense sequences disclosed as duplex in any of Tables 1-3, Tables 1A-3A. As described herein, it will be understood that the sense and antisense strands in a duplex of the invention may be independently selected.

5

Mismatches

It is known to skilled in art, mismatches are tolerated for efficacy in dsRNA, especially the mismatches are within terminal region of dsRNA. Certain mismatches tolerate better, for example mismatches with wobble base pairs G:U and A:C are tolerated better for efficacy (Du et al., A systematic analysis of the silencing effects of an active siRNA at all single-nucleotide mismatched target sites. *Nucleic Acids Res.* 2005 Mar 21;33(5):1671-7. Doi: 10.1093/nar/gki312. *Nucleic Acids Res.* 2005;33(11):3698). Some embodiments of methods and compounds of the invention a HTT dsRNA agent may contain one or more mismatches to the HTT target sequence. In some embodiments, HTT dsRNA agent of the invention includes no mismatches. In certain embodiments, HTT dsRNA agent of the invention includes no more than 1 mismatch. In some embodiments, HTT dsRNA agent of the invention includes no more than 2 mismatches. In certain embodiments, HTT dsRNA agent of the invention includes no more than 3 mismatches. In some embodiments of the invention, an antisense strand of a HTT dsRNA agent contains mismatches to a HTT target sequence that are not located in the center of the region of complementarity. In some embodiments, the antisense strand of the HTT dsRNA agent includes 1, 2, 3, 4, or more mismatches that are within the last 5, 4, 3, 2, or 1 nucleotide from one or both of the 5' or 3' end of the region of complementarity. Methods described herein and/or methods known in the art can be used to determine whether a HTT dsRNA agent containing a mismatch to a HTT target sequence is effective in inhibiting the expression of the HTT gene.

25

Complementarity

As used herein, unless otherwise indicated, the term “complementary,” when used to describe a first nucleotide sequence (e.g., HTT dsRNA agent sense strand or targeted HTT mRNA) in relation to a second nucleotide sequence (e.g., HTT dsRNA agent antisense strand or a single-stranded antisense polynucleotide), means the ability of an oligonucleotide or polynucleotide including the first nucleotide sequence to hybridize [form base pair hydrogen bonds under mammalian physiological conditions (or similar conditions *in vitro*)] and form a duplex or double helical structure under certain conditions with an oligonucleotide or polynucleotide including the second nucleotide sequence. Other conditions, such as physiologically relevant conditions as can be encountered inside an organism, can apply. A skilled artisan will be able to determine the set of conditions most appropriate for a test of complementarity of two sequences in accordance with the ultimate application of the hybridized nucleotides. Complementary sequences include Watson-Crick base pairs or non-Watson-Crick

35

base pairs and include natural or modified nucleotides or nucleotide mimics, at least to the extent that the above hybridization requirements are fulfilled. Sequence identity or complementarity is independent of modification.

Complementary sequences, for example, within a HTT dsRNA as described herein, include base-pairing of the oligonucleotide or polynucleotide comprising a first nucleotide sequence to an oligonucleotide or polynucleotide comprising a second nucleotide sequence over the entire length of one or both nucleotide sequences. Such sequences can be referred to as “fully complementary” with respect to each other herein. It will be understood that in embodiments when two oligonucleotides are designed to form, upon hybridization, one or more single stranded overhangs, such overhangs are not regarded herein as mismatches with regard to the determination of complementarity. For example, a HTT dsRNA agent comprising one oligonucleotide 19 nucleotides in length and another oligonucleotide 20 nucleotides in length, wherein the longer oligonucleotide comprises a sequence of 19 nucleotides that is fully complementary to the shorter oligonucleotide, can yet be referred to as “fully complementary” for the purposes described herein. Thus, as used herein, “fully complementary” means that all (100%) of the bases in a contiguous sequence of a first polynucleotide will hybridize with the same number of bases in a contiguous sequence of a second polynucleotide. The contiguous sequence may comprise all or a part of a first or second nucleotide sequence.

The term “substantially complementary” as used herein means that in a hybridized pair of nucleobase sequences, at least about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, but not all, of the bases in a contiguous sequence of a first polynucleotide will hybridize with the same number of bases in a contiguous sequence of a second polynucleotide. The term “substantially complementary” can be used in reference to a first sequence with respect to a second sequence if the two sequences include one or more, for example at least 1, 2, 3, 4, or 5 mismatched base pairs upon hybridization for a duplex up to 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 base pairs (bp), while retaining the ability to hybridize under the conditions most relevant to their ultimate application, e.g., inhibition of HTT gene expression via a RISC pathway.

The term, “partially complementary” may be used herein in reference to a hybridized pair of nucleobase sequences, in which at least 75%, but not all, of the bases in a contiguous sequence of a first polynucleotide will hybridize with the same number of bases in a contiguous sequence of a second polynucleotide. In some embodiments, “partially complementary” means at least 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of the bases in a contiguous sequence of a first polynucleotide will hybridize with the same number of bases in a contiguous sequence of a second polynucleotide.

The terms “complementary,” “fully complementary,” “substantially complementary,” and “partially complementary” are used herein in reference to the base matching between the sense strand and the antisense strand of a HTT dsRNA agent, between the antisense strand of a

HTT dsRNA agent and a sequence of a target HTT mRNA, or between a single-stranded antisense oligonucleotide and a sequence of a target HTT mRNA. It will be understood that the term “antisense strand of a HTT dsRNA agent” may refer to the same sequence of an “HTT antisense polynucleotide agent”.

5 As used herein, the term “substantially identical” or “substantial identity” used in reference to a nucleic acid sequence means a nucleic acid sequence comprising a sequence with at least about 85% sequence identity or more, preferably at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, compared to a reference sequence. Percentage of sequence identity is determined by comparing
10 two optimally aligned sequences over a comparison window. The percentage is calculated by determining the number of positions at which the identical nucleic acid base occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison and multiplying the result by 100 to yield the percentage of sequence identity. The inventions disclosed herein encompasses
15 nucleotide sequences substantially identical to those disclosed herein. e.g., in Tables 1-3, Tables 1A-3A. In some embodiments, the sequences disclosed herein are exactly identical, or at least about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% percent identical to those disclosed herein, e.g., in Tables 1-3, Tables 1A-3A.

As used herein, the term “strand comprising a sequence” means an oligonucleotide
20 comprising a chain of nucleotides that is described by the sequence referred to using the standard nucleotide nomenclature. The term “double-stranded RNA” or “dsRNA,” as used herein, refers to an RNAi that includes an RNA molecule or complex of molecules having a hybridized duplex region comprising two anti-parallel and substantially or fully complementary nucleic acid strands, which are referred to as having “sense” and “antisense” orientations with respect to a
25 target HTT RNA. The duplex region can be of any length that permits specific degradation of a desired target HTT RNA through a RISC pathway but will typically range from 9 to 30 base pairs in length, e.g., 15-30 base pairs in length. Considering a duplex between 9 and 30 base pairs, the duplex can be any length in this range, for example, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30, and any sub-range therein between, including,
30 but not limited to 15-30 base pairs, 15-26 base pairs, 15-23 base pairs, 15-22 base pairs, 15-21 base pairs, 15-20 base pairs, 15-19 base pairs, 15-18 base pairs, 15-17 base pairs, 18-30 base pairs, 18-26 base pairs, 18-23 base pairs, 18-22 base pairs, 18-21 base pairs, 18-20 base pairs, 19-30 base pairs, 19-26 base pairs, 19-23 base pairs, 19-22 base pairs, 19-21 base pairs, 19-20 base pairs, 20-30 base pairs, 20-26 base pairs, 20-25 base pairs, 20-24 base pairs, 20-23 base
35 pairs, 20-22 base pairs, 20-21 base pairs, 21-30 base pairs, 21-26 base pairs, 21-25 base pairs, 21-24 base pairs, 21-23 base pairs, or 21-22 base pairs. HTT dsRNA agents generated in the cell by processing with Dicer and similar enzymes are generally in the range of 19-22 base pairs in length. One strand of the duplex region of a HTT dsDNA agent comprises a sequence that is substantially complementary to a region of a target HTT RNA. The two strands forming the

duplex structure can be from a single RNA molecule having at least one self-complementary region, or can be formed from two or more separate RNA molecules. Where the duplex region is formed from two strands of a single molecule, the molecule can have a duplex region separated by a single stranded chain of nucleotides (herein referred to as a “hairpin loop”) between the 3'-end of one strand and the 5'-end of the respective other strand forming the duplex structure. In some embodiments of the invention, a hairpin look comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more unpaired nucleotides. Where the two substantially complementary strands of a HTT dsRNA agent are comprised by separate RNA molecules, those molecules need not, but can be covalently connected. Where the two strands are connected covalently by means other than a hairpin loop, the connecting structure is referred to as a “linker.” The term “siRNA” is also used herein to refer to a dsRNA agent as described herein.

In some embodiments of the invention a HTT dsRNA agent may include a sense and antisense sequence that have no-unpaired nucleotides or nucleotide analogs at one or both terminal ends of the dsRNA agent. An end with no unpaired nucleotides is referred to as a “blunt end” and as having no nucleotide overhang. If both ends of a dsRNA agent are blunt, the dsRNA is referred to as “blunt ended.” In some embodiments of the invention, a first end of a dsRNA agent is blunt, in some embodiments a second end of a dsRNA agent is blunt, and in certain embodiments of the invention, both ends of a HTT dsRNA agent are blunt.

In some embodiments of dsRNA agents of the invention, the dsRNA does not have one or two blunt ends. In such instances there is at least one unpaired nucleotide at the end of a strand of a dsRNA agent. For example, when a 3'-end of one strand of a dsRNA extends beyond the 5'-end of the other strand, or vice versa, there is a nucleotide overhang. A dsRNA can comprise an overhang of at least 1, 2, 3, 4, 5, 6, or more nucleotides. A nucleotide overhang can comprise or consist of a nucleotide/nucleoside analog, including a deoxynucleotide/nucleoside. It will be understood that in some embodiments a nucleotide overhang is on a sense strand of a dsRNA agent, on an antisense strand of a dsRNA agent, or on both ends of a dsRNA agent and nucleotide(s) of an overhang can be present on the 5' end, 3' end or both ends of either an antisense or sense strand of a dsRNA. In certain embodiments of the invention, one or more of the nucleotides in an overhang is replaced with a nucleoside thiophosphate.

As used herein, the term “antisense strand” or “guide strand” refers to the strand of a HTT dsRNA agent that includes a region that is substantially complementary to a HTT target sequence. As used herein the term “sense strand,” or “passenger strand” refers to the strand of a HTT dsRNA agent that includes a region that is substantially complementary to a region of the antisense strand of the HTT dsRNA agent.

Modifications

In some embodiments of the invention the RNA of a HTT RNAi agent is chemically modified to enhance stability and/or one or more other beneficial characteristics. Nucleic acids

in certain embodiments of the invention may be synthesized and/or modified by methods well established in the art, for example, those described in "Current protocols in Nucleic Acid Chemistry," Beaucage, S. L. et al. (Eds.), John Wiley & Sons, Inc., New York, N.Y., USA, which is incorporated herein by reference. Modifications that can be present in certain

5 embodiments of HTT dsRNA agents of the invention include, for example, (a) end modifications, e.g., 5' end modifications (phosphorylation, conjugation, inverted linkages, etc.) 3' end modifications (conjugation, DNA nucleotides, inverted linkages, etc.), (b) base modifications, e.g., replacement with stabilizing bases, destabilizing bases, or bases that base pair with an expanded repertoire of partners, removal of bases (abasic nucleotides), or conjugated bases, (c)

10 sugar modifications (e.g., at the 2' position or 4' position) or replacement of the sugar, as well as (d) backbone modifications, including modification or replacement of the phosphodiester linkages. Specific examples of RNA compounds useful in certain embodiments of HTT dsRNA agents, HTT antisense polynucleotides, and HTT sense polynucleotides of the invention include, but are not limited to RNAs comprising modified backbones or no natural internucleoside

15 linkages. As a non-limiting example, an RNA having a modified backbone may not have a phosphorus atom in the backbone. RNAs that do not have a phosphorus atom in their internucleoside backbone may be referred to as oligonucleosides. In certain embodiments of the invention, a modified RNA has a phosphorus atom in its internucleoside backbone.

It will be understood that the term "RNA molecule" or "RNA" or "ribonucleic acid

20 molecule" encompasses not only RNA molecules as expressed or found in nature, but also analogs and derivatives of RNA comprising one or more ribonucleotide/ribonucleoside analogs or derivatives as described herein or as known in the art. The terms "ribonucleoside" and "ribonucleotide" may be used interchangeably herein. An RNA molecule can be modified in the nucleobase structure or in the ribose-phosphate backbone structure, e.g., as described herein

25 below, and molecules comprising ribonucleoside analogs or derivatives must retain the ability to form a duplex. As non-limiting examples, an RNA molecule can also include at least one modified ribonucleoside including but not limited to a 2'-O-methyl modified nucleoside, a nucleoside comprising a 5' phosphorothioate group, a terminal nucleoside linked to a cholesteryl derivative or dodecanoic acid bisdecylamide group, a locked nucleoside, an abasic nucleoside, a

30 2'-deoxy-2'-fluoro modified nucleoside, a 2'-amino-modified nucleoside, 2'-alkyl-modified nucleoside, morpholino nucleoside, a phosphoramidate or a non-natural base comprising nucleoside, or any combination thereof. In some embodiments of the invention, an RNA molecule comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or up to the full length of the HTT dsRNA agent molecule's ribonucleosides that are modified

35 ribonucleosides. The modifications need not be the same for each of such a plurality of modified ribonucleosides in an RNA molecule.

DsRNA agents, HTT antisense polynucleotides, and/or HTT sense polynucleotides of the invention may, in some embodiments comprise one or more independently selected modified nucleotide and/or one or more independently selected non-phosphodiester linkage. As used

herein the term “independently selected” used in reference to a selected element, such as a modified nucleotide, non-phosphodiester linkage, etc., means that two or more selected elements can but need not be the same as each other.

As used herein, a “nucleotide base,” “nucleotide,” or “nucleobase” is a heterocyclic pyrimidine or purine compound, which is a standard constituent of all nucleic acids, and includes the bases that form the nucleotides adenine, guanine, cytosine, thymine, and uracil. A nucleobase may further be modified to include, though not intended to be limiting: universal bases, hydrophobic bases, promiscuous bases, size-expanded bases, and fluorinated bases. The term “ribonucleotide” or “nucleotide” may be used herein to refer to an unmodified nucleotide, a modified nucleotide, or a surrogate replacement moiety. Those in the art will recognize that guanine, cytosine, adenine, and uracil can be replaced by other moieties without substantially altering the base pairing properties of an oligonucleotide comprising a nucleotide bearing such replacement moiety.

In one embodiment, modified RNAs contemplated for use in methods and compositions described herein are peptide nucleic acids (PNAs) that have the ability to form the required duplex structure and that permit or mediate the specific degradation of a target RNA via a RISC pathway. In certain embodiments of the invention, a HTT RNA interference agent includes a single stranded RNA that interacts with a target HTT RNA sequence to direct the cleavage of the target HTT RNA.

Modified RNA backbones can include, for example, phosphorothioates, chiral phosphorothioates, phosphorodithioates, phosphotriesters, aminoalkylphosphotriesters, methyl and other alkyl phosphonates including 3'-alkylene phosphonates and chiral phosphonates, phosphinates, phosphoramidates including 3'-amino phosphoramidate and aminoalkylphosphoramidates, thionophosphoramidates, thionoalkylphosphonates, thionoalkylphosphotriesters, and boranophosphates having normal 3'-5' linkages, 2'-5' linked analogs of these, and those) having inverted polarity wherein the adjacent pairs of nucleoside units are linked 3'-5' to 5'-3' or 2'-5' to 5'-2'. Various salts, mixed salts and free acid forms are also included. Means of preparing phosphorus-containing linkages are routinely practiced in the art and such methods can be used to prepare certain modified HTT dsRNA agents, certain modified HTT antisense polynucleotides, and/or certain modified HTT sense polynucleotides of the invention.

Modified RNA backbones that do not include a phosphorus atom therein have backbones that are formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatoms and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages. These include those having morpholino linkages (formed in part from the sugar portion of a nucleoside); siloxane backbones; sulfide, sulfoxide and sulfone backbones; formacetyl and thioformacetyl backbones; methylene formacetyl and thioformacetyl backbones; alkene containing backbones; sulfamate backbones; methyleneimino and methylenehydrazino backbones; sulfonate and sulfonamide backbones; amide backbones;

and others having mixed N, O, S and CH₂ component parts. Means of preparing modified RNA backbones that do not include a phosphorus atom are routinely practiced in the art and such methods can be used to prepare certain modified HTT dsRNA agents, certain modified HTT antisense polynucleotides, and/or certain modified HTT sense polynucleotides of the invention.

5 In certain embodiments of the invention, RNA mimetics are included in HTT dsRNAs, HTT antisense polynucleotides, and/or HTT sense polynucleotides, such as, but not limited to: replacement of the sugar and the internucleoside linkage, i.e., the backbone, of the nucleotide units with novel groups. In such embodiments, base units are maintained for hybridization with an appropriate HTT nucleic acid target compound. One such oligomeric compound, an RNA
10 mimetic that has been shown to have excellent hybridization properties, is referred to as a peptide nucleic acid (PNA). In PNA compounds, the sugar backbone of an RNA is replaced with an amide containing backbone, in particular an aminoethylglycine backbone. The nucleobases are retained and are bound directly or indirectly to aza nitrogen atoms of the amide portion of the backbone. Means of preparing RNA mimetics are routinely practiced in the art and such
15 methods can be used to prepare certain modified HTT dsRNA agents of the invention.

Some embodiments of the invention include RNAs with phosphorothioate backbones and oligonucleosides with heteroatom backbones, and in particular -CH₂-NH-CH₂-, -CH₂-N(CH₃)-O-CH₂-[known as a methylene (methylimino) or MMI backbone], -CH₂-O-N(CH₃)-CH₂-, -CH₂-N(CH₃)-N(CH₃)-CH₂- and -N(CH₃)-CH₂-[wherein the native phosphodiester
20 backbone is represented as -O-P-O-CH₂-]. Means of preparing RNAs with phosphorothioate backbones and oligonucleosides with heteroatom backbones are routinely practiced in the art and such methods can be used to prepare certain modified HTT dsRNA agents, certain HTT antisense polynucleotides, and/or certain HTT sense polynucleotides of the invention.

Modified RNAs can also contain one or more substituted sugar moieties. HTT dsRNAs,
25 HTT antisense polynucleotides, and/or HTT sense polynucleotides of the invention may comprise one of the following at the 2' position: OH; F; O-, S-, or N-alkyl; O-, S-, or N-alkenyl; O-, S- or N-alkynyl; or O-alkyl-O-alkyl, wherein the alkyl, alkenyl and alkynyl may be substituted or unsubstituted C₁ to C₁₀ alkyl or C₂ to C₁₀ alkenyl and alkynyl. Exemplary suitable modifications include O[(CH₂)_nO]_mCH₃, O(CH₂)_nOCH₃, O(CH₂)_nNH₂, O(CH₂)_nCH₃,
30 O(CH₂)_nONH₂, and O(CH₂)_nON[(CH₂)_nCH₃]₂, where n and m are from 1 to about 10. In other embodiments, dsRNAs include one of the following at the 2' position: C₁ to C₁₀ lower alkyl, substituted lower alkyl, alkaryl, aralkyl, O-alkaryl or O-aralkyl, SH, SCH₃, OCN, Cl, Br, CN, CF₃, OCF₃, SOCH₃, SO₂CH₃, ONO₂, NO₂, N₃, NH₂, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino, substituted silyl, an RNA cleaving group, a reporter group,
35 an intercalator, a group for improving the pharmacokinetic properties of a HTT dsRNA agent, or a group for improving the pharmacodynamic properties of a HTT dsRNA agent, HTT antisense polynucleotide, and/or HTT sense polynucleotide, and other substituents having similar properties. In some embodiments, the modification includes a 2'-methoxyethoxy (2'-O-CH₂CH₂OCH₃, also known as 2'-O-(2-methoxyethyl) or 2'-MOE) (Martin et al., *Helv. Chim.*

Acta, 1995, 78:486-504) i.e., an alkoxy-alkoxy group. Another exemplary modification is 2'-dimethylaminoethoxy, i.e., a $\text{O}(\text{CH}_2)_2\text{ON}(\text{CH}_3)_2$ group, also known as 2'-DMAOE, as described in examples herein below, and 2'-dimethylaminoethoxyethoxy (also known in the art as 2'-O-dimethylaminoethoxyethyl or 2'-DMAEOE), i.e., $2'\text{-O-CH}_2\text{-O-CH}_2\text{-N}(\text{CH}_3)_2$. Means of preparing modified RNAs such as those described are routinely practiced in the art and such methods can be used to prepare certain modified HTT dsRNA agents of the invention.

Other modifications include 2'-methoxy ($2'\text{-OCH}_3$), 2'-aminopropoxy ($2'\text{-OCH}_2\text{CH}_2\text{CH}_2\text{NH}_2$) and 2'-fluoro ($2'\text{-F}$). Similar modifications can also be made at other positions on the RNA of a HTT dsRNA agent, HTT antisense polynucleotide, and/or HTT sense polynucleotide of the invention, particularly the 3' position of the sugar on the 3' terminal nucleotide or in 2'-5' linked HTT dsRNAs, HTT antisense polynucleotides, or HTT sense polynucleotides, and the 5' position of 5' terminal nucleotide. HTT dsRNA agents, HTT antisense polynucleotides, and/or HTT sense polynucleotides may also have sugar mimetics such as cyclobutyl moieties in place of the pentofuranosyl sugar. Means of preparing modified RNAs such as those described are routinely practiced in the art and such methods can be used to prepare certain modified HTT dsRNA agents, HTT antisense polynucleotides, and/or HTT sense polynucleotides of the invention.

An HTT dsRNA agent, HTT antisense polynucleotide, and/or HTT sense polynucleotide may, in some embodiments, include nucleobase (often referred to in the art simply as "base") modifications or substitutions. As used herein, "unmodified" or "natural" nucleobases include the purine bases adenine and guanine, and the pyrimidine bases thymine, cytosine and uracil. Modified nucleobases include other synthetic and natural nucleobases such as 5-methylcytosine (5-Me-C), 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine and guanine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-halouracil and cytosine, 5-propynyl uracil and cytosine, 6-azo uracil, cytosine and thymine, 5-uracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl and other 8-substituted adenines and guanines, 5-halo, particularly 5-bromo, 5-trifluoromethyl and other 5-substituted uracils and cytosines, 7-methylguanine and 7-methyladenine, 8-azaguanine and 8-azaadenine, 7-deazaguanine and 7-daazaadenine and 3-deazaguanine and 3-deazaadenine. Additional nucleobases that may be included in certain embodiments of HTT dsRNA agents of the invention are known in the art, see for example: Modified Nucleosides in Biochemistry, Biotechnology and Medicine, Herdewijn, P. Ed. Wiley-VCH, 2008; The Concise Encyclopedia Of Polymer Science And Engineering, pages 858-859, Kroschwitz, J. L., Ed. John Wiley & Sons, 1990, English et al., Angewandte Chemie, International Edition, 1991, 30, 613, Sanghvi, Y S., Chapter 15, dsRNA Research and Applications, pages 289-302, Crooke, S. T. and Lebleu, B., Ed., CRC Press, 1993. Means of preparing dsRNAs, HTT antisense strand polynucleotides and/or HTT sense strand polynucleotides that comprise nucleobase modifications and/or substitutions such as those described herein are routinely practiced in the art and such methods can be used to

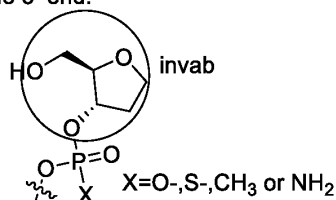
prepare certain modified HTT dsRNA agents, HTT sense polynucleotides, and/or HTT antisense polynucleotides of the invention.

Certain embodiments of HTT dsRNA agents, HTT antisense polynucleotides, and/or HTT sense polynucleotides of the invention include RNA modified to include one or more locked nucleic acids (LNA). A locked nucleic acid is a nucleotide with a modified ribose moiety comprising an extra bridge connecting the 2' and 4' carbons. This structure effectively “locks” the ribose in the 3'-endo structural conformation. The addition of locked nucleic acids in a HTT dsRNA agent, HTT antisense polynucleotides, and/or HTT sense polynucleotides of the invention may increase stability in serum, and to reduce off-target effects (Elmen, J. et al., (2005) *Nucleic Acids Research* 33(1):439-447; Mook, O R. et al., (2007) *Mol Canc Ther* 6(3):833-843; Grunweller, A. et al., (2003) *Nucleic Acids Research* 31(12):3185-3193). Means of preparing dsRNA agents, HTT antisense polynucleotides, and/or HTT sense polynucleotides that comprise locked nucleic acid(s) are routinely practiced in the art and such methods can be used to prepare certain modified HTT dsRNA agents of the invention.

Certain embodiments of HTT dsRNA compounds, sense polynucleotides, and/or antisense polynucleotides of the invention, include at least one modified nucleotide, wherein the at least one modified nucleotide comprises: a 2'-O-methyl nucleotide, 2'-Fluoro nucleotide, 2'-deoxy nucleotide, 2'3'-seco nucleotide mimic, locked nucleotide, 2'-F-Arabino nucleotide, 2'-methoxyxyethyl nucleotide, 2'-amino-modified nucleotide, 2'-alkyl-modified nucleotide, morpholino nucleotide, and 3'-OMe nucleotide, a nucleotide comprising a 5'-phosphorothioate group, a nucleotide comprising vinyl phosphate, a nucleotide comprising adenosine- glycol nucleic acid (GNA), a nucleotide comprising thymidine-glycol nucleic acid (GNA) S- Isomer, a nucleotide comprising 2-hydroxymethyl-tetrahydrofuran-5-phosphate, a nucleotide comprising 2'-deoxythymidine-3'phosphate, a nucleotide comprising 2'-deoxyguanosine-3'- phosphate, or a terminal nucleotide linked to a cholesteryl derivative or dodecanoic acid bisdecylamide group, a 2'-amino-modified nucleotide, a phosphoramidate, or a non-natural base comprising nucleotide. In some embodiments, a HTT dsRNA compound includes an E-vinylphosphonate nucleotide at the 5' -end of the antisense strand, also referred to herein as the guide strand.

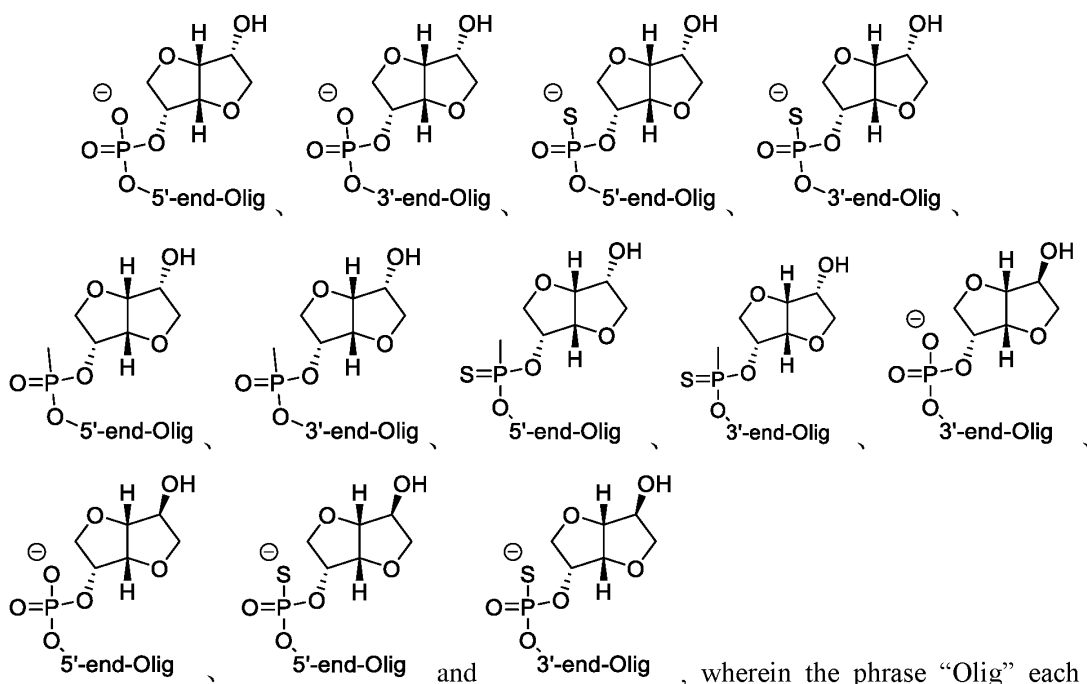
Certain embodiments of HTT dsRNA compounds, 3' and 5' end of sense polynucleotides, and/or 3' end of antisense polynucleotides of the invention, include at least one modified nucleotide, wherein the at least one modified nucleotide comprises: abasic nucleotide, ribitol, inverted nucleotide, inverted abasic nucleotide, inverted 2'-OMe nucleotide, inverted 2'-deoxy nucleotide. It is known to skilled in art, including an abasic or inverted abasic nucleotide at the end of oligonucleotide enhances stability (Czaderna et al. *Structural variations and stabilizing modifications of synthetic siRNAs in mammalian cells. Nucleic Acids Res.* 2003;31(11):2705-2716. doi:10.1093/nar/gkg393). In some embodiments, a HTT dsRNA compound includes one or more inverted abasic residues (invab) at either 3'-end or 5'-end, or both 3'-end and 5'-end. Exemplified inverted abasic residues (invab) include, but are not limited to the following:

when at the 3'-end:

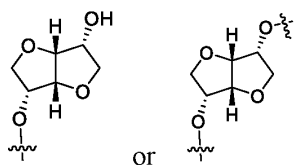


attached to 3'-end of oligonucleotide

Certain embodiments of HTT dsRNA compounds, 3' and 5' end of sense polynucleotides, and/or 3' end of antisense polynucleotides of the invention, include at least one modified nucleotide, wherein the at least one modified nucleotide comprises: isomannide nucleotide or stereoisomer of said isomannide nucleotide. Specific examples of isomannide nucleotides or stereoisomers of said isomannide nucleotides include, but are not limited to:



10 independently represents a polynucleotide moiety. Exemplified isomannide residues (imann) include, but are not limited to, the following:



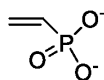
In certain embodiments, the isomannide nucleotides may further conjugate to one or more targeting groups or delivery molecules, such as GalNAc moieties.

15 Certain embodiments of HTT dsRNA compounds, antisense polynucleotides of the invention, include at least one modified nucleotide, wherein the at least one modified nucleotide comprises unlocked nucleic acid nucleotide (UNA) or/and glycol nucleic acid nucleotide (GNA).

It is known to skilled in art, UNA and GNA are thermally destabilizing chemical modifications, can significantly improves the off-target profile of a siRNA compound (Janas, et al., Selection of GalNAc-conjugated siRNAs with limited off-target-driven rat hepatotoxicity. Nat Commun. 2018;9(1):723. doi:10.1038/s41467-018-02989-4; Laursen et al., Utilization of unlocked nucleic acid (UNA) to enhance siRNA performance in vitro and in vivo. Mol BioSyst. 2010;6:862–70).

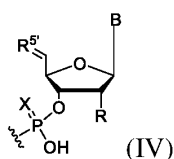
Certain embodiments of HTT dsRNA compounds, antisense polynucleotides of the invention, further comprise a 5'-phosphate mimic. Certain embodiments, 5'-phosphate mimic on the antisense strand of a RNAi agent. As used herein, a "5'-phosphate mimic" or "phosphate mimic" refers to a phosphate analogs corresponding to are bound to the 4'-carbon of the sugar moiety (e.g., a ribose or deoxyribose or analog thereof) of the a nucleotide. Typically, the phosphate analog is a vinyl phosphonate, where the carbon atom of the vinyl phosphonate group is bound to the 4'- carbon of the sugar moiety or analog thereof. In other embodiments, the phosphate analog is Ethylphosphonate, cyclic phosphonate, oxymethylphosphonate, oxymethylphosphonate, thiomethylphosphonate or an aminomethylphosphonate, where the carbon, oxygen, sulfur or amine atom of the thiomethyl group or the nitrogen atom of the aminomethyl group is bound to the 4'-carbon of the sugar moiety or analog thereof. In such instances, it is desirable to stabilize the phosphorous mimic against degradation or de-phosphorylation, which may inactivate the compound. Thus, in certain embodiments, oligonucleotides in which the 5'-phosphorous mimic have been stabilized are desired. In certain such embodiments, the phosphorous mimic is resistant to removal in biological systems, relative to unmodified nucleosides and/or the 5'-nucleoside is resistant to cleavage by nucleases. Suitable phosphate mimics are disclosed in, for example WO2011005860, WO2011/139702, WO2013/033230, WO2010/048585, WO2010/048549, WO2011/139699, WO2017214112, WO2018045317, the contents of which are incorporated herein by reference for the methods provided therein.

In some embodiments, the phosphate mimic is a 5'-vinyl phosphonate (VP). In exemplary embodiments, a vinyl phosphonate of the disclosure has the following structure:



A vinyl phosphonate of the instant disclosure may be attached to either the antisense or the sense strand of a dsRNA of the disclosure. In certain preferred embodiments, a vinyl phosphonate of the instant disclosure is attached to the antisense strand of a dsRNA, optionally at the 5' end of the antisense strand of the dsRNA.

In certain embodiments, a vinyl phosphonate modified nucleotide of the disclosure has the structure of formula (IV):



wherein X is O or S;

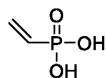
R is hydrogen, hydroxy, fluoro, or C₁₋₂₀ alkoxy (e.g., methoxy or n-hexadecyloxy);

R^{5'} is =C(H)-P(O)(OH)₂ and the double bond between the C5' carbon and R^{5'} is in the E or Z orientation (e.g., E orientation); and

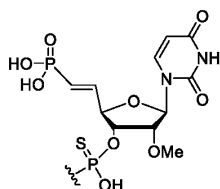
B is a nucleobase or a modified nucleobase, optionally where B is adenine, guanine, cytosine, thymine, or uracil.

In certain embodiments, R^{5'} is =C(H)-P(O)(OH)₂ and the double bond between the C5' carbon and R^{5'} is in the E orientation. In certain embodiments, R is methoxy and R^{5'} is =C(H)-P(O)(OH)₂ and the double bond between the C5' carbon and R^{5'} is in the E orientation. In certain embodiments, X is S, R is methoxy, and R^{5'} is =C(H)-P(O)(OH)₂ and the double bond between the C5' carbon and R^{5'} is in the E orientation.

Vinyl phosphate modifications are also contemplated for the dsRNAs, the compositions and methods of the instant disclosure. An exemplary vinyl phosphate structure is:



In certain embodiments, a vinyl phosphonate modified nucleotide is VPU* which has the structure of as follows:



In many cases, protecting groups are used during the preparation of the compounds of the invention. As used herein, the term "protected" means that the indicated moiety has a protecting group appended thereon. In some embodiments of the invention, compounds contain one or more protecting groups. A wide variety of protecting groups can be employed in the methods of the invention. In general, protecting groups render chemical functionalities inert to specific reaction conditions, and can be appended to and removed from such functionalities in a molecule without substantially damaging the remainder of the molecule. Protecting groups in general and hydroxyl protecting groups in particular are well known in the art (Greene and

Wuts, Protective Groups in Organic Synthesis, Chapter 2, 2d ed., John Wiley & Sons, New York, 1991).

As used herein, examples of protecting groups (e.g., hydroxyl protecting groups) include, but are not limited to, methyl, ethyl, benzyl (Bn), phenyl, isopropyl, tert-butyl, acetyl, chloroacetyl, trichloro acetyl, trifluoroacetyl, pivaloyl, tert-butoxymethyl, methoxymethyl, 1-ethoxyethyl, 1-(2-chloroethoxy)ethyl, allyl, cyclohexyl, 9-fluorenylmethoxycarbonyl (Fmoc), methanesulfonate, toluenesulfonate, triflate, benzoyl, benzoylformate, p-phenylbenzoyl, 4-methoxybenzyl, monomethoxytrityl, dimethoxytrityl, trimethoxytrityl, 4-chlorobenzyl, 4-nitrobenzyl, 2,4-dinitrophenyl, 4-acyloxybenzyl, 2-methylphenyl, 2,6-dimethylphenyl, 2-chlorophenyl, 2,6-dichlorobenzyl, diphenylmethyl, triphenylmethyl, 4-methylthio-1-butyl, S-acetylthioacetate (SATA), 2-cyanoethyl, 2-cyano-1,1-dimethylethyl (CDM), 4-cyano-2-butenyl, 2-(trimethylsilyl)ethyl (TSE), 2-(phenylthio)ethyl, 2-(triphenylsilyl)ethyl, 2-(benzylsulfonyl)ethyl, 2,2,2-trichloroethyl, 2,2,2-tribromoethyl, 2,3-dibromopropyl, 2,2,2-trifluoroethyl, phenylthio, 2-chloro-4-tritylphenyl, 2-bromophenyl, 2-[N-isopropyl-N-(4-methoxybenzoyl)amino]ethyl, 4-(N-trifluoroacetyl)amino]butyl, 4-oxopentyl, 4-tritylaminophenyl, 4-benzyl aminophenyl, tetrahydropyranyl, morpholino, trimethylsilyl, triethylsilyl, tert-butyl dimethylsilyl, tert-butyl diphenylsilyl, triphenyl silyl, triisopropylsilyl, pivaloyloxymethyl (POM) and 9-phenylxanthine-9-yl.

As used herein, examples of amino protecting groups include, but are not limited to, carbamate protecting groups, such as 2-trimethylsilylethoxycarbonyl (Teoc), 1-methyl-1-(4-biphenyl)ethoxycarbonyl (Bpoc), tert-butyloxycarbonyl (BOC), allyloxycarbonyl (Alloc), 9-fluorenyl-methoxycarbonyl (Fmoc), benzyloxycarbonyl (Cbz); amide protecting groups, such as formyl, acetyl, pivaloyl, trihaloacetyl, benzoyl, 2-nitrobenzenesulfonyl; and imine and cyclic imide protecting groups, such as phthalimido and dithiasuccinoyl. Equivalents of these amino-protecting groups are also encompassed by the compounds and methods of the invention.

Another modification that may be included in the RNA of certain embodiments of HTT dsRNA agents, HTT antisense polynucleotides, and/or HTT sense polynucleotides of the invention, comprises chemically linking to the RNA one or more ligands, moieties or conjugates that enhance one or more characteristics of the HTT dsRNA agent, HTT antisense polynucleotide, and/or HTT sense polynucleotide, respectively. Non-limiting examples of characteristics that may be enhanced are: HTT dsRNA agent, HTT antisense polynucleotide, and/or HTT sense polynucleotide activity, cellular distribution, delivery of a HTT dsRNA agent, pharmacokinetic properties of a HTT dsRNA agent, and cellular uptake of the HTT dsRNA agent. In some embodiments of the invention, a HTT dsRNA agent comprises one or more

targeting groups or linking groups, which in certain embodiments of HTT dsRNA agents of the invention are conjugated to the sense strand. A non-limiting example of a targeting group is a compound comprising N-acetyl-galactosamine (GalNAc). The terms “targeting group”, “targeting agent”, “linking agent”, “targeting compound”, “delivery molecule”, “delivery compound” and “targeting ligand” may be used interchangeably herein. In certain embodiments of the invention a HTT dsRNA agent comprises a targeting compound that is conjugated to the 5'-terminal end of the sense strand. In certain embodiments of the invention a HTT dsRNA agent comprises a targeting compound that is conjugated to the 3'-terminal end of the sense strand. In some embodiments of the invention, a HTT dsRNA agent comprises a targeting group that comprises GalNAc. In certain embodiments of the invention a HTT dsRNA agent does not include a targeting compound conjugated to one or both of the 3'-terminal end and the 5'-terminal end of the sense strand. In certain embodiments of the invention a HTT dsRNA agent does not include a GalNAc containing targeting compound conjugated to one or both of the 5'-terminal end and the 3'-terminal end of the sense strand.

Additional targeting and linking agents are well known in the art, for example, targeting and linking agents that may be used in certain embodiments of the invention include but are not limited to lipid moieties such as a cholesterol moiety (Letsinger et al., Proc. Natl. Acad. Sci. USA, 1989, 86: 6553-6556), cholic acid (Manoharan et al., Biorg. Med. Chem. Lett., 1994, 4:1053-1060), a thioether, e.g., beryl-S-tritylthiol (Manoharan et al., Ann. N.Y. Acad. Sci., 1992, 660:306-309; Manoharan et al., Biorg. Med. Chem. Lett., 1993, 3:2765-2770), a thiocholesterol (Oberhauser et al., Nucl. Acids Res., 1992, 20:533-538), an aliphatic chain, e.g., dodecandiol or undecyl residues (Saison-Behmoaras et al., EMBO J, 1991, 10:1111-1118; Kabanov et al., FEBS Lett., 1990, 259:327-330; Svinarchuk et al., Biochimie, 1993, 75:49-54), a phospholipid, e.g., di-hexadecyl-rac-glycerol or triethyl-ammonium 1,2-di-O-hexadecyl-rac-glycero-3-phosphonate (Manoharan et al., Tetrahedron Lett., 1995, 36:3651-3654; Shea et al., Nucl. Acids Res., 1990, 18:3777-3783), a polyamine or a polyethylene glycol chain (Manoharan et al., Nucleosides & Nucleotides, 1995, 14:969-973), or adamantane acetic acid (Manoharan et al., Tetrahedron Lett., 1995, 36:3651-3654), a palmityl moiety (Mishra et al., Biochim. Biophys. Acta, 1995, 1264:229-237), or an octadecylamine or hexylamino-carboxycholesterol moiety (Crooke et al., J. Pharmacol. Exp. Ther., 1996, 277:923-937).

Certain embodiments of a composition comprising a HTT dsRNA agent, HTT antisense polynucleotide, and/or HTT sense polynucleotide may comprise a ligand that alters distribution, targeting, or etc. of the HTT dsRNA agent. In some embodiments of a composition comprising a HTT dsRNA agent of the invention, the ligand increases affinity for a selected target, e.g., molecule, cell or cell type, compartment, e.g., a cellular or organ compartment, tissue, organ or region of the body, as, e.g., compared to a species absent such a ligand. A ligand useful in a composition and/or method of the invention may be a naturally occurring substance, such as a protein (e.g., human serum albumin (HSA), low-density lipoprotein (LDL), or globulin); a carbohydrate (e.g., a dextran, pullulan, chitin, chitosan, inulin, cyclodextrin or hyaluronic acid);

or a lipid. A ligand may also be a recombinant or synthetic molecule, such as a synthetic polymer, e.g., a synthetic polyamino acid or polyamine. Examples of polyamino acids are a polylysine (PLL), poly L-aspartic acid, poly L-glutamic acid, styrene-maleic acid anhydride copolymer, poly(L-lactide-co-glycolide) copolymer, divinyl ether-maleic anhydride copolymer, N-(2-hydroxypropyl)methacrylamide copolymer (HMPA), polyethylene glycol (PEG), polyvinyl alcohol (PVA), polyurethane, poly(2-ethylacrylic acid), N-isopropylacrylamide polymers, or polyphosphazene. Example of polyamines include: polyethylenimine, polylysine (PLL), spermine, spermidine, polyamine, pseudopeptide-polyamine, peptidomimetic polyamine, dendrimer polyamine, arginine, amidine, protamine, cationic lipid, cationic porphyrin, quaternary salt of a polyamine, or an alpha helical peptide.

A ligand included in a composition and/or method of the invention may comprise a targeting group, non-limiting examples of which are a cell or tissue targeting agent, e.g., a lectin, glycoprotein, lipid or protein, e.g., an antibody that binds to a specified cell type such as a kidney cell or a liver cell. A targeting group can be a thyrotropin, melanotropin, lectin, glycoprotein, surfactant protein A, Mucin carbohydrate, multivalent lactose, multivalent galactose, N-acetyl-galactosamine, N-acetyl-gulucosamine multivalent mannose, multivalent fucose, glycosylated polyaminoacids, multivalent galactose, transferrin, bisphosphonate, polyglutamate, polyaspartate, a lipid, cholesterol, a steroid, bile acid, folate, vitamin B12, vitamin A, biotin, or an RGD peptide or RGD peptide mimetic.

Other examples of ligands include dyes, intercalating agents (e.g. acridines), cross-linkers (e.g. psoralene, mitomycin C), porphyrins (TPPC4, texaphyrin, Sapphyrin), polycyclic aromatic hydrocarbons (e.g., phenazine, dihydrophenazine), artificial endonucleases (e.g. EDTA), lipophilic molecules, e.g., cholesterol, cholic acid, adamantane acetic acid, 1-pyrene butyric acid, dihydrotestosterone, 1,3-Bis-O(hexadecyl)glycerol, geranyloxyhexyl group, hexadecylglycerol, borneol, menthol, 1,3-propanediol, heptadecyl group, palmitic acid, myristic acid, O3-(oleoyl)lithocholic acid, O3-(oleoyl)cholenic acid, dimethoxytrityl, or phenoxazine) and peptide conjugates (e.g., antennapedia peptide, Tat peptide), alkylating agents, phosphate, amino, mercapto, PEG (e.g., PEG-40K), MPEG, [MPEG]₂, polyamino, alkyl, substituted alkyl, radiolabeled markers, enzymes, haptens (e.g., biotin), transport/absorption facilitators (e.g., aspirin, vitamin E, folic acid), synthetic ribonucleases (e.g., imidazole, bisimidazole, histamine, imidazole clusters, acridine-imidazole conjugates, Eu³⁺ complexes of tetraazamacrocycles), dinitrophenyl, HRP, or AP.

A ligand included in a composition and/or method of the invention may be a protein, e.g., glycoprotein, or peptide, for example a molecule with a specific affinity for a co-ligand, or an antibody, for example an antibody, that binds to a specified cell type such as a cancer cell, endothelial cell, cardiac cell, or bone cell. A ligand useful in an embodiment of a composition and/or method of the invention can be a hormone or hormone receptor. A ligand useful in an embodiment of a composition and/or method of the invention can be a lipid, lectin, carbohydrates, vitamin, cofactors, multivalent lactose, multivalent galactose, N-acetyl-galactosamine, N-acetyl-

gulucosamine multivalent mannose, or multivalent fucose. A ligand useful in an embodiment of a composition and/or method of the invention can be a substance that can increase uptake of the HTT dsRNA agent into the cell, for example, by disrupting the cell's cytoskeleton, e.g., by disrupting the cell's microtubules, microfilaments, and/or intermediate filaments. Non-limiting
5 examples of this type of agent are: taxon, vincristine, vinblastine, cytochalasin, nocodazole, japlakinolide, latrunculin A, phalloidin, swinholide A, indanocine, and myoservin.

In some embodiments, a ligand attached to a HTT dsRNA agent of the invention functions as a pharmacokinetic (PK) modulator. An example of a PK modulator that may be used in compositions and methods of the invention includes but is not limited to: a lipophiles, a
10 bile acid, a steroid, a phospholipid analogue, a peptide, a protein binding agent, PEG, a vitamin, cholesterol, a fatty acid, cholic acid, lithocholic acid, dialkylglycerides, diacylglyceride, a phospholipid, a sphingolipid, naproxen, ibuprofen, vitamin E, biotin, an aptamer that binds a serum protein, etc. Oligonucleotides comprising a number of phosphorothioate linkages are also known to bind to serum protein, thus short oligonucleotides, e.g., oligonucleotides of about
15 5 bases, 10 bases, 15 bases or 20 bases, comprising multiple of phosphorothioate linkages in the backbone may also be used in compositions and/or methods of the invention as ligands.

HTT dsRNA agent compositions

In some embodiments of the invention, a HTT dsRNA agent is in a composition. A
20 composition of the invention may include one or more HTT dsRNA agent and optionally one or more of a pharmaceutically acceptable carrier, a delivery agent, a targeting agent, detectable label, etc. A non-limiting example of a targeting agent that may be useful according to some embodiments of methods of the invention is an agent that directs a HTT dsRNA agent of the invention to and/or into a cell to be treated. A targeting agent of choice will depend upon such
25 elements as: the nature of the HTT-associated disease or condition, and on the cell type being targeted. In a non-limiting example, in some embodiments of the invention it may be desirable to target a HTT dsRNA agent to and/or into a liver cell. It will be understood that in some embodiments of methods of the invention, a therapeutic agent comprises a HTT dsRNA agent with only a delivery agent, such as a delivery agent comprising N-Acetylgalactosamine
30 (GalNAc), without any additional attached elements. For example, in some aspects of the invention a HTT dsRNA agent may be attached to a delivery compound comprising GalNAc and included in a composition comprising a pharmaceutically acceptable carrier and administered to a cell or subject without any detectable labels, or targeting agents, etc. attached to the HTT dsRNA agent.

35 In cases where a HTT dsRNA agent of the invention is administered with and/or attached to one or more delivery agents, targeting agents, labeling agents, etc. a skilled artisan will be aware of and able to select and use suitable agents for use in methods of the invention. Labeling agents may be used in certain methods of the invention to determine the location of a HTT dsRNA agent in cells and tissues and may be used to determine a cell, tissue, or organ location

of a treatment composition comprising a HTT dsRNA agent that has been administered in methods of the invention. Procedures for attaching and utilizing labeling agents such as enzymatic labels, dyes, radiolabels, etc. are well known in the art. It will be understood that in some embodiments of compositions and methods of the invention, a labeling agent is attached to one or both of a sense polynucleotide and an antisense polynucleotide included in a HTT dsRNA agent.

Delivery of HTT dsRNA agents and HTT antisense polynucleotide agents

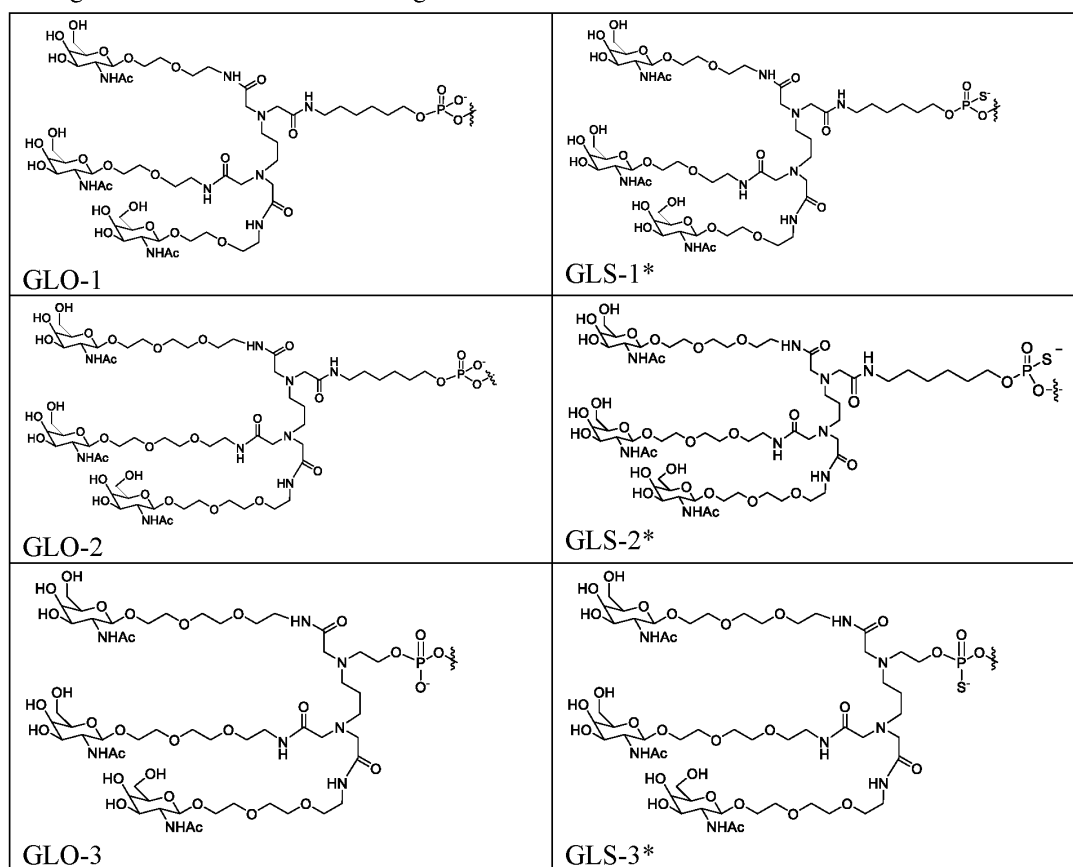
Certain embodiments of methods of the invention, includes delivery of a HTT dsRNA agent into a cell. As used herein the term, “delivery” means facilitating or effecting uptake or absorption into the cell. Absorption or uptake of a HTT dsRNA agent can occur through unaided diffusive or active cellular processes, or by use of delivery agents, targeting agents, etc. that may be associated with a HTT dsRNA agent of the invention. Delivery means that are suitable for use in methods of the invention include, but are not limited to: *in vivo* delivery, in which a HTT dsRNA agent is injected into a tissue site or administered systemically. In some embodiments of the invention, a HTT dsRNA agent is attached to a delivery agent.

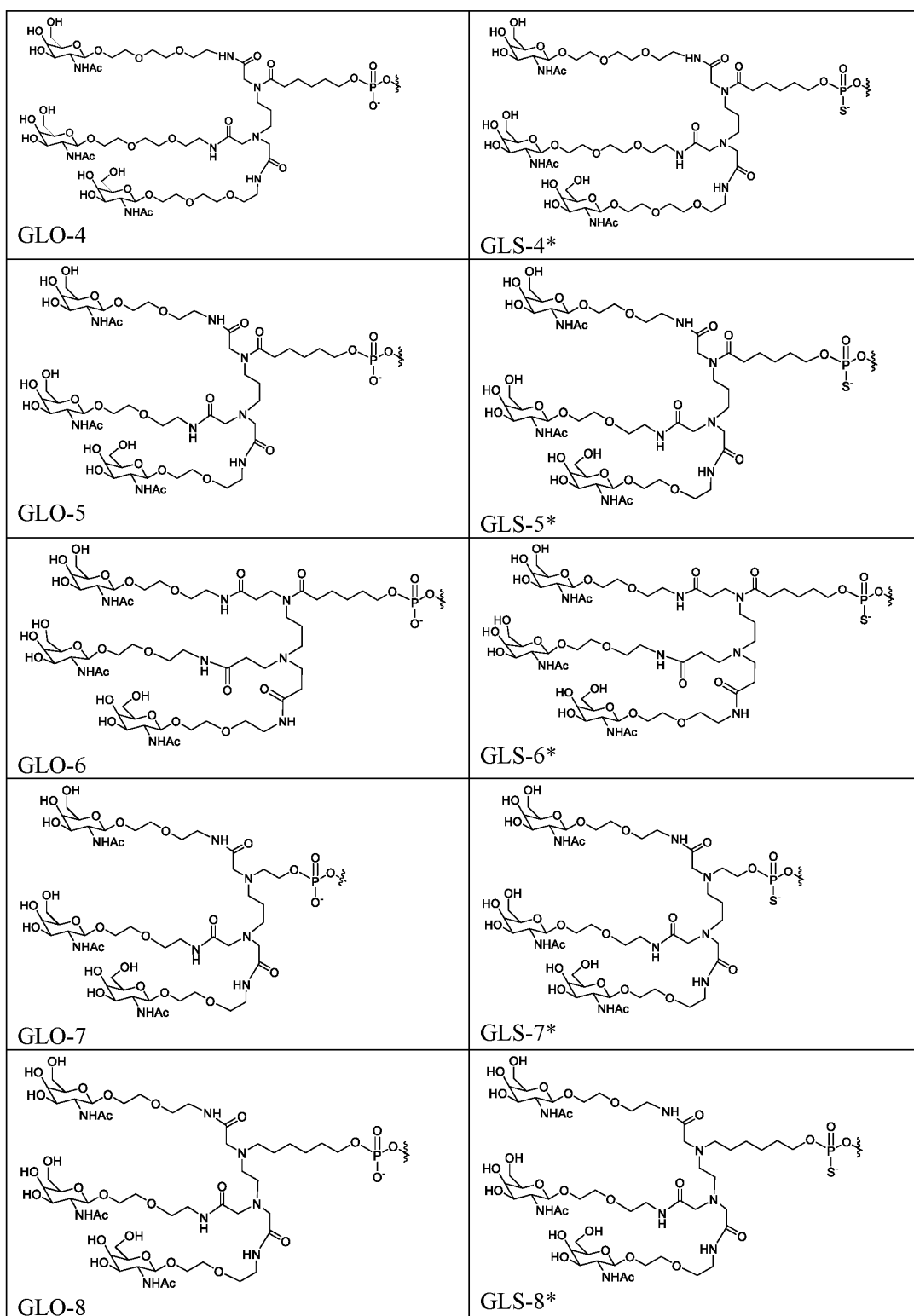
Non-limiting examples of methods that can be used to deliver HTT dsRNA agents to cells, tissues and/or subjects include: HTT dsRNA-GalNAc conjugates, SAMiRNA technology, LNP-based delivery methods, and naked RNA delivery. These and other delivery methods have been used successfully in the art to deliver therapeutic RNAi agents for treatment of various diseases and conditions, such as but not limited to: liver diseases, acute intermittent porphyria (AIP), hemophilia, pulmonary fibrosis, etc. Details of various delivery means are found in publications such as: Nikam, R.R. & K. R. Gore (2018) *Nucleic Acid Ther*, 28 (4), 209-224 Aug 2018; Springer A.D. & S.F. Dowdy (2018) *Nucleic Acid Ther*. Jun 1; 28(3): 109–118; Lee, K. et al., (2018) *Arch Pharm Res*, 41(9), 867-874; and Nair, J.K. et al., (2014) *J. Am. Chem. Soc.* 136:16958-16961, the content each of which is incorporated by reference herein.

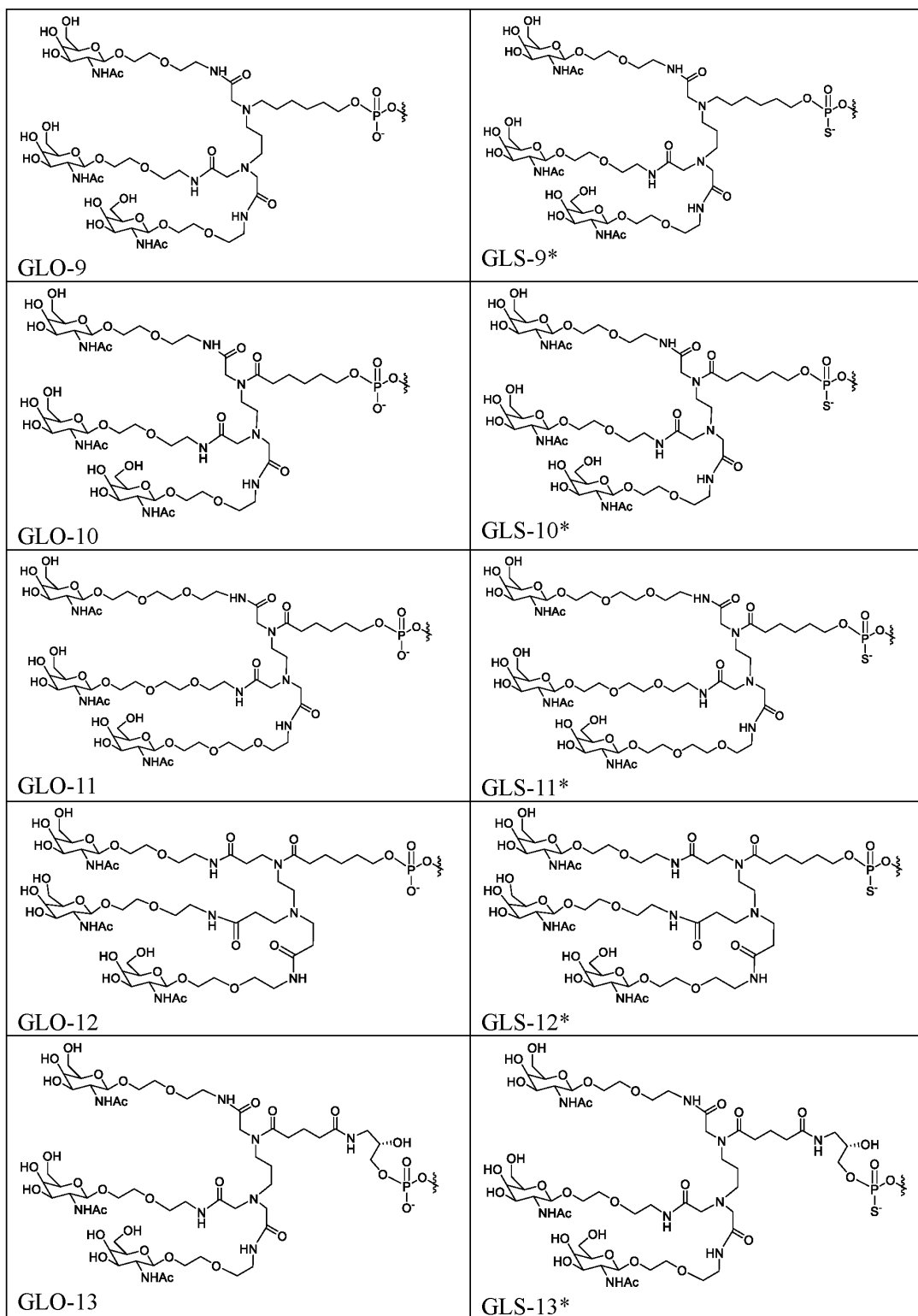
Some embodiments of the invention comprise use of lipid nanoparticles (LNPs) to deliver a HTT dsRNA agent of the invention to a cell, tissue, and/or subject. LNPs are routinely used for *in vivo* delivery of HTT dsRNA agents, including therapeutic HTT dsRNA agents. One benefit of using an LNP or other delivery agent is an increased stability of the HTT RNA agent when it is delivered to a subject using the LNP or other delivery agent. In some embodiments of the invention an LNP comprises a cationic LNP that is loaded with one or more HTT RNAi molecules of the invention. The LNP comprising the HTT RNAi molecule(s) is administered to a subject, the LNPs and their attached HTT RNAi molecules are taken up by cells via endocytosis, their presence results in release of RNAi trigger molecules, which mediate RNAi.

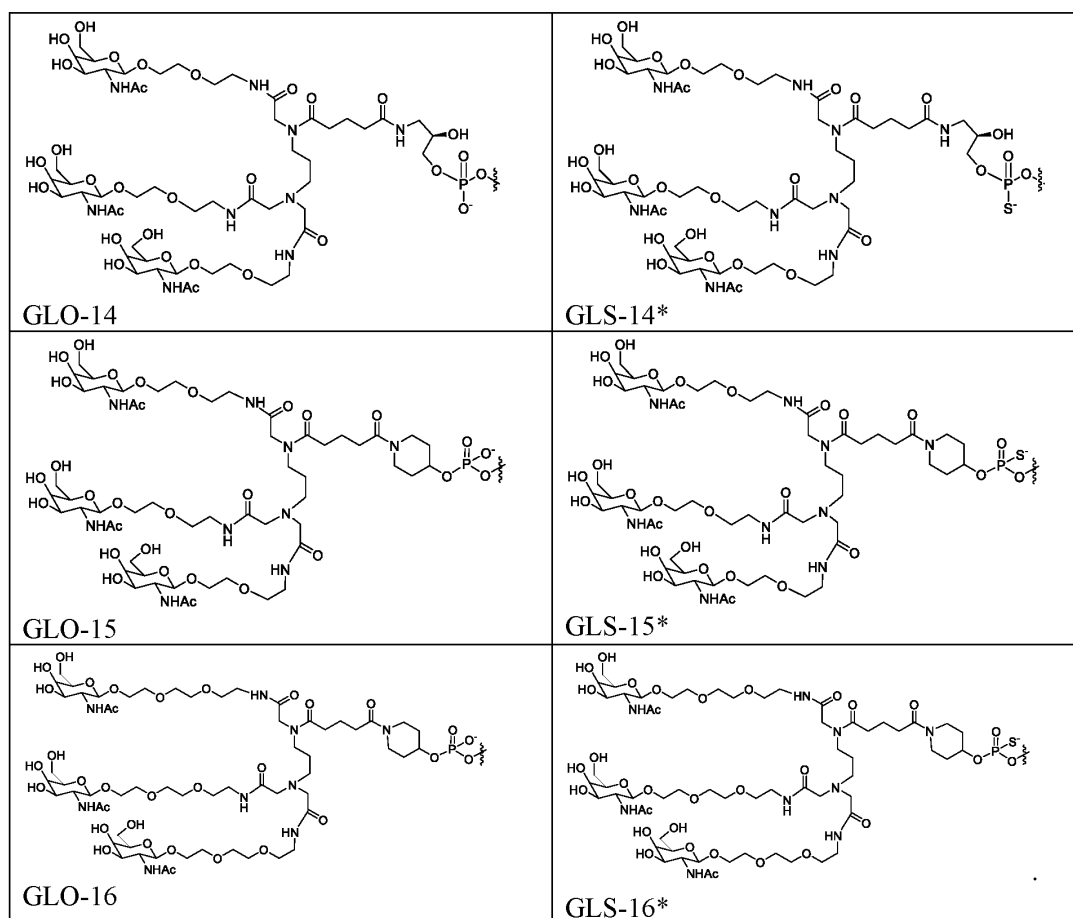
Another non-limiting example of a delivery agent that may be used in embodiments of the invention to delivery a HTT dsRNA agent of the invention to a cell, tissue and/or subject is an agent comprising GalNAc that is attached to a HTT dsRNA agent of the invention and delivers the HTT dsRNA agent to a cell, tissue, and/or subject. Examples of certain additional delivery

agents comprising GalNAc that can be used in certain embodiments of methods and composition of the invention are disclosed in PCT Application: WO2020191183A1 (incorporated herein in its entirety). A non-limiting example of a GalNAc targeting ligand that can be used in compositions and methods of the invention to deliver a HTT dsRNA agent to a cell is a targeting ligand cluster. Examples of targeting ligand clusters that are presented herein are referred to as: GalNAc Ligand with phosphodiester link (GLO) and GalNAc Ligand with phosphorothioate link (GLS). The term “GLX-n” may be used herein to indicate the attached GalNAc-containing compound is any one of compounds GLS-1*, GLS-2*, GLS-3*, GLS-4*, GLS-5*, GLS-6*, GLS-7*, GLS-8*, GLS-9*, GLS-10*, GLS-11*, GLS-12*, GLS-13*, GLS-14*, GLS-15*, GLS-16*, GLO-1, GLO-2, GLO-3, GLO-4, GLO-5, GLO-6, GLO-7, GLO-8, GLO-9, GLO-10, GLO-11, GLO-12, GLO-13, GLO-14, GLO-15, and GLO-16, the structure of each of which is shown below, with the below with location of attachment of the GalNAc-targeting ligand to an RNAi agent of the invention at far right of each (shown with “}”). It will be understood that any RNAi and dsRNA molecule of the invention can be attached to the GLS-1*, GLS-2*, GLS-3*, GLS-4*, GLS-5*, GLS-6*, GLS-7*, GLS-8*, GLS-9*, GLS-10*, GLS-11*, GLS-12*, GLS-13*, GLS-14*, GLS-15*, GLS-16*, GLO-1, GLO-2, GLO-3, GLO-4, GLO-5, GLO-6, GLO-7, GLO-8, GLO-9, GLO-10, GLO-11, GLO-12, GLO-13, GLO-14, GLO-15, and GLO-16, GLO-1 through GLO-16 and GLS-1* through GLS-16* structures are shown below.

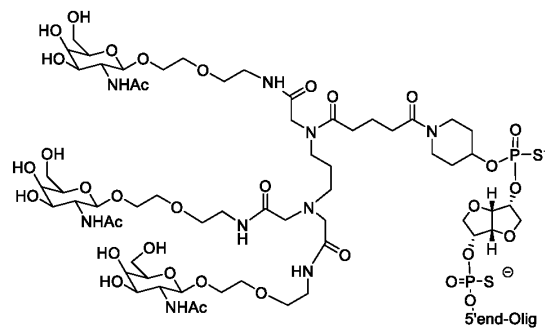








In certain embodiments, the aforesaid isomannide nucleotides may further conjugate to one or more GalNAc targeting ligands. Specific examples of isomannide nucleotides conjugated to a GalNAc targeting ligand include, but are not limited to:



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, wherein the phrase "olig" each independently represents a polynucleotide moiety.

In some embodiments of the invention, *in vivo* delivery can also be by a beta-glucan delivery system, such as those described in U.S. Pat. Nos. 5,032,401 and 5,607,677, and U.S. Publication No. 2005/0281781, which are hereby incorporated by reference in their entirety. *In vitro* introduction of a HTT RNAi agent into a cell may also be done using art-known methods

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such as electroporation and lipofection. In certain embodiments of methods of the invention, a HTT dsRNA is delivered without a targeting agent. These RNAs may be delivered as “naked” RNA molecules. As a non-limiting example, a HTT dsRNA of the invention may be administered to a subject to treat a HTT-associated disease or condition in the subject, such as a cardiovascular disease, in a pharmaceutical composition comprising the RNAi agent, but not including a targeting agent such as a GalNAc targeting compound.

In addition to certain delivery means described herein, it will be understood that RNAi delivery means, such as but not limited to those described herein and those used in the art, can be used in conjunction with embodiments of HTT RNAi agents and treatment methods described herein.

HTT dsRNA agents of the invention may be administered to a subject in an amount and manner effective to reduce a level and activity of HTT polypeptide in a cell and/or subject. In some embodiments of methods of the invention one or more HTT dsRNA agents are administered to a cell and/or subject to treat a disease or condition associated with HTT expression and activity. Methods of the invention, in some embodiments, include administering one or more HTT dsRNA agents to a subject in need of such treatment to reduce a disease or condition associated with HTT expression in the subject. HTT dsRNA agents or HTT antisense polynucleotide agents of the invention can be administered to reduce HTT expression and/or activity in one more of *in vitro*, *ex vivo*, and *in vivo* cells.

In some embodiments of the invention, a level, and thus an activity, of HTT polypeptide in a cell is reduced by delivering (e.g. introducing) an HTT dsRNA agent or HTT antisense polynucleotide agent into a cell. Targeting agents and methods may be used to aid in delivery of a HTT dsRNA agent or HTT antisense polynucleotide agent to a specific cell type, cell subtype, organ, spatial region within a subject, and/or to a sub-cellular region within a cell. An HTT dsRNA agent can be administered in certain methods of the invention singly or in combination with one or more additional HTT dsRNA agents. In some embodiments, 2, 3, 4, or more independently selected HTT dsRNA agents are administered to a subject.

In certain embodiments of the invention, an HTT dsRNA agent is administered to a subject to treat a HTT-associated disease or condition in conjunction with one or more additional therapeutic regimens for treating the HTT-associated disease or condition. Non-limiting examples of additional therapeutic regimens are: administering one or more HTT antisense polynucleotides of the invention, administering a non-HTT dsRNA therapeutic agent, and a behavioral modification. An additional therapeutic regimen may be administered at a time that is one or more of: prior to, simultaneous with, and following administration of a HTT dsRNA agent of the invention. It will be understood that simultaneous with as used herein, within five minutes of time zero, within 10 minutes of time zero, within 30 minutes of time zero, within 45 minutes of time zero, and within 60 minutes of time zero, with “time zero” the time of administration of the HTT dsRNA agent of the invention to the subject. Non-limiting examples of non-HTT dsRNA therapeutic agents are a monoamine inhibitor. These and other therapeutic

agents and behavior modifications are known in the art and used to treat a HTT-associated disease or condition in a subject and may be administered to a subject in combination with the administration of one or more HTT dsRNA agents of the invention to treat the HTT-associated disease or condition. A HTT dsRNA agent of the invention administered to a cell or subject to
5 treat a HTT-associated disease or condition may act in a synergistic manner with one or more other therapeutic agents or activities and increase the effectiveness of the one or more therapeutic agents or activities and/or to increase the effectiveness of the HTT dsRNA agent at treating the HTT-associated disease or condition.

Treatment methods of the invention that include administration of a HTT dsRNA agent
10 can be used prior to the onset of an HTT-associated disease or condition and/or when a HTT-associated disease or condition is present, including at an early stage, mid-stage, and late stage of the disease or condition and all times before and after any of these stages. Methods of the invention may also be to treat subjects who have previously been treated for a HTT-associated disease or condition with one or more other therapeutic agents and/or therapeutic activities that
15 were not successful, were minimally successful, and/or are no longer successful at treating the HTT-associated disease or condition in the subject.

Vector Encoded dsRNAs

In certain embodiments of the invention, a HTT dsRNA agent can be delivered into a
20 cell using a vector. HTT dsRNA agent transcription units can be included in a DNA or RNA vector. Prepare and use of such vectors encoding transgenes for delivering sequences into a cell and or subject are well known in the art. Vectors can be used in methods of the invention that result in transient expression of HTT dsRNA, for example for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more hours, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more weeks. The length of the transient expression
25 can be determined using routine methods based on elements such as, but not limited to the specific vector construct selected and the target cell and/or tissue. Such transgenes can be introduced as a linear construct, a circular plasmid, or a viral vector, which can be an integrating or non-integrating vector. The transgene can also be constructed to permit it to be inherited as an extrachromosomal plasmid (Gassmann, et al., Proc. Natl. Acad. Sci. USA (1995) 92:1292).

An individual strand or strands of a HTT dsRNA agent can be transcribed from a
30 promoter on an expression vector. Where two separate strands are to be expressed to generate, for example, a dsRNA, two separate expression vectors can be co-introduced to a cell using means such as transfection or infection. In certain embodiments each individual strand of a HTT dsRNA agent of the invention can be transcribed by promoters that are both included on
35 the same expression vector. In certain embodiments of the invention a HTT dsRNA agent is expressed as inverted repeat polynucleotides joined by a linker polynucleotide sequence such that the HTT dsRNA agent has a stem and loop structure.

Non-limiting examples of RNA expression vectors are DNA plasmids or viral vectors. Expression vectors useful in embodiments of the invention can be compatible with eukaryotic

cells. Eukaryotic cell expression vectors are routinely used in the art and are available from a number of commercial sources. Delivery of HTT dsRNA expressing vectors can be systemic, such as by intravenous or intramuscular administration, by administration to target cells explanted from a subject followed by reintroduction into the subject, or by any other means that allows for introduction into a desired target cell.

Viral vector systems that may be included in an embodiment of a method of the include, but are not limited to, (a) adenovirus vectors; (b) retrovirus vectors, including but not limited to lentiviral vectors, moloney murine leukemia virus, etc.; (c) adeno-associated virus vectors; (d) herpes simplex virus vectors; (e) SV 40 vectors; (f) polyoma virus vectors; (g) papilloma virus vectors; (h) picornavirus vectors; (i) pox virus vectors such as an orthopox, e.g., vaccinia virus vectors or avipox, e.g. canary pox or fowl pox; and (j) a helper-dependent or gutless adenovirus. Constructs for the recombinant expression of a HTT dsRNA agent may include regulatory elements, such as promoters, enhancers, etc., which may be selected to provide constitutive or regulated/inducible expression. Viral vector systems, and the use of promoters and enhancers, etc. are routine in the art and can be used in conjunction with methods and compositions described herein.

Certain embodiments of the invention include use of viral vectors for delivery of HTT dsRNA agents into cells. Numerous adenovirus-based delivery systems are routinely used in the art for deliver to, for example, lung, liver, the central nervous system, endothelial cells, and muscle. Non-limiting examples of viral vectors that may be used in methods of the invention are: AAV vectors, a pox virus such as a vaccinia virus, a Modified Virus Ankara (MVA), NYVAC, an avipox such as fowl pox or canary pox.

Certain embodiments of the invention include methods of delivering HTT dsRNA agents into cells using a vector and such vectors may be in a pharmaceutically acceptable carrier that may, but need not, include a slow-release matrix in which the gene delivery vehicle is imbedded. In some embodiments, a vector for delivering a HTT dsRNA can be produced from a recombinant cell, and a pharmaceutical composition of the invention may include one or more cells that produced the HTT dsRNA delivery system.

Pharmaceutical Compositions Containing HTT dsRNA or ssRNA agents

Certain embodiments of the invention include use of pharmaceutical compositions containing a HTT dsRNA agent or HTT antisense polynucleotide agent and a pharmaceutically acceptable carrier. The pharmaceutical composition containing the HTT dsRNA agent or HTT antisense polynucleotide agent can be used in methods of the invention to reduce HTT gene expression and HTT activity in a cell and is useful to treat a HTT-associated disease or condition. Such pharmaceutical compositions can be formulated based on the mode of delivery. Non-limiting examples of formulations for modes of delivery are: a composition formulated for subcutaneous delivery, a composition formulated for systemic administration via parenteral delivery, a composition formulated for intravenous (IV) delivery, a composition formulated for

intrathecally delivery, a composition formulated for intracerebroventricular (ICV) delivery, composition formulated for intrastriatal (IS) injection delivery, a composition formulated for direct delivery into brain, etc, a composition formulated for direct delivery into CNS cell, etc. Administration of a pharmaceutic composition of the invention to deliver a HTT dsRNA agent or HTT antisense polynucleotide agent into a cell may be done using one or more means such as: topical (e.g., by a transdermal patch), pulmonary, e.g., by inhalation or insufflation of powders or aerosols, including by nebulizer; intratracheal, intranasal, epidermal and transdermal, oral or parenteral. Parenteral administration includes intravenous, intraarterial, subcutaneous, intraperitoneal or intramuscular injection or infusion; subdermal, e.g., via an implanted device; or intracranial, e.g., by intraparenchymal, intrathecal or intraventricular, administration. A HTT dsRNA agent or HTT antisense polynucleotide agent can also be delivered directly to a target tissue, for example directly into the liver, directly into a Central Nervous System, directly into brain, etc. It will be understood that “delivering a HTT dsRNA agent” or “delivering a HTT antisense polynucleotide agent” into a cell encompasses delivering a HTT dsRNA agent or HTT antisense polynucleotide agent, respectively, directly as well as expressing a HTT dsRNA agent in a cell from an encoding vector that is delivered into a cell, or by any suitable means with which the HTT dsRNA or HTT antisense polynucleotide agent becomes present in a cell. Preparation and use of formulations and means for delivering inhibitory RNAs are well known and routinely used in the art.

As used herein, a “pharmaceutical composition” comprises a pharmacologically effective amount of a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention and a pharmaceutically acceptable carrier. The term “pharmaceutically acceptable carrier” refers to a carrier for administration of a therapeutic agent. Such carriers include, but are not limited to, saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof. The term specifically excludes cell culture medium. For drugs administered orally, pharmaceutically acceptable carriers include, but are not limited to pharmaceutically acceptable excipients such as inert diluents, disintegrating agents, binding agents, lubricating agents, sweetening agents, flavoring agents, coloring agents and preservatives. Suitable inert diluents include sodium and calcium carbonate, sodium and calcium phosphate, and lactose, while corn starch and alginic acid are suitable disintegrating agents. Binding agents may include starch and gelatin, while the lubricating agent, if present, will generally be magnesium stearate, stearic acid or talc. If desired, the tablets may be coated with a material such as glyceryl monostearate or glyceryl distearate, to delay absorption in the gastrointestinal tract. Agents included in drug formulations are described further herein below.

As used herein terms such as: “pharmacologically effective amount,” “therapeutically effective amount” and “effective amount” refers to that amount of a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention to produce the intended pharmacological, therapeutic or preventive result. For example, if a given clinical treatment is considered effective when there is at least a 10% reduction in a measurable parameter associated with a

disease or disorder, a therapeutically effective amount of a drug for the treatment of that disease or disorder is the amount necessary to effect at least a 10% reduction in that parameter. For example, a therapeutically effective amount of a HTT dsRNA agent or HTT antisense polynucleotide agent can reduce HTT polypeptide levels by at least 10%.

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Effective amounts

Methods of the invention, in some respects comprise contacting a cell with a HTT dsRNA agent or HTT antisense polynucleotide agent in an effective amount to reduce HTT gene expression in the contacted cell. Certain embodiments of methods of the invention comprise administering a HTT dsRNA agent or a HTT antisense polynucleotide agent to a subject in an amount effective to reduce HTT gene expression and treat a HTT-associated disease or condition in the subject. An “effective amount” used in terms of reducing expression of HTT and/or for treating a HTT-associated disease or condition, is an amount necessary or sufficient to realize a desired biologic effect. For example, an effective amount of a HTT dsRNA agent or HTT antisense polynucleotide agent to treat a HTT-associated disease or condition could be that amount necessary to (i) slow or halt progression of the disease or condition; or (ii) reverse, reduce, or eliminate one or more symptoms of the disease or condition. In some aspects of the invention, an effective amount is that amount of a HTT dsRNA agent or HTT antisense polynucleotide agent that when administered to a subject in need of a treatment of a HTT-associated disease or condition, results in a therapeutic response that prevents and/or treats the disease or condition. According to some aspects of the invention, an effective amount is that amount of a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention that when combined or co-administered with another therapeutic treatment for a HTT-associated disease or condition, results in a therapeutic response that prevents and/or treats the disease or condition. In some embodiments of the invention, a biologic effect of treating a subject with a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention may be the amelioration and or absolute elimination of symptoms resulting from the HTT-associated disease or condition. In some embodiments of the invention, a biologic effect is the complete abrogation of the HTT-associated disease or condition, as evidenced for example, by a diagnostic test that indicates the subject is free of the HTT-associated disease or condition. A non-limiting example of a physiological symptom that may be detected includes a reduction in HTT level in liver of a subject following administration of an agent of the invention. Additional art-known means of assessing the status of a HTT-associated disease or condition can be used to determine an effect of an agent and/or methods of the invention on a HTT-associated disease or condition.

Typically, an effective amount of a HTT dsRNA agent or HTT antisense polynucleotide agent to decrease HTT polypeptide activity to a level to treat a HTT-associated disease or condition will be determined in clinical trials, establishing an effective dose for a test population versus a control population in a blind study. In some embodiments, an effective amount will be that results in a desired response, e.g., an amount that diminishes a HTT-associated disease or

condition in cells, tissues, and/or subjects with the disease or condition. Thus, an effective amount of a HTT dsRNA agent or HTT antisense polynucleotide agent to treat a HTT-associated disease or condition that can be treated by reducing HTT polypeptide activity may be the amount that when administered decreases the amount of HTT polypeptide activity in the subject to an amount that is less than the amount that would be present in the cell, tissue, and/or subject without the administration of the HTT dsRNA agent or HTT antisense polynucleotide agent. In certain aspects of the invention the level of HTT polypeptide activity, and/or HTT gene expression present in a cell, tissue, and/or subject that has not been contacted with or administered a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention is referred to as a “control” amount. In some embodiments of methods of the invention a control amount for a subject is a pre-treatment amount for the subject, in other words, a level in a subject before administration of a HTT agent can be a control level for that subject and compared to a level of HTT polypeptide activity and/or HTT gene expression in the subject following siRNA administered to the subject. In the case of treating a HTT-associated disease or condition the desired response may be reducing or eliminating one or more symptoms of the disease or condition in the cell, tissue, and/or subject. The reduction or elimination may be temporary or may be permanent. It will be understood that the status of a HTT-associated disease or condition can be monitored using methods of determining HTT polypeptide activity, HTT gene expression, symptom evaluation, clinical testing, etc. In some aspects of the invention, a desired response to treatment of a HTT-associated disease or condition is delaying the onset or even preventing the onset of the disease or condition.

An effective amount of a compound that decreases HTT polypeptide activity may also be determined by assessing physiological effects of administration of a HTT dsRNA agent or HTT antisense polynucleotide agent on a cell or subject, such as a decrease of a HTT-associated disease or condition following administration. Assays and/or symptomatic monitoring of a subject can be used to determine efficacy of a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention, which may be administered in a pharmaceutical compound of the invention, and to determine the presence or absence of a response to the treatment. A non-limiting example, is that one or more art-known tests of a decrease in biological activity of HTT, e.g., or additional pathologies associated with elevated levels of HTT, preferably or the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P.

Some embodiments of the invention include methods of determining an efficacy of an dsRNA agent or HTT antisense polynucleotide agent of the invention administered to a subject, to treat a HTT-associated disease or condition by assessing and/or monitoring one or more “physiological characteristics” of the HTT-associated disease or condition in the subject. Non-limiting examples of physiological characteristics of a HTT-associated disease or condition are the HTT mRNA level, the HTT protein level, or the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P.

It will be understood that the amount of a HTT dsRNA agent or HTT antisense polynucleotide agent administered to a subject can be modified based, at least in part, on such determinations of disease and/or condition status and/or physiological characteristics determined for a subject. The amount of a treatment may be varied for example by increasing or decreasing the amount of a HTT-dsRNA agent or HTT antisense polynucleotide agent, by changing the composition in which the HTT dsRNA agent or HTT antisense polynucleotide agent, respectively, is administered, by changing the route of administration, by changing the dosage timing and so on. The effective amount of a HTT dsRNA agent or HTT antisense polynucleotide agent will vary with the particular condition being treated, the age and physical condition of the subject being treated; the severity of the condition, the duration of the treatment, the nature of the concurrent therapy (if any), the specific route of administration, and additional factors within the knowledge and expertise of the health practitioner. For example, an effective amount may depend upon the desired level of HTT polypeptide activity and or HTT gene expression that is effective to treat the HTT-associated disease or condition. A skilled artisan can empirically determine an effective amount of a particular HTT dsRNA agent or HTT antisense polynucleotide agent of the invention for use in methods of the invention without necessitating undue experimentation. Combined with the teachings provided herein, by selecting from among various HTT dsRNA agents or HTT antisense polynucleotide agents of the invention, and weighing factors such as potency, relative bioavailability, patient body weight, severity of adverse side-effects and preferred mode of administration, an effective prophylactic or therapeutic treatment regimen can be planned that is effective to treat the particular subject. As used in embodiments of the invention, an effective amount of a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention can be that amount that when contacted with a cell results in a desired biological effect in the cell.

It will be recognized that HTT gene silencing may be determined in any cell expressing HTT, either constitutively or by genomic engineering, and by any appropriate assay. In some embodiments of the invention, HTT gene expression is reduced by at least 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% by administration of a HTT dsRNA agent of the invention. In some embodiments of the invention, HTT gene expression is reduced by at between 5% and 10%, 5% and 25%, 10% and 50%, 10% and 75%, 25% and 75%, 25% and 100%, or 50% and 100% by administration of a HTT dsRNA agent of the invention.

Dosing

HTT dsRNA agents and HTT antisense polynucleotide agents are delivered in pharmaceutical compositions in dosages sufficient to inhibit expression of HTT genes. In certain embodiments of the invention, a dose of HTT dsRNA agent or HTT antisense polynucleotide agent is in a range of 0.01 to 200.0 milligrams per kilogram body weight of the recipient per day, generally in the range of 1 to 50 mg per kilogram body weight, 5 to 40 mg/kg

body weight, 10 to 30 mg/kg body weight, 1 to 20 mg/kg body weight, 1 to 10 mg/kg body weight, 4 to 15 mg/kg body weight per day, inclusive. For example, the HTT dsRNA agent or HTT antisense polynucleotide agent can be administered in an amount that is from about 0.01 mg/kg, 0.05 mg/kg, 0.1 mg/kg, 0.2 mg/kg, 0.3 mg/kg, 0.4 mg/kg, 0.5 mg/kg, 1 mg/kg, 1.1 mg/kg, 1.2 mg/kg, 1.3 mg/kg, 1.4 mg/kg, 1.5 mg/kg, 1.6 mg/kg, 1.7 mg/kg, 1.8 mg/kg, 1.9 mg/kg, 2 mg/kg, 2.1 mg/kg, 2.2 mg/kg, 2.3 mg/kg, 2.4 mg/kg, 2.5 mg/kg, 2.6 mg/kg, 2.7 mg/kg, 2.8 mg/kg, 2.9 mg/kg, 3.0 mg/kg, 3.1 mg/kg, 3.2 mg/kg, 3.3 mg/kg, 3.4 mg/kg, 3.5 mg/kg, 3.6 mg/kg, 3.7 mg/kg, 3.8 mg/kg, 3.9 mg/kg, 4 mg/kg, 4.1 mg/kg, 4.2 mg/kg, 4.3 mg/kg, 4.4 mg/kg, 4.5 mg/kg, 4.6 mg/kg, 4.7 mg/kg, 4.8 mg/kg, 4.9 mg/kg, 5 mg/kg, 5.1 mg/kg, 5.2 mg/kg, 5.3 mg/kg, 5.4 mg/kg, 5.5 mg/kg, 5.6 mg/kg, 5.7 mg/kg, 5.8 mg/kg, 5.9 mg/kg, 6 mg/kg, 6.1 mg/kg, 6.2 mg/kg, 6.3 mg/kg, 6.4 mg/kg, 6.5 mg/kg, 6.6 mg/kg, 6.7 mg/kg, 6.8 mg/kg, 6.9 mg/kg, 7 mg/kg, 7.1 mg/kg, 7.2 mg/kg, 7.3 mg/kg, 7.4 mg/kg, 7.5 mg/kg, 7.6 mg/kg, 7.7 mg/kg, 7.8 mg/kg, 7.9 mg/kg, 8 mg/kg, 8.1 mg/kg, 8.2 mg/kg, 8.3 mg/kg, 8.4 mg/kg, 8.5 mg/kg, 8.6 mg/kg, 8.7 mg/kg, 8.8 mg/kg, 8.9 mg/kg, 9 mg/kg, 9.1 mg/kg, 9.2 mg/kg, 9.3 mg/kg, 9.4 mg/kg, 9.5 mg/kg, 9.6 mg/kg, 9.7 mg/kg, 9.8 mg/kg, 9.9 mg/kg, 10 mg/kg, 11 mg/kg, 12 mg/kg, 13 mg/kg, 14 mg/kg, 15 mg/kg, 16 mg/kg, 17 mg/kg, 18 mg/kg, 19 mg/kg, 20 mg/kg, 21 mg/kg, 22 mg/kg, 23 mg/kg, 24 mg/kg, 25 mg/kg, 26 mg/kg, 27 mg/kg, 28 mg/kg, 29 mg/kg, 30 mg/kg, 31 mg/kg, 32 mg/kg, 33 mg/kg, 34 mg/kg, 35 mg/kg, 36 mg/kg, 37 mg/kg, 38 mg/kg, 39 mg/kg, 40 mg/kg, 41 mg/kg, 42 mg/kg, 43 mg/kg, 44 mg/kg, 45 mg/kg, 46 mg/kg, 47 mg/kg, 48 mg/kg, 49 mg/kg, through 50 mg/kg body per single dose.

Various factors may be considered in the determination of dosage and timing of delivery of a HTT dsRNA agent of the invention. The absolute amount of a HTT dsRNA agent or HTT antisense polynucleotide agent delivered will depend upon a variety of factors including a concurrent treatment, the number of doses and the individual subject parameters including age, physical condition, size and weight. These are factors well known to those of ordinary skill in the art and can be addressed with no more than routine experimentation. In some embodiments, a maximum dose can be used, that is, the highest safe dose according to sound medical judgment.

Methods of the invention may in some embodiments include administering to a subject 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more doses of a HTT dsRNA agent or HTT antisense polynucleotide agent. In some instances, a pharmaceutical compound, (e.g., comprising a HTT dsRNA agent or comprising a HTT antisense polynucleotide agent) can be administered to a subject at least daily, every other day, weekly, every other week, monthly, etc. Doses may be administered once per day or more than once per day, for example, 2, 3, 4, 5, or more times in one 24-hour period. A pharmaceutical composition of the invention may be administered once daily, or the HTT dsRNA agent or HTT antisense polynucleotide agent may be administered as two, three, or more sub-doses at appropriate intervals throughout the day or even using continuous infusion or delivery through a controlled release formulation. In some embodiments of methods of the invention, a pharmaceutical composition of the invention is administered to a subject one or

more times per day, one or more times per week, one or more times per month, or one or more times per year.

Methods of the invention, in some aspects, include administration of a pharmaceutical compound alone, in combination with one or more other HTT dsRNA agents or HTT antisense polynucleotide agents, and/or in combination with other drug therapies or treatment activities or regimens that are administered to subjects with a HTT-associated disease or condition. Pharmaceutical compounds may be administered in pharmaceutical compositions. Pharmaceutical compositions used in methods of the invention may be sterile and contain an amount of a HTT dsRNA agent or HTT antisense polynucleotide agent that will reduce activity of a HTT polypeptide to a level sufficient to produce the desired response in a unit of weight or volume suitable for administration to a subject. A dose administered to a subject of a pharmaceutical composition that includes a HTT dsRNA agent or HTT antisense polynucleotide agent to reduce HTT protein activity can be chosen in accordance with different parameters, in particular in accordance with the mode of administration used and the state of the subject. Other factors include the desired period of treatment. In the event that a response in a subject is insufficient at the initial doses applied, higher doses (or effectively higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits.

Treatment

As used herein, “HTT-associated disease”, “HTT-associated diseases and conditions” and “diseases and conditions caused and/or modulated by HTT” is intended to include any disease associated with the HTT gene or protein. Such diseases may be caused, for example, by overproduction of HTT protein, by mutation of the HTT gene, by abnormal cleavage of the HTT protein, by abnormal interaction between HTT and other proteins or other endogenous or exogenous substances. Exemplary HTT -associated diseases is HD (Huntington's disease).

As used herein, “symptom” or “hallmark” means any physical feature or test result that indicates the existence or extent of a disease or disorder. In certain embodiments, a symptom is apparent to a subject or to a medical professional examining or testing the subject. In certain embodiments, a hallmark is apparent upon invasive diagnostic testing, including, but not limited to, abnormal body movements called chorea and lack of coordination.

In certain aspects of the invention, a subject may be administered a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention at a time that is one or more of before or after diagnosis of a HTT-associated disease or condition. In some aspects of the invention, a subject is at risk of having or developing a HTT-associated disease or condition. A subject at risk of developing a HTT-associated disease or condition is one who has an increased probability of developing the HTT-associated disease or condition, compared to a control risk of developing the HTT-associated disease or condition. In some embodiments of the invention, a level of risk may be statistically significant compared to a control level of risk. A subject at risk may include, for instance, a subject who is, or will be, a subject who has a preexisting disease and/or a genetic

abnormality that makes the subject more susceptible to a HTT-associated disease or condition than a control subject without the preexisting disease or genetic abnormality; a subject having a family and/or personal medical history of the HTT-associated disease or condition; and a subject who has previously been treated for a HTT-associated disease or condition. It will be understood that a preexisting disease and/or a genetic abnormality that makes the subject more susceptible to a HTT-associated disease or condition, may be a disease or genetic abnormality that when present has been previously identified as having a correlative relation to a higher likelihood of developing a HTT-associated disease or condition.

It will be understood that a HTT dsRNA agent or HTT antisense polynucleotide agent may be administered to a subject based on a medical status of the individual subject. For example, a health-care provider for a subject may assess a HTT level measured in a sample obtained from a subject and determine it is desirable to reduce the subject's HTT level, by administration of a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention. In this example, the HTT level may be considered to be a physiological characteristic of a HTT-associated condition, even if the subject is not diagnosed as having a HTT-associated disease such as one disclosed herein. A healthcare provider may monitor changes in the subject's HTT level, as a measure of efficacy of the administered HTT dsRNA agent or HTT antisense polynucleotide agent of the invention. In a non-limiting example, a biological sample, such as a blood, serum sample may be obtained from a subject and a HTT level for the subject determined in the sample. A HTT dsRNA agent or HTT antisense polynucleotide agent is administered to the subject and a blood sample is obtained from the subject following the administration and the HTT level determined using the sample and the results compared to the results determined in the subject's pre-administration (prior) sample. A reduction in the subject's HTT level in the later sample compared to the pre-administration level indicates the administered HTT dsRNA agent or HTT antisense polynucleotide agent efficacy in reducing the lipid level in the subject. Certain embodiments of methods of the invention include adjusting a treatment that includes administering a dsRNA agent or a HTT antisense polynucleotide agent of the invention to a subject based at least in part on assessment of a change in one or more of the subject's physiological characteristics of a HTT-associated disease or condition resulting from the treatment. For example, in some embodiments of the invention, an effect of an administered dsRNA agent or HTT antisense polynucleotide agent of the invention may be determined for a subject and used to assist in adjusting an amount of a dsRNA agent or HTT antisense polynucleotide agent of the invention subsequently administered to the subject. In a non-limiting example, a subject is administered a dsRNA agent or HTT antisense polynucleotide agent of the invention, the subject's HTT level is determined after the administration, and based at least in part on the determined level, a greater amount of the dsRNA agent or HTT antisense polynucleotide agent is determined to be desirable in order to increase the physiological effect of the administered agent, for example to reduce or further reduce the subject's HTT level. In another non-limiting example, a subject is administered a dsRNA agent or HTT antisense

polynucleotide agent of the invention, the subject's HTT level is determined after the administration and based at least in part on the determined level, a lower amount of the dsRNA agent or HTT antisense polynucleotide agent is desirable to administer to the subject.

Thus, some embodiments of the invention include assessing a change in one or more physiological characteristics of resulting from a subject's previous treatment to adjust an amount of a dsRNA agent or HTT antisense polynucleotide agent of the invention subsequently administered to the subject. Some embodiments of methods of the invention include 1, 2, 3, 4, 5, 6, or more determinations of a physiological characteristic of a HTT-associated disease or condition to assess and/or monitor the efficacy of an administered HTT dsRNA agent or HTT antisense polynucleotide agent of the invention, and optionally using the determinations to adjust one or more of: a dose, administration regimen, and or administration frequency of a dsRNA agent or HTT antisense polynucleotide agent of the invention to treat a HTT-associated disease or condition in a subject. In some embodiments of methods of the invention, a desired result of administering an effective amount of a dsRNA agent or HTT antisense polynucleotide agent of the invention to a subject is a reduction of the subject's the HTT mRNA level, the HTT protein level in the subject, or the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P in the subject.

As used herein, the terms "treat", "treated", or "treating" when used with respect to a HTT-associated disease or condition may refer to a prophylactic treatment that decreases the likelihood of a subject developing the HTT-associated disease or condition, and also may refer to a treatment after the subject has developed a HTT-associated disease or condition in order to eliminate or reduce the level of the HTT-associated disease or condition, prevent the HTT-associated disease or condition from becoming more advanced (e.g., more severe), and/or slow the progression of the HTT-associated disease or condition in a subject compared to the subject in the absence of the therapy to reduce activity in the subject of HTT polypeptide.

Certain embodiments of agents, compositions, and methods of the invention can be used to inhibit HTT gene expression. As used herein in reference to expression of a HTT gene, the terms "inhibit," "silence," "reduce," "down-regulate," and "knockdown" mean the expression of the HTT gene, as measured by one or more of: a level of RNA transcribed from the gene, a level of activity of HTT expressed, and a level of HTT polypeptide, protein or protein subunit translated from the mRNA in a cell, group of cells, tissue, organ, or subject in which the HTT gene is transcribed, is reduced when the cell, group of cells, tissue, organ, or subject is contacted with (e.g., treated with) a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention, compared to a control level of RNA transcribed from the HTT gene, a level of activity of expressed HTT, or a level of HTT translated from the MRNA, respectively. In some embodiments, a control level is a level in a cell, tissue, organ or subject that has not been contacted with (e.g., treated with) the HTT dsRNA agent or HTT antisense polynucleotide agent.

Administration methods

A variety of administration routes for a HTT dsRNA agent or HTT antisense polynucleotide agent are available for use in methods of the invention. The particular delivery mode selected will depend at least in part, upon the particular condition being treated and the dosage required for therapeutic efficacy. Methods of this invention, generally speaking, may be practiced using any mode of administration that is medically acceptable, meaning any mode that produces effective levels of treatment of a HTT-associated disease or condition without causing clinically unacceptable adverse effects. In some embodiments of the invention, a HTT dsRNA agent or HTT antisense polynucleotide agent may be administered via an oral, enteral, mucosal, subcutaneous, and/or parenteral route. The term “parenteral” includes subcutaneous, intravenous, intrathecal, intramuscular, intraperitoneal, and intrasternal injection, or infusion techniques. Other routes include but are not limited to nasal (e.g., via a gastro-nasal tube), dermal, vaginal, rectal, sublingual, and inhalation. Delivery routes of the invention may include intrathecal, intraventricular, or intracranial. In some embodiments of the invention, a HTT dsRNA agent or HTT antisense polynucleotide agent may be placed within a slow-release matrix and administered by placement of the matrix in the subject. In some aspects of the invention, a HTT dsRNA agent or HTT antisense polynucleotide agent may be delivered to a subject cell using nanoparticles coated with a delivery agent that targets a specific cell or organelle. Various delivery means, methods, agents are known in the art. Non-limiting examples of delivery methods and delivery agents are additionally provided elsewhere herein. In some aspects of the invention, the term “delivering” in reference to a HTT dsRNA agent or HTT antisense polynucleotide agent may mean administration to a cell or subject of one or more “naked” HTT dsRNA agent or HTT antisense polynucleotide agent sequences and in certain aspects of the invention “delivering” means administration to a cell or subject via transfection means, delivering a cell comprising a HTT dsRNA agent or HTT antisense polynucleotide agent to a subject, delivering a vector encoding a HTT dsRNA agent or HTT antisense polynucleotide agent into a cell and/or subject, etc. Delivery of a HTT dsRNA agent or HTT antisense polynucleotide agent using a transfection means may include administration of a vector to a cell and/or subject.

In some methods of the invention one or more HTT dsRNA agents or HTT antisense polynucleotide agents may be administered in formulations, which may be administered in pharmaceutically acceptable solutions, which may routinely contain pharmaceutically acceptable concentrations of salt, buffering agents, preservatives, compatible carriers, adjuvants, and optionally other therapeutic ingredients. In some embodiments of the invention a HTT dsRNA agent or HTT antisense polynucleotide agent may be formulated with another therapeutic agent for simultaneous administration. According to methods of the invention, a HTT dsRNA agent or HTT antisense polynucleotide agent may be administered in a pharmaceutical composition. In general, a pharmaceutical composition comprises a HTT dsRNA agent or HTT antisense polynucleotide agent and optionally, a pharmaceutically acceptable carrier. Pharmaceutically acceptable carriers are well-known to those of ordinary

skill in the art. As used herein, a pharmaceutically acceptable carrier means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredients, e.g., the ability of the HTT dsRNA agent or HTT antisense polynucleotide agent to inhibit HTT gene expression in a cell or subject. Numerous methods to administer and deliver dsRNA agents or HTT antisense polynucleotide agents for therapeutic use are known in the art and may be utilized in methods of the invention.

Pharmaceutically acceptable carriers include diluents, fillers, salts, buffers, stabilizers, solubilizers and other materials that are well-known in the art. Exemplary pharmaceutically acceptable carriers are described in U.S. Pat. No. 5,211,657 and others are known by those skilled in the art. Such preparations may routinely contain salt, buffering agents, preservatives, compatible carriers, and optionally other therapeutic agents. When used in medicine, the salts should be pharmaceutically acceptable, but non-pharmaceutically acceptable salts may conveniently be used to prepare pharmaceutically acceptable salts thereof and are not excluded from the scope of the invention. Such pharmacologically and pharmaceutically acceptable salts include, but are not limited to, those prepared from the following acids: hydrochloric, hydrobromic, sulfuric, nitric, phosphoric, maleic, acetic, salicylic, citric, formic, malonic, succinic, and the like. Also, pharmaceutically acceptable salts can be prepared as alkaline metal or alkaline earth salts, such as sodium, potassium or calcium salts.

Some embodiments of methods of the invention include administering one or more HTT dsRNA agents or HTT antisense polynucleotide agents directly to a tissue. In some embodiments, the tissue to which the compound is administered is a tissue in which the HTT-associated disease or condition is present or is likely to arise, non-limiting examples of which are the heart. Direct tissue administration may be achieved by direct injection or other means. Many orally delivered compounds naturally travel to and through the liver, brain, and some other organs. Some embodiments of treatment methods of the invention include oral administration of one or more HTT dsRNA agents to a subject. HTT dsRNA agents or HTT antisense polynucleotide agents, either alone or in conjunction with other therapeutic agents, may be administered once, or alternatively they may be administered in a plurality of administrations. If administered multiple times, the HTT dsRNA agent or HTT antisense polynucleotide agent may be administered via different routes. For example, though not intended to be limiting, a first (or first several) administrations may be made via subcutaneous means and one or more additional administrations may be oral and/or systemic administrations. In some embodiments, the dsRNA agent is administered to the subject subcutaneously. In certain embodiments, the dsRNA agent is administered to the subject by IV administration. In some embodiments, the dsRNA agent is administered to the subject by intrathecally. In some embodiments, the dsRNA agent is administered to the subject by intracerebroventricular (ICV) injection. In yet another embodiment, the dsRNA agent is administered to the subject intrastriatal (IS) injection. A non-limiting exemplary intracisternal administration comprises an injection into the cisterna magna (cerebellomedullary cistern) by suboccipital puncture. In certain embodiments, the dsRNA is

administered by intracerebroventricular (ICV) injection, intrastriatal (IS) injection, intravenous (IV) injection, subcutaneous (SQ) injection, or a combination thereof.

For embodiments of the invention in which it is desirable to administer a HTT dsRNA agent or HTT antisense polynucleotide agent systemically, the HTT dsRNA agent or HTT antisense polynucleotide agent may be formulated for parenteral administration by injection, e.g., by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, e.g., in ampoules or in multi-dose containers, with or without an added preservative. HTT dsRNA agent formulations (also referred to as pharmaceutical compositions) may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

Preparations for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. Parenteral vehicles include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's, or fixed oils. Intravenous vehicles include fluid and nutrient replenishers, electrolyte replenishers (such as those based on Ringer's dextrose), and the like. Preservatives and other additives may also be present such as, for example, antimicrobials, anti-oxidants, chelating agents, and inert gases and the like. Lower doses will result from other forms of administration, such as intravenous administration. In the event that a response in a subject is insufficient at the initial doses applied, higher doses (or effectively higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits. Multiple doses per day may be used as needed to achieve appropriate systemic or local levels of one or more HTT dsRNA agents or HTT antisense polynucleotide agents and to achieve appropriate reduction in HTT protein activity.

In yet other embodiments, methods of the invention include use of a delivery vehicle such as biocompatible microparticle, nanoparticle, or implant suitable for implantation into a recipient, e.g., a subject. Exemplary bioerodible implants that may be useful in accordance with this method are described in PCT Publication No. WO 95/24929 (incorporated by reference herein), which describes a biocompatible, biodegradable polymeric matrix for containing a biological macromolecule.

Both non-biodegradable and biodegradable polymeric matrices can be used in methods of the invention to deliver one or more HTT dsRNA agents or HTT antisense polynucleotide agents to a subject. In some embodiments, a matrix may be biodegradable. Matrix polymers may be natural or synthetic polymers. A polymer can be selected based on the period of time over which release is desired, generally in the order of a few hours to a year or longer. Typically, release over a period ranging from between a few hours and three to twelve months can be used. The polymer optionally is in the form of a hydrogel that can absorb up to about 90% of its weight in water and further, optionally is cross-linked with multivalent ions or other polymers.

In general, HTT dsRNA agents or HTT antisense polynucleotide agents may be delivered in some embodiments of the invention using the bioerodible implant by way of diffusion, or by degradation of the polymeric matrix. Exemplary synthetic polymers for such use are well known in the art. Biodegradable polymers and non-biodegradable polymers can be used for delivery of HTT dsRNA agents or HTT antisense polynucleotide agents using art-known methods. Bioadhesive polymers such as bioerodible hydrogels (see H. S. Sawhney, C. P. Pathak and J. A. Hubbell in *Macromolecules*, 1993, 26, 581-587, the teachings of which are incorporated by reference herein) may also be used to deliver HTT dsRNA agents or HTT antisense polynucleotide agents for treatment of a HTT-associated disease or condition. Additional suitable delivery systems can include time-release, delayed release or sustained release delivery systems. Such systems can avoid repeated administrations of a HTT dsRNA agent or HTT antisense polynucleotide agent, increasing convenience to the subject and the medical care professional. Many types of release delivery systems are available and known to those of ordinary skill in the art. (See for example: U.S. Pat. Nos. 5,075,109; 4,452,775; 4,675,189; 5,736,152; 3,854,480; 5,133,974; and 5,407,686 (the teaching of each of which is incorporated herein by reference). In addition, pump-based hardware delivery systems can be used, some of which are adapted for implantation.

Use of a long-term sustained release implant may be suitable for prophylactic treatment of subjects and for subjects at risk of developing a recurrent HTT-associated disease or condition. Long-term release, as used herein, means that the implant is constructed and arranged to deliver a therapeutic level of a HTT dsRNA agent or HTT antisense polynucleotide agent for at least up to 10 days, 20 days, 30 days, 60 days, 90 days, six months, a year, or longer. Long-term sustained release implants are well-known to those of ordinary skill in the art and include some of the release systems described above.

Therapeutic formulations of HTT dsRNA agents or HTT antisense polynucleotide agents may be prepared for storage by mixing the molecule or compound having the desired degree of purity with optional pharmaceutically acceptable carriers, excipients or stabilizers [Remington's *Pharmaceutical Sciences* 21st edition, (2006)], in the form of lyophilized formulations or aqueous solutions. Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride, benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium;

metal complexes (e.g., Zn-protein complexes); and/or non-ionic surfactants such as TWEEN®, PLURONICS® or polyethylene glycol (PEG).

Cells, Subjects, and Controls

5 Methods of the invention may be used in conjunction with cells, tissues, organs and/or subjects. In some aspects of the invention a subject is a human or vertebrate mammal including but not limited to a dog, cat, horse, cow, goat, mouse, rat, and primate, e.g., monkey. Thus, the invention can be used to treat HTT-associated diseases or conditions in human and non-human subjects. In some aspects of the invention a subject may be a farm animal, a zoo animal, a
10 domesticated animal or non-domesticated animal and methods of the invention can be used in veterinary prevention and treatment regimens. In some embodiments of the invention, the subject is a human and methods of the invention can be used in human prevention and treatment regimens.

 Non-limiting examples of subjects to which the present invention can be applied are
15 subjects who are diagnosed with, suspected of having, or at risk of having a disease or condition associated with a higher than desirable HTT expression and/or activity, also referred to as “elevated levels of HTT expression”. Non-limiting examples of diseases and conditions associated with a higher than desirable levels of HTT expression and/or activity are described elsewhere herein. Methods of the invention may be applied to a subject who, at the time of
20 treatment, has been diagnosed as having the disease or condition associated with a higher than desirable HTT expression and/or activity, or a subject who is considered to be at risk for having or developing a disease or condition associated with a higher than desirable HTT expression and/or activity. In some aspects of the invention a disease or condition associated with a higher than desirable HTT level of expression and/or activity is an acute disease or condition, and in
25 certain aspects of the invention a disease or condition associated with a higher than desirable HTT level of expression and/or activity is a chronic disease or condition.

 In a non-limiting example, a HTT dsRNA agent of the invention is administered to a subject diagnosed with, suspected of having, or at risk of having, statin resistant hypercholesterolemia, which is a disease in which it is desirable to reduce HTT expression.
30 Methods of the invention may be applied to the subject who, at the time of treatment, has been diagnosed as having the disease or condition, or a subject who is considered to be at risk for having or developing the disease or condition.

 In another non-limiting example, a HTT dsRNA agent of the invention is administered to a subject diagnosed with HD, which is a disease in which it is desirable to reduce HTT
35 expression. Methods of the invention may be applied to the subject who, at the time of treatment, has been diagnosed as having the disease or condition, or a subject who is considered to be at risk for having or developing the disease or condition.

 A cell to which methods of the invention may be applied include cells that are *in vitro*, *in vivo*, *ex vivo* cells. Cells may be in a subject, in culture, and/or in suspension, or in any other

suitable state or condition. A cell to which a method of the invention may be applied can be a liver cell, a hepatocyte, a cardiac cell, a pancreatic cell, a cardiovascular cell, kidney cell or other type of vertebrate cell, including human and non-human mammalian cells. In certain aspects of the invention, a cell to which methods of the invention may be applied is a healthy, normal cell
5 that is not known to be a disease cell. In certain embodiments of the invention a cell to which methods and compositions of the invention are applied to a liver cell, a hepatocyte, a cardiac cell, a pancreatic cell, a cardiovascular cell, a CNS cell, and/or a kidney cell. In certain aspects of the invention, a control cell is a normal cell, but it will be understood that a cell having a disease or condition may also serve as a control cell in particular circumstances for example to compare
10 results in a treated cell having a disease or condition versus an untreated cell having the disease or condition, etc.

A level of HTT polypeptide activity can be determined and compared to control level of HTT polypeptide activity, according to methods of the invention. A control may be a predetermined value, which can take a variety of forms. It can be a single cut-off value, such
15 as a median or mean. It can be established based upon comparative groups, such as in groups having normal levels of HTT polypeptide and/or HTT polypeptide activity and groups having increased levels of HTT polypeptide and/or HTT polypeptide activity. Another non-limiting example of comparative groups may be groups having one or more symptoms of or a diagnosis of a HTT-associated disease or condition; groups without having one or more symptoms of or a
20 diagnosis of the disease or condition; groups of subjects to whom an siRNA treatment of the invention has been administered; groups of subjects to whom an siRNA treatment of the invention has not been administered. Typically, a control may be based on apparently healthy normal individuals in an appropriate age bracket or apparently healthy cells. It will be understood that controls according to the invention may be, in addition to predetermined values,
25 samples of materials tested in parallel with the experimental materials. Examples include samples from control populations or control samples generated through manufacture to be tested in parallel with the experimental samples. In some embodiments of the invention, a control may include a cell or subject not contacted or treated with a HTT dsRNA agent of the invention and in such instances, a control level of HTT polypeptide and/or HTT polypeptide activity can
30 be compared to a level of HTT polypeptide and/or HTT polypeptide activity in a cell or subject contacted with a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention.

In some embodiments of the invention a level of HTT polypeptide determined for a subject can be a control level against which a level of HTT polypeptide determined for the same subject at a different time is compared. In a non-limiting example, a level of HTT is determined
35 in a biological sample obtained from a subject who has not been administered a HTT treatment of the invention. In some embodiments, the biological sample is a serum sample. The level of HTT polypeptide determined in the sample obtained from the subject can serve as a baseline or control value for the subject. After one or more administrations of a HTT dsRNA agent to the subject in a treatment method of the invention, one or more additional serum samples can be

obtained from the subject and the level of HTT polypeptide in the subsequent sample or samples can be compared to the control/baseline level for the subject. Such comparisons can be used to assess onset, progression, or recession of a HTT associated disease or condition in the subject. For example, a level of HTT polypeptide in the baseline sample obtained from the subject that is higher than a level obtained from the same subject after the subject has been administered a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention indicates regression of the HTT-associated disease or condition and indicates efficacy of the administered HTT dsRNA agent of the invention for treatment of the HTT-associated disease or condition.

In some aspects of the invention, values of one or more of a level of HTT polypeptide and/or HTT polypeptide activity determined for a subject may serve as control values for later comparison of levels of HTT polypeptide and/or HTT activity, in that same subject, thus permitting assessment of changes from a “baseline” HTT polypeptide activity in a subject. Thus, an initial HTT polypeptide level and/or initial HTT polypeptide activity level may be present and/or determined in a subject and methods and compounds of the invention may be used to decrease the level of HTT polypeptide and/or HTT polypeptide activity in the subject, with the initial level serving as a control level for that subject.

Using methods of the invention, HTT dsRNA agents and/or HTT antisense polynucleotide agents of the invention may be administered to a subject. Efficacy of the administration and treatment of the invention can be assessed when a level of HTT polypeptide in a serum sample obtained from a subject is decreased by at least 0.5%, 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or more compared to a pre-administration level of HTT polypeptide in a serum sample obtained from the subject at a prior time point, or compared to a non-contacted control level, for example a level of HTT polypeptide in a control serum sample. It will be understood that a level of HTT polypeptide and a level of HTT polypeptide activity both correlate with a level of HTT gene expression. Certain embodiments of methods of the invention comprise administering a HTT dsRNA and/or HTT antisense agent of the invention to a subject in an amount effective to inhibit HTT gene expression and thereby reduce a level of HTT polypeptide and reduce a level of HTT polypeptide activity in the subject.

Some embodiments of the invention, include determining presence, absence, and/or an amount (also referred to herein as a level) of HTT polypeptide in one or more biological samples obtained from one or more subjects. The determination can be used to assess efficacy of a treatment method of the invention. For example, methods and compositions of the invention can be used to determine a level of HTT polypeptide in a biological sample obtained from a subject previously treated with administration of a HTT dsRNA agent and/or a HTT antisense agent of the invention. A level of HTT polypeptide determined in a serum sample obtained from the treated subject that is lower by at least 0.5%, 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or more compared to a pretreatment level of HTT polypeptide determined for the subject, or compared to a non-contacted control biological sample level, indicates a level of efficacy of the treatment administered to the subject.

In some embodiments of the invention a physiological characteristic of a HTT-associated disease or condition determined for a subject can be a control determination against which a determination of the physiological characteristic in the same subject at a different time is compared. In a non-limiting example, a physiological characteristic such as the reduction in the expression of HTT may also be assessed indirectly by measuring a decrease in biological activity of HTT, e.g., or additional pathologies associated with elevated levels of HTT, preferably in the blood, serum. In a non-limiting example, a physiological characteristic such as at least one indicia of abnormal body movements called chorea and lack of coordination.

The HTT mRNA level (and/or other physiological characteristic of a HTT disease or condition) determined in the sample obtained from the subject can serve as a baseline or control value for the subject. After one or more administrations of a HTT dsRNA agent to the subject in a treatment method of the invention, one or more additional serum samples can be obtained from the subject and HTT mRNA level and/or HTT protein level in the subsequent sample or samples are compared to the control/baseline level and/or ratio, respectively, for the subject. Such comparisons can be used to assess onset, progression, or recession of a HTT associated disease or condition in the subject. For example, HTT mRNA level in the baseline sample obtained from the subject that is higher than HTT mRNA level determined in a sample obtained from the same subject after the subject has been administered a HTT dsRNA agent or HTT antisense polynucleotide agent of the invention indicates regression of the HTT-associated disease or condition and indicates efficacy of the administered HTT dsRNA agent of the invention for treatment of the HTT-associated disease or condition.

In some aspects of the invention, values of one or more of a physiological characteristic of a HTT-associated disease or condition determined for a subject may serve as control values for later comparison of the physiological characteristics in that same subject, thus permitting assessment of changes from a “baseline” physiological characteristic in a subject. Thus, an initial physiological characteristic may be present and/or determined in a subject and methods and compounds of the invention may be used to decrease the level of HTT polypeptide and/or HTT polypeptide activity in the subject, with the initial physiological characteristic determination serving as a control for that subject.

Using methods of the invention, HTT dsRNA agents and/or HTT antisense polynucleotide agents of the invention may be administered to a subject in an effective amount to treat a HTT disease or condition. Efficacy of the administration and treatment of the invention can be assessed by determining a change in one or more physiological characteristics of the HTT disease or condition. In a non-limiting example, a HTT mRNA level in a serum sample obtained from a subject is decreased by at least 0.5%, 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or more compared to a pre-administration lipid in a serum sample obtained from the subject at a prior time point, or compared to a non-contacted control level, for example HTT mRNA level in a control serum sample. It will be understood that the HTT mRNA level, the HTT protein level in the subject, or the lipid level. Certain embodiments

of methods of the invention comprise administering a HTT dsRNA and/or HTT antisense agent of the invention to a subject in an amount effective to inhibit HTT gene expression and thereby reduce the HTT mRNA level, the HTT protein level in the subject, or otherwise positively impact a physiological characteristic of a HTT-associated disease or condition in the subject.

- 5 Some embodiments of the invention, include determining presence, absence, and/or a change in a physiological characteristic of a HTT-associated disease or condition using methods such as but not limited to: (1) assessing one or more biological samples obtained from one or more subjects for the physiological characteristic; (2) imaging a subject (for example but not limited to obtaining a liver image); and (3) or physical examination of the subject. The
10 determination can be used to assess efficacy of a treatment method of the invention.

Kits

- Also within the scope of the invention are kits that comprise one or more HTT dsRNA agents and/or HTT antisense polynucleotide agents and instructions for its use in methods of the
15 invention. Kits of the invention may include one or more of a HTT dsRNA agent, HTT sense polynucleotide, and HTT antisense polynucleotide agent that may be used to treat a HTT-associated disease or condition. Kits containing one or more HTT dsRNA agents, HTT sense polynucleotides, and HTT antisense polynucleotide agents can be prepared for use in treatment methods of the invention. Components of kits of the invention may be packaged either in
20 aqueous medium or in lyophilized form. A kit of the invention may comprise a carrier being compartmentalized to receive in close confinement therein one or more container means or series of container means such as test tubes, vials, flasks, bottles, syringes, or the like. A first container means or series of container means may contain one or more compounds such as a HTT dsRNA agent and/or HTT sense or antisense polynucleotide agent. A second container
25 means or series of container means may contain a targeting agent, a labelling agent, a delivery agent, etc. that may be included as a portion of a HTT dsRNA agent and/or HTT antisense polynucleotide to be administered in an embodiment of a treatment method of the invention.

- A kit of the invention may also include instructions. Instructions typically will be in written form and will provide guidance for carrying-out a treatment embodied by the kit and
30 for making a determination based upon that treatment.

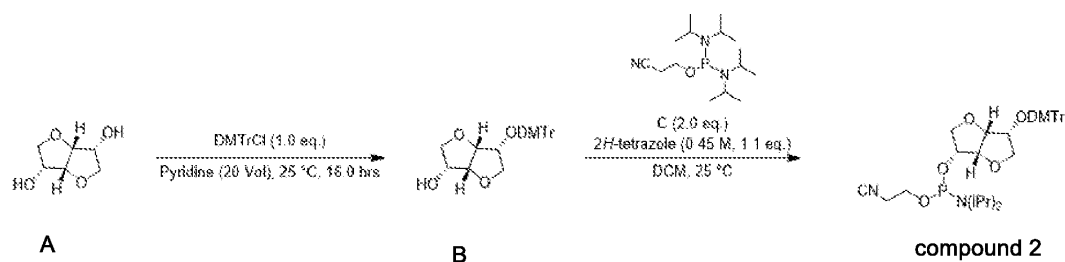
- The following examples are provided to illustrate specific instances of the practice of the present invention and are not intended to limit the scope of the invention. As will be apparent to one of ordinary skill in the art, the present invention will find application in a variety of compositions and methods.

35

Examples

Example 1.

Phosphoramidite Compound 2 (isomannide residues (imann) Phosphoramidite)



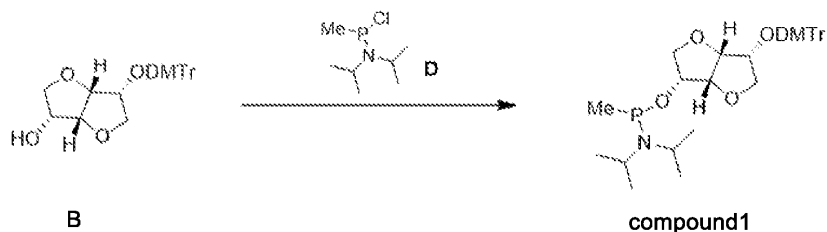
DMTrCl (232 g, 684 mmol, 1.0 *eq*) in pyridine (400 mL) was added to the solution of isomannide compound **A** (100 g, 684 mmol, 1.0 *eq*) in pyridine (600 mL), and the mixture was stirred at 25 °C for 12 hrs. LC-MS showed compound **A** was consumed completely and one main peak with desired mass was detected. The resulting reaction mixture was diluted with water (500 mL), extracted with DCM (500 mL *2), and the combined organic phases were washed with brine (500 mL), dried over Na₂SO₄ and concentrated in vacuum to get the residue. The residue was purified by column chromatography (DCM/MeOH=100/1 to 50/1, 0.1% Et₃N) to give compound **B** (150 g, 48.9% yield) a yellow solid.

¹H NMR: EC4783-404-P1B1_C (400 MHz, DMSO-*d*₆) δ ppm 7.46 (br d, *J*=7.63 Hz, 2 H) 7.28 - 7.37 (m, 6 H) 7.19 - 7.25 (m, 1 H) 6.90 (br d, *J*=7.88 Hz, 4 H) 4.70 (d, *J*=6.50 Hz, 1 H) 3.99 - 4.09 (m, 6 H) 3.88 - 3.96 (m, 2 H) 3.83 (br dd, *J*=7.82, 6.94 Hz, 1 H) 3.74 (s, 6 H) 3.41 (br t, *J*=8.13 Hz, 1 H) 3.05 (t, *J*=8.44 Hz, 1 H) 2.85 (br t, *J*=7.50 Hz, 1 H).

To a solution of compound **B** (80.0 g, 178 mmol, 1.0 *eq*) in DCM (800 mL) at 25 °C under N₂ atmosphere was added dropwise 2H-tetrazole (0.45 M, 436 mL, 1.1 *eq*), then compound **C** (80.6 g, 267 mmol, 85.0 mL, 1.5 *eq*) in DCM (200 mL) was added dropwise to the mixture. The reaction mixture was stirred at 25 °C under for 1.0 hr. LC-MS showed compound **B** was consumed completely and one main peak with desired mass was detected. The resulting reaction mixture was cooled to -20 °C and poured into ice cold sat. NaHCO₃ (500 mL), extracted with DCM (500 mL *3), the combined organic layers were washed with sat. NaHCO₃/brine=1:1 (300 mL/300 mL), dried over Na₂SO₄ and concentrated in vacuum (35 °C) to get the residue (100 mL). The residue was purified by column chromatography (Al₂O₃, DCM/MeOH=100/1 to 50/1, 0.1% Et₃N) to give compound2 (77 g, 119 mmol, 66.5% yield) as a white solid.

¹H NMR: EC4783-423-P1B1_C (400 MHz, DMSO-*d*₆) δ ppm 7.22 (br d, *J*=7.50 Hz, 2 H) 7.05 - 7.14 (m, 6 H) 6.96 - 7.02 (m, 1 H) 6.67 (br dd, *J*=8.82, 1.81 Hz, 4 H) 3.95 - 4.07 (m, 2 H) 3.73 - 3.83 (m, 1 H) 3.62 - 3.72 (m, 2 H) 3.48 - 3.53 (m, 6 H) 3.27 - 3.37 (m, 3 H) 3.11 (s, 6 H) 2.82 (td, *J*=8.54, 2.31 Hz, 1 H) 2.47 - 2.63 (m, 3 H) 2.28 (br d, *J*=1.63 Hz, 3 H) 0.82 - 1.00 (m, 13 H).

Phosphoramidite Compound 1



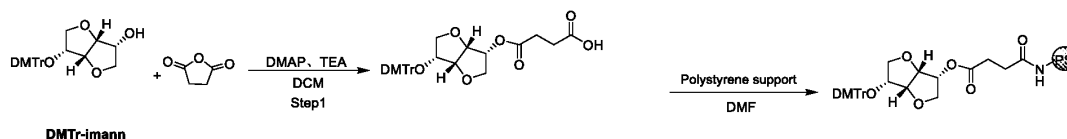
To a solution of compound **B** (500 mg, 1.11 mmol, 1.0 eq) in DCM (5.0 mL) was added compound **D** (607 mg, 3.34 mmol, 3.0 eq) and DIEA (432 mg, 3.34 mmol, 582 μ L, 3.0 eq) under N_2 atmosphere at 0-5 $^{\circ}$ C, the mixture was stirred at 25 $^{\circ}$ C for 1.0 hrs. LC-MS showed Compound **B** was consumed completely, several new peaks were shown on LC-MS and ~70.9% of desired compound was detected. The resulting reaction mixture was cooled to -20 $^{\circ}$ C and poured into cold (0-5 $^{\circ}$ C) sat.NaHCO₃ (5.0 mL) solution, extracted with DCM (5.0 mL *2), the combined organic layers were washed with cold (0-5 $^{\circ}$ C) sat.NaHCO₃/brine =1:1 (5.0 mL/5.0 mL), dried over Na₂SO₄ and concentrated in vacuum to get the residue (~5 mL). The residue was purified by column chromatography (alkaline Al₂O₃, Petroleum ether/Ethyl acetate=10/1 to 5/1, 0.1% Et₃N) to give compound **1** (280 mg, 471 μ mol, 42.3% yield) was obtained as a white solid.

¹H NMR: EC10615-49-P1N (400 MHz, DMSO-*d*₆) δ ppm 7.44 (br d, *J*=7.63 Hz, 2 H), 7.31 (br t, *J*=7.94 Hz, 6 H), 7.18 - 7.26 (m, 1 H), 6.89 (brd, *J*=8.00 Hz, 4 H), 4.08 - 4.13 (m, 1 H), 3.95 - 4.03 (m, 1 H), 3.84 - 3.93 (m, 1 H), 3.77 - 3.83 (m, 1 H), 3.74 (s, 6 H), 3.43 - 3.53 (m, 3 H), 3.38 (br d, *J*=6.75 Hz, 1 H), 2.94 - 3.04 (m, 1 H), 2.70 - 2.85 (m, 1 H), 1.09 - 1.15 (m, 12 H), 1.07 (br s, 3 H).

Other phosphoramidites may be prepared according to procedures described herein and/or prior arts such as, but are not limited to, US426,220 and WO02/36743.

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Example 2. Preparation of a solid support comprising phosphoramidites monomers of the present invention



25 represents amine methyl polyethylene macroporous resin carrier part

Dichloromethane (19.50kg) was added to the 50 L glass kettle under the protection of nitrogen and started stirring. The temperature was controlled at 20~30 $^{\circ}$ C, and DMTr imann (1.47 kg), triethylamine (1.50 kg), 4-dimethylaminopyridine (0.164 kg) and succinic anhydride (1.34 kg) was added to the glass kettle. The system was kept at 20~30 $^{\circ}$ C for 18h, samples were taken and the reaction was ended. Saturated sodium bicarbonate solution (22.50 kg) was added

30

into the reaction system, stirred for 10-20 min, and allowed to separate into layers. The organic phase was separated, and the aqueous phase was extracted twice with dichloromethane, and the organic phase was combined and dried over anhydrous sodium sulfate, filtered, and concentrated in vacuum to get the residue forming a gray to off-white solid of 1.83 kg.

- 5 N, N-dimethylformamide (23.50 kg) was added into a 100L glass kettle and stirred. The temperature was controlled at 20~30 °C. Under the protection of nitrogen, the products of the previous step, O-benzotriazole tetramethylurea hexafluorophosphate (0.33 kg) and N, N-diisopropylethylamine (0.13 kg) were added into the aforesaid 100L glass kettle through the solid feeding funnel and stirred for 10~30 minutes and were discharged into a 50 L zinc barrel
- 10 for use. Macroporous amine methyl resin (3.25 kg) (purchased from Tianjin Nankai Hecheng Science and Technology Co., Ltd., batch number HA2X1209, load capacity 0.48 mmol/g) were added into the aforesaid 100 L solid phase synthesis reactor through the solid feeding funnel, the temperature was controlled at 20~30 °C, N, N-dimethylformamide (21.00 kg+21.00 kg) and the reaction solution in the zinc barrel of the previous step were add into the solid phase synthesis
- 15 reactor. The system was subject to thermal insulation reaction, and the solid load was tracked to $\geq 250\mu\text{mol/g}$, and the load detection method was UV. The system was filtered under the pressure of nitrogen, the filter cake was washed with N, N-dimethylformamide for three times (26.00kg+26.10kg+26.00kg), and the filter cake was left in the kettle. CAP.A (50% acetonitrile and 50% acetic anhydride, 4.40kg+4.42kg+4.30kg) and CAP.B (20% pyridine and 30% N-
- 20 methylimidazole and 50% acetonitrile, 4.40kg+4.40kg+4.47kg) were added into the 80L glass kettle, and stirred for 3~8min before use. This operation was repeated for three times to cap, and acetonitrile (18.00 kg+18.00 kg+18.00 kg+17.50 kg+17.50 kg) was added into the solid phase synthesis kettle. Filter-pressed after nitrogen bubbling for 10~30 min. This operation was repeated for four times, the filter cake was purged in the solid phase synthesis kettle with nitrogen
- 25 for 2-4 h, and then was transferred to a 50 L filter press tank. The temperature was controlled at 15~30 °C, continued drying, and obtained yellow to white solid product after drying, weight: 3.516 kg.
- The isomannide residue can be added to the 5' -end or 3' -end of the oligonucleotide chain by a method well known to those skilled in the art, such as the reverse abasic (invab) method, and
- 30 further added to the target to the group.

Example 3. Synthesis of HTT RNAi Agents.

HTT RNAi agent duplexes shown in Table 2-3, Table 2A-3A, above, were synthesized in accordance with the following general procedures:

- 35 Sense and antisense strand sequences of siRNA were synthesized on oligonucleotide synthesizers using a well-established solid phase synthesis method based on phosphoramidite chemistry. Oligonucleotide chain propagation is achieved through 4-step cycles: a deprotection, a condensation, a capping and an oxidation or a sulfurization step for addition of each nucleotide. Syntheses were performed on a solid support made of controlled pore glass (CPG, 1000 Å).

Monomer phosphoramidites may be purchased from commercial sources or may be the phosphoramidite compounds in example 1-2 and/or in WO2023/045995 and/or in WO2016/028649. The phosphoramidite compounds herein may be attached to the 3'-end as a monomeric phosphoramidite, and further be attached to the CPG solid support. In the case of attachment at the 5'-end, the phosphoramidite compounds may be used for the final coupling reaction and can be further conjugated to target ligands if necessary.

Phosphoramidites with GalNAc ligand cluster (GLS-5* or GLS-15* Phosphoramidites as non-limiting examples) were public in WO2023/045995A1 (incorporated herein in its entirety). For siRNAs used for *in vitro* screening (Table 2, Table 2A), syntheses were carried out at 2 μ mol scale, and for siRNAs used for *in vivo* testing (Table 3, Table 3A), syntheses were carried out at scale of 5 μ mol or larger. In the case where the GalNAc ligand (GLO-n Phosphoramidites as non-limiting examples) were public in WO2023/045995A1 (incorporated herein in its entirety) is attached at 3'-end of sense strand, GalNAc ligand attached CPG solid support was used. In the case where the GalNAc ligand (GLS-5* or GLS-15* as non-limiting example are attached at 5'-end of sense strand, GLS-5* or GLS-15* Phosphoramidites with GalNAc ligand cluster are attached at 5'-end of sense strand, a GalNAc phosphoramidite was used for the last coupling reaction. The sense strands and the antisense strands were synthesis by solid phase synthesis with 4-step cycles, which detailed as below: Trichloroacetic acid (TCA) 3% in dichloromethane was used for deprotection of 4,4'-dimethoxytrityl protecting group (DMT). 5-Ethylthio-1H-tetrazole was used as an activator. I₂ in THF/Py/H₂O and phenylacetyl disulfide (PADS) in pyridine/MeCN was used for oxidation and sulfurization reactions, respectively. After the final solid phase synthesis step, solid support bound oligomer was cleaved and protecting groups were removed by treating with a 1:1 volume solution of 40 wt. % methylamine in water and 28% ammonium hydroxide solution. For the synthesis of siRNAs used for *in vitro* screening, crude mixture was concentrated. The remaining solid was dissolved in 1.0 M NaOAc, and ice cold EtOH was added to precipitate out the single strand product as the sodium salt, which was used for annealing without further purification. For the synthesis of siRNAs used for *in vivo* testing, crude single strand product was further purified by ion pairing reversed phase HPLC (IP-RP-HPLC). Purified single strand oligonucleotide product from IP-RP-HPLC was converted to sodium salt by dissolving in 1.0 M NaOAc and precipitation by addition of ice cold EtOH. Annealing of equimolar complementary sense stand and antisense strand oligonucleotide in water was performed to form the double strand siRNA product, which was lyophilized to afford a fluffy white solid.

In certain studies, a method used to attach a targeting group comprising GalNAc (also referred to herein as a GalNAc delivery compound) to the 5'-end of a sense strand included use of a GalNAc phosphoramidite (GLS-5* or GLS-15* Phosphoramidites) in the last coupling step in the solid phase synthesis, using a synthetic process such as the process used if oligonucleotide chain propagation of adding a nucleotide to the 5'-end of the sense strand is performed.

In some studies, a method of attaching a targeting group comprising GalNAc to the 3'-end of a sense strand comprised use of a solid support (CPG) that included a GLO-n. In some studies, a method of attaching a targeting group comprising GalNAc to the 3'-end of a sense strand comprises attaching a GalNAc targeting group to CPG solid support through an ester bond and using the resulting CPG with the attached GalNAc targeting group when synthesizing the sense strand, which results in the GalNAc targeting group attached at the 3'-end of the sense strand.

The imann residues can be added to the 5' end or 3' end of the oligonucleotide chain by a method well known to those skilled in the art, such as the inverted abasic residues (invab) method, and/or further added to the target to the GalNAc targeting group.

Example 4. *In Vitro* Screening of HTT siRNA Duplexes

BE2C cells were trypsinized and adjusted to appropriate density and seeded into 96-well plates. Cells were transfected with test siRNAs or a control siRNA using Lipofectamine RNAiMax (Invitrogen) at the same time of seeding following the protocol according to manufacturer's recommendation. The siRNAs were tested at three concentrations (10 nM, 3.3nM and 1.1 nM).

Cells were incubated for 24 hours after transfection. The medium was removed, and cells were harvested for RNA extraction. Total RNA was extracted by RNeasy® 96 Kit (QIAGEN) according to the manual.

The cDNA was Synthesized with FastKing RT Kit (With gDNase, Tiangen- KR116-02) according to the manual. The human HTT cDNA expression was determined by qPCR, and HTT normalized to expression of GAPDH. Percent of inhibition was calculated by comparing expression of HTT of siRNA to control siRNA- treated samples.

The duplex sequences used correspond to those shown in Table 2 and Table 2A. Results from these experiments were summarized in Table 5-8.

Table 5 provides experimental results of *in vitro* studies using various HTT RNAi agents to inhibit HTT expression. The duplex sequences used correspond to those shown in Table 2 and Table 2A.

Duplex AV#	Inhibition % relative to control group		
	10nM	3.3nM	1.1nM
AV02743	20.3	18.9	-1.6
AV02744	53.3	37.5	8.5
AV02745	39.4	39.4	36.2
AV02746	39.8	40.1	33.7
AV02747	44.8	44.6	51.0
AV02748	41.3	42.3	28.2
AV02749	30.7	33.5	31.9

AV02750	23.1	-9.9	-28.5
AV02751	32.8	10.1	31.1
AV02752	27.0	29.7	25.4
AV02753	47.6	39.8	47.2
AV02754	3.6	20.1	32.1
AV02755	14.0	9.1	14.0
AV02756	56.6	42.3	48.4
AV02757	-3.6	17.0	25.4
AV02758	-27.2	-37.2	-22.8
AV02759	1.3	-18.6	-38.7
AV02760	18.4	-17.0	5.3
AV02761	22.8	24.9	12.8
AV02762	22.5	14.3	4.3
AV02763	11.3	39.4	-0.5
AV02764	36.0	20.6	43.1
AV02765	33.5	28.2	-17.8
AV02766	18.4	-8.4	-19.5
AV02767	35.1	-11.1	-6.2
AV02768	29.7	14.3	-3.6
AV02769	24.9	32.3	12.5
AV02770	12.5	-11.1	10.1
AV02771	45.8	16.7	-5.5
AV02772	63.5	46.2	24.1
AV02773	47.8	7.6	-11.5
AV02774	10.1	33.0	11.0
AV02775	33.7	NA	23.9
AV02776	48.9	42.7	11.3
AV02777	44.0	35.9	15.8
AV02778	-8.4	-19.8	-41.0
AV02779	41.7	42.5	33.1
AV02780	48.6	34.4	36.7
AV02781	39.5	35.3	15.3
AV02782	24.2	15.0	14.7
AV02783	45.1	45.3	36.2
AV02784	-3.2	32.1	22.3
AV02785	38.8	21.9	19.5
AV02786	0.3	5.3	-11.8
AV02787	23.4	20.1	1.0
AV02788	14.7	36.5	18.2
AV02789	34.7	31.7	-11.0
AV02790	36.9	27.5	29.5
AV02791	34.2	54.0	43.9
AV02792	27.0	28.3	1.7
AV02793	63.6	37.0	44.0
AV02794	-46.0	1.7	-55.4
AV02795	30.5	40.1	-7.6
AV02796	39.9	11.4	18.7
AV02797	29.0	-32.0	-11.0

AV02798	33.1	7.0	-7.6
AV02799	42.3	17.6	24.4
AV02800	4.4	18.2	-2.5
AV02801	56.4	36.4	34.1
AV02802	-39.6	-28.0	-32.5
AV02803	34.0	16.7	16.7
AV02804	52.0	36.9	11.7
AV02805	28.8	43.1	6.6
AV02806	17.0	36.7	21.0
AV02807	25.2	35.1	37.5
AV02808	50.7	49.6	35.1
AV02809	56.4	63.5	61.4
AV02810	50.4	50.4	50.4
AV02811	61.9	60.7	47.8
AV02812	59.7	56.8	53.8
AV02813	62.3	70.2	61.4
AV02814	59.6	68.0	48.7
AV02815	65.8	58.9	40.6
AV02816	67.9	67.2	41.1
AV02817	43.5	43.1	37.0
AV02818	57.9	47.6	49.9
AV02819	61.4	52.6	51.3
AV02820	57.7	55.8	35.3
AV02821	61.4	58.9	47.8
AV02822	56.2	41.3	42.3
AV02823	67.1	51.8	59.2
AV02824	57.3	43.1	34.1
AV02825	46.9	58.5	48.1

Table 6 provides experimental results of *in vitro* studies using various HTT RNAi agents to inhibit HTT expression. The duplex sequences used correspond to those shown in Table 2.

Duplex AV#	Inhibition % relative to control group		
	10nM	3.3nM	1.1nM
AV02826	37.9	25.3	41.2
AV02827	40.6	37.2	46.7
AV02828	47.8	56.2	48.1
AV02829	46.1	27.6	21.6
AV02830	39.6	30.1	26.6
AV02831	-8.9	19.1	8.7
AV02832	30.8	46.5	42.0
AV02833	26.1	29.6	25.1
AV02834	41.2	35.0	34.8
AV02835	53.9	31.1	36.6
AV02836	58.9	55.0	54.8
AV02837	48.3	42.4	34.6
AV02838	32.7	12.7	2.2
AV02839	-10.8	9.0	8.1

AV02840	49.0	39.8	31.8
AV02841	29.1	27.4	16.0
AV02842	39.1	15.1	36.1
AV02843	47.4	37.0	41.2
AV02844	58.3	59.4	49.5
AV02845	50.1	38.1	28.1
AV02846	48.3	45.7	47.4
AV02847	15.7	-17.1	17.7
AV02848	29.9	32.0	28.4
AV02849	32.5	22.7	35.5
AV02850	43.2	31.8	35.9
AV02851	47.9	51.4	26.1
AV02852	60.0	53.7	46.3
AV02853	51.9	43.6	43.8
AV02854	43.6	49.5	38.5
AV02855	21.1	NA	25.1
AV02856	34.8	49.2	34.6
AV02857	40.4	40.2	40.4
AV02858	27.7	-0.1	16.7
AV02859	38.6	29.0	34.2
AV02860	42.1	34.9	31.4
AV02861	46.3	43.5	54.6
AV02862	48.4	28.2	50.6
AV02863	40.5	46.9	23.6
AV02864	27.7	41.9	33.9
AV02865	17.7	-5.2	0.5
AV02866	29.2	26.7	23.1
AV02867	40.9	47.1	49.6
AV02868	54.3	49.6	44.6
AV02869	30.9	54.3	50.8
AV02870	39.6	17.8	29.7
AV02871	37.7	42.9	16.1
AV02872	42.3	43.7	40.7
AV02873	37.4	11.8	36.1
AV02874	14.3	23.9	1.6
AV02875	32.8	51.5	31.4
AV02876	53.5	30.9	49.2
AV02877	50.6	57.2	26.5
AV02878	45.4	27.7	38.2
AV02879	51.8	21.2	17.5
AV02880	33.5	16.7	41.1
AV02881	33.6	35.9	31.5
AV02882	16.7	15.2	20.9
AV02883	44.3	47.3	31.9
AV02884	30.7	31.6	25.4
AV02885	55.0	50.6	39.0
AV02886	51.5	48.0	43.7
AV02887	46.3	43.9	41.9

AV02888	42.9	37.7	37.7
AV02889	38.6	50.8	22.5
AV02890	23.8	19.4	16.0
AV02891	34.6	29.6	13.6
AV02892	37.9	24.6	20.3
AV02893	43.4	33.9	16.0
AV02894	53.2	31.5	31.3
AV02895	40.2	22.7	21.6
AV02896	32.7	41.8	37.2
AV02897	14.0	-6.2	37.1
AV02898	33.9	19.1	14.8
AV02899	45.5	40.6	25.1
AV02900	23.8	31.5	41.6
AV02901	21.6	33.4	38.3
AV02902	16.6	27.1	38.7
AV02903	27.6	44.0	18.9
AV02904	47.8	22.4	29.6
AV02905	8.5	16.1	37.9
AV02906	42.8	20.8	24.8
AV02907	27.1	23.0	9.7
AV02908	23.8	25.9	16.9
AV02909	10.9	25.6	16.0
AV02910	34.1	27.4	23.8
AV02911	27.6	25.6	38.1
AV02912	30.8	24.0	32.7

Table 7 provides experimental results of *in vitro* studies using various HTT RNAi agents to inhibit HTT expression. The duplex sequences used correspond to those shown in Table 2.

Duplex AV#	Inhibition % relative to control group		
	10nM	3.3nM	1.1nM
AV02913	45.0	35.5	6.3
AV02914	51.5	47.1	43.9
AV02915	59.2	63.4	56.2
AV02916	65.6	61.7	55.9
AV02917	50.3	34.7	30.5
AV02918	58.1	51.4	45.3
AV02919	34.9	49.5	46.6
AV02920	46.0	54.1	43.0
AV02921	44.6	36.4	36.2
AV02922	61.3	58.7	48.8
AV02923	62.2	45.3	34.7
AV02924	61.6	60.5	46.4
AV02925	37.1	39.5	23.4
AV02926	47.3	36.3	22.6
AV02927	21.0	14.7	4.4
AV02928	37.6	29.5	15.3

AV02929	33.5	12.2	28.0
AV02930	46.4	58.1	43.7
AV02931	55.7	53.8	52.4
AV02932	56.8	55.9	48.6
AV02933	51.4	29.3	6.0
AV02934	49.3	44.7	11.4
AV02936	42.8	25.0	26.0
AV02937	10.7	32.1	39.0
AV02938	59.1	49.5	39.7
AV02939	58.0	57.2	45.1
AV02940	63.7	58.0	47.5
AV02941	20.4	48.8	40.1
AV02942	51.9	40.1	31.0
AV02943	1.4	39.3	19.9
AV02944	41.0	37.1	2.4
AV02945	32.3	44.5	49.4
AV02946	22.8	13.2	3.0
AV02947	52.7	20.1	34.4
AV02948	54.3	30.2	38.2
AV02949	45.6	31.9	38.4
AV02950	51.0	35.3	40.3
AV02951	49.4	46.0	41.9
AV02952	38.2	38.8	0.3
AV02953	12.2	39.2	31.6
AV02954	17.6	15.3	22.8
AV02955	47.1	43.5	29.5
AV02956	52.2	33.3	38.4
AV02957	47.8	38.0	14.7
AV02958	43.9	31.9	39.3
AV02959	29.0	35.3	2.3
AV02960	37.3	19.8	-11.8
AV02961	33.5	46.9	40.3
AV02962	28.0	19.8	9.5
AV02963	49.8	43.7	33.3
AV02964	23.9	39.9	36.2
AV02965	40.7	36.9	33.3
AV02966	43.7	35.1	39.0
AV02967	40.3	34.9	16.7
AV02968	44.1	38.6	-1.5
AV02969	42.9	41.5	27.0
AV02971	33.3	12.3	27.5
AV02972	50.3	44.5	39.7
AV02973	47.5	38.0	30.9
AV02974	48.4	12.3	33.5
AV02975	29.5	15.0	28.0
AV02976	9.5	6.0	30.2
AV02977	40.3	35.8	26.2
AV02978	28.5	17.3	22.3

AV02979	33.9	25.2	19.0
AV02980	26.7	32.6	21.5
AV02981	20.4	5.3	19.2
AV02982	35.5	33.9	18.4
AV02983	32.6	27.5	16.7
AV02984	33.5	32.6	-4.0
AV02985	44.5	37.5	34.9
AV02986	38.4	41.7	29.5
AV02987	32.6	38.2	31.4
AV02988	10.1	31.4	19.0
AV02989	39.0	19.5	5.0
AV02990	18.4	-2.6	21.2
AV02991	14.6	30.9	24.7
AV02992	10.7	27.7	-5.5
AV02993	25.9	26.7	10.4

Table 8 provides experimental results of *in vitro* studies using various HTT RNAi agents to inhibit HTT expression. The duplex sequences used correspond to those shown in Table 2.

Duplex AV#	Inhibition % relative to control group		
	10nM	3.3nM	1.1nM
AV02994	53.9	54.3	40.3
AV02995	53.0	40.1	32.1
AV02996	60.3	52.3	44.8
AV02997	53.8	65.1	50.1
AV02998	62.8	48.9	36.9
AV02999	45.8	23.1	-11.9
AV03000	37.9	45.4	41.5
AV03001	45.1	30.7	46.0
AV03002	41.1	54.6	58.2
AV03003	46.5	33.5	41.3
AV03004	36.0	49.8	53.0
AV03005	10.1	-6.2	37.1
AV03006	3.0	17.5	43.7
AV03007	-1.9	-11.1	-16.6
AV03008	44.5	37.9	25.4
AV03009	35.8	31.9	43.0
AV03010	42.1	47.8	35.5
AV03011	21.5	42.9	49.4
AV03012	54.7	31.6	41.1
AV03013	35.5	10.4	37.9
AV03014	37.3	38.8	45.8
AV03015	2.3	-20.3	18.4
AV03016	30.9	40.3	36.9
AV03017	19.1	30.0	30.0
AV03018	44.3	53.3	47.1
AV03019	45.6	32.6	52.5

AV03020	46.2	55.0	53.6
AV03021	51.8	40.3	50.1
AV03022	54.1	24.7	63.0
AV03023	12.2	-19.5	33.5
AV03024	57.0	40.7	45.8
AV03025	43.6	22.4	22.4
AV03026	65.1	53.9	62.7
AV03027	67.6	57.3	52.6
AV03028	56.8	31.3	47.8
AV03029	58.7	6.9	11.6
AV03030	62.7	47.1	41.7
AV03031	44.6	30.9	31.6
AV03032	39.4	30.1	26.9
AV03033	-46.4	14.1	34.3
AV03034	57.9	59.3	59.7
AV03035	30.4	37.5	7.8
AV03036	51.8	45.0	59.9
AV03037	15.2	-0.2	20.6
AV03038	33.9	24.1	41.9
AV03039	11.9	16.3	15.8
AV03040	29.4	11.6	21.9
AV03041	28.6	9.9	24.5
AV03042	48.0	56.8	58.7
AV03043	60.7	56.5	44.8
AV03044	63.5	37.7	45.4
AV03045	43.1	5.6	20.9
AV03046	30.6	6.9	35.5
AV03047	39.4	10.7	-0.5
AV03048	37.9	34.4	31.6
AV03049	28.3	33.6	33.6
AV03050	56.1	47.4	52.1
AV03051	58.9	43.5	61.4
AV03052	63.1	62.2	66.1
AV03053	34.6	45.4	58.9
AV03054	23.6	60.7	61.4
AV03055	-5.2	39.4	53.1
AV03056	54.9	51.5	46.5
AV03057	15.6	3.4	15.3
AV03058	43.6	27.8	35.8
AV03059	47.3	38.0	16.2
AV03060	47.1	25.3	1.4
AV03061	54.0	41.4	37.1
AV03062	59.7	46.0	26.5
AV03063	45.9	34.9	34.9
AV03064	49.1	45.3	41.8
AV03065	6.4	4.4	11.4
AV03066	47.3	35.6	38.9
AV03067	27.8	28.3	17.4

AV03068	29.3	14.1	27.3
AV03069	43.4	26.0	38.0
AV03070	27.0	25.0	19.3
AV03071	22.6	25.8	36.1
AV03072	36.7	31.0	33.6
AV03073	31.2	37.6	48.9

Example 5. *In Vitro* Screening of HTT siRNA Duplexes

Huh7 cells were trypsinized and adjusted to appropriate density, mixed with the complexes of psiCHECK^(TM)-2 (fused to HTT target sequence comprising nucleotides of SEQ ID NO: 7) and Lipofectamine 2000 (Invitrogen-11668-019) and seeded into 96-well plates on day 1. On day 2, cells were then transfected with test siRNAs or a control siRNA using Lipofectamine RNAiMax (Invitrogen -13778-150) following the protocol according to manufacturer's recommendation. The siRNAs were tested at three concentrations (10 nM, 1nM and 0.1 nM) in triplicate. On day 3, the inhibition of HTT mRNA expression was analyzed by Dual-Glo® luciferase assay.

The calculation formula was showed as followed,

Ratio of sample well= (sample Renilla luminescence-background blank)/ (sample Fireflyluminescence-background blank)

Ratio of no compound control well= (control Renilla luminescence-background blank)/ (control sample Fireflyluminescence-background blank)

% inhibition= 100-(Ratio of sample well/ the average Ratio of no compound control) ×100%

Table 9 provides experimental results of *in vitro* studies using various HTT RNAi agents to inhibit HTT expression. The duplex sequences used correspond to those shown in Table 2A.

Duplex AV#	Inhibition % relative to control group		
	10nM	1nM	0.1nM
	MEAN±SD		
AV04179	79.38±0.15	49.29±4.51	5.60±5.57
AV04180	29.63±1.62	1.22±4.91	-1.77±9.41
AV04181	81.02±1.06	26.59±2.97	0.86±1.82
AV04182	44.32±4.28	1.67±2.75	1.92±11.29
AV04183	83.29±1.08	69.81±1.22	14.51±10.37
AV04184	72.41±0.82	23.85±3.20	7.11±1.33
AV04185	73.25±4.08	45.61±0.81	8.67±0.07
AV04186	74.80±2.55	52.54±6.52	3.29±3.25
AV04187	78.52±0.78	58.70±0.47	7.41±2.53
AV04188	73.03±1.16	38.27±1.45	-2.27±6.28

AV04189	83.06±0.21	71.47±0.99	26.96±4.32
AV04190	86.69±0.00	80.01±2.10	38.72±2.24
AV04191	75.53±0.15	24.97±4.30	-3.48±6.16
AV04192	67.44±0.10	15.84±5.34	-8.35±10.45
AV04193	65.19±1.18	10.50±1.92	-10.08±3.56
AV04194	36.03±0.91	-8.97±6.22	-13.32±4.36
AV04195	52.37±3.71	17.08±8.71	3.79±8.59
AV04196	73.35±4.83	26.08±0.23	-1.70±8.28
AV04197	60.14±5.64	18.07±0.60	1.73±1.39
AV04198	81.25±1.48	43.41±1.70	2.93±0.88
AV04199	22.56±9.82	0.00±0.38	3.43±8.43
AV04200	60.69±1.45	10.67±4.45	-3.86±4.21
AV04201	55.21±7.74	2.46±8.48	-1.83±3.11
AV04202	71.10±4.02	21.07±1.58	-7.84±1.29
AV04203	77.22±2.79	53.41±1.59	11.26±4.30
AV04204	63.72±3.54	14.24±0.62	-5.71±3.10
AV04205	39.84±1.67	-5.31±2.68	-4.25±9.32
AV04206	64.62±0.15	6.66±1.52	-4.59±0.80
AV04207	73.83±1.23	49.77±5.28	-0.62±4.10
AV04208	75.29±1.37	26.21±0.90	-2.12±2.31
AV04209	41.02±1.67	1.71±4.05	-5.90±10.89
AV04210	65.73±0.33	42.81±6.87	-12.10±23.03
AV04211	75.71±0.22	60.39±5.61	14.24±1.17
AV04212	71.69±0.14	40.81±0.93	11.11±6.15
AV04213	40.55±1.06	7.10±0.02	4.75±4.19
AV04214	60.76±6.15	21.52±1.78	-4.30±2.10
AV04215	68.87±0.95	27.83±1.71	-7.62±4.91
AV04216	79.12±0.68	59.36±3.42	-5.58±10.75
AV04217	71.55±1.13	26.59±3.18	-9.14±5.16
AV04218	59.42±0.43	37.08±4.19	-2.10±2.05
AV04219	53.63±4.70	26.16±6.53	-4.21±0.29
AV04220	31.76±3.42	-6.92±6.66	-13.83±9.97
AV04221	60.43±1.39	14.50±0.22	-13.90±5.24
AV04222	66.42±0.82	49.10±3.05	2.17±4.62
AV04223	34.07±0.13	5.01±2.89	-14.74±13.26
AV04224	64.64±1.82	44.33±3.59	-0.37±4.46
AV04225	55.63±0.50	26.25±2.70	-5.91±0.92
AV04226	51.34±0.26	25.21±5.83	-16.15±5.06
AV04227	67.96±3.19	46.94±3.77	11.45±11.36
AV04228	36.47±1.02	5.75±2.45	-3.09±9.45
AV04229	62.99±1.16	25.18±3.17	3.65±4.04
AV04230	49.78±1.56	8.75±11.34	-0.44±6.19
AV04231	72.36±1.47	25.72±5.85	1.72±5.06
AV04232	70.52±0.87	39.10±3.11	2.65±2.53
AV04233	63.98±3.13	33.64±4.12	-5.30±3.39
AV04234	53.20±0.55	17.35±4.91	-12.71±11.27

AV04235	66.56±4.96	44.50±3.00	12.26±7.30
AV04236	69.91±0.89	39.88±7.07	2.05±1.32
AV04237	77.21±0.52	59.74±2.29	9.92±5.48
AV04238	66.73±2.35	53.72±2.45	6.32±0.13
AV04239	70.95±1.63	56.02±1.75	15.49±0.73
AV04240	74.62±3.19	59.59±2.86	17.15±12.97
AV04241	64.43±3.34	25.01±2.02	-4.18±0.96
AV03469	74.60±0.28	63.17±0.12	1.34±1.81

Example 6 *In Vivo* testing of HTT siRNA Duplexes

At day 1, female C57BL/6J mice (4 mice in each group) were infected by intravenous administration of a solution of adeno-associated virus 8 (AAV8) vector encoding human HTT (respectively fused to HTT target sequence comprising nucleotides 408-2944, 2842-5863, 5722-8716, 8601-11391 Of SEQ ID NO: 1) and luciferase gene. on day 8, mice were subcutaneously administered a single 3 mg/kg of HTT siRNA agents or saline solution. plasma samples were collected on day 8 (pre-dosing plasma sample), day 15, day 22 and day 29, for quantification of HTT mRNA inhibition by luciferase assay. The results were shown in Tables 10-15.

Table 10 provides experimental results of *in vivo* studies using various HTT RNAi agents to inhibit HTT expression (fused to HTT target sequence comprising nucleotides 408-2944 Of SEQ ID NO: 1). The duplex sequences used correspond to those shown in Table 3.

Duplex AD#	remaining percent relative to D8 (Mean ± SD)			Dosage mg/kg
	D15	D22	D29	
AD01471	0.47±0.16	0.42±0.07	0.31±0.06	3
AD01245	0.23±0.07	0.2±0.05	0.19±0.04	3
AD01246	0.24±0.12	0.24±0.08	0.3±0.11	3
AD01247	0.33±0.1	0.23±0.04	0.33±0.13	3
AD01248	1.03±0.31	1.09±0.19	1.09±0.27	3
AD01249	0.23±0.03	0.25±0.06	0.22±0.03	3

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Table 11 provides experimental results of *in vivo* studies using various HTT RNAi agents to inhibit HTT expression (fused to HTT target sequence comprising nucleotides 2842-5863 Of SEQ ID NO: 1). The duplex sequences used correspond to those shown in Table 3.

Duplex AD#	remaining percent relative to D8 (Mean ± SD)			Dosage mg/kg
	D15	D22	D29	
AD01250	0.32±0.1	0.44±0.08	0.45±0.19	3
AD01251	0.34±0.04	0.28±0.03	0.28±0.08	3

AD01252	0.29±0.19	0.24±0.15	0.21±0.09	3
AD01253	0.3±0.05	0.37±0.06	0.27±0.12	3
AD01254	0.21±0.08	0.22±0.08	0.27±0.22	3
AD01255	0.5±0.24	0.41±0.14	0.46±0.31	3
AD01256	0.31±0.08	0.36±0.17	0.29±0.06	3
AD01257	0.37±0.11	0.43±0.14	0.58±0.21	3

Table 12 provides experimental results of in vivo studies using various HTT RNAi agents to inhibit HTT expression (fused to HTT target sequence comprising nucleotides 5722-8716 Of SEQ ID NO: 1). The duplex sequences used correspond to those shown in Table 3.

Duplex AD#	remaining percent relative to D8 (Mean ± SD)			Dosage mg/kg
	D15	D22	D29	
AD01473	0.53±0.14	0.72±0.33	0.69±0.24	3
AD01258	0.32±0.19	0.24±0.07	0.28±0.11	3
AD01259	0.34±0.17	0.36±0.12	0.41±0.42	3
AD01260	0.27±0.12	0.28±0.07	0.18±0.06	3

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Table 13 provides experimental results of in vivo studies using various HTT RNAi agents to inhibit HTT expression (fused to HTT target sequence comprising nucleotides 408-2944 Of SEQ ID NO: 1). The duplex sequences used correspond to those shown in Table 3.

Duplex AD#	remaining percent relative to D8 (Mean ± SD)			Dosage mg/kg
	D15	D22	D29	
AD01919	0.47±0.12	0.72±0.28	0.54±0.04	3
AD01920	0.52±0.17	0.42±0.14	0.43±0.12	3
AD01921	0.44±0.06	0.76±0.33	0.47±0.06	3
AD01922	0.35±0.07	0.45±0.19	0.52±0.31	3
AD01923	0.37±0.11	0.53±0.25	0.36±0.11	3
AD01924	0.4±0.06	0.6±0.16	0.31±0.08	3
AD01925	0.13±0.05	0.19±0.05	0.2±0.06	3
AD01926	0.07±0.02	0.13±0.05	0.13±0.03	3
AD01927	0.11±0.02	0.15±0.06	0.12±0.05	3
AD01928	0.15±0.04	0.2±0.12	0.15±0.07	3
AD01929	0.1±0.02	0.1±0.02	0.11±0.07	3
AD01930	0.1±0.03	0.12±0.02	0.12±0.03	3
AD01931	0.14±0.08	0.13±0.06	0.17±0.06	3
AD01932	0.08±0.03	0.08±0.02	0.09±0.03	3
AD01933	0.11±0.05	0.09±0.01	0.11±0.03	3
AD01934	0.28±0.07	0.31±0.07	0.43±0.14	3
AD01935	0.17±0.09	0.15±0.05	0.17±0.13	3

AD01936	0.12±0.01	0.18±0.08	0.18±0.05	3
AD01937	0.15±0.03	0.2±0.05	0.23±0.14	3
AD01938	0.28±0.15	0.25±0.02	0.21±0.04	3
AD01939	0.27±0.04	0.26±0.13	0.17±0.05	3
AD01962	2.26±0.59	1.4±0.26	0.97±0.27	3

Table 14 provides experimental results of in vivo studies using various HTT RNAi agents to inhibit HTT expression (fused to HTT target sequence comprising nucleotides 2842-5863 Of SEQ ID NO: 1) . The duplex sequences used correspond to those shown in Table 3.

Duplex AD#	remaining percent relative to D8 (Mean ± SD)			Dosage mg/kg
	D15	D22	D29	
AD01472	0.39±0.13	0.4±0.26	0.48±0.3	3
AD01940	0.62±0.15	0.41±0.05	0.52±0.11	3
AD01941	0.61±0.06	0.36±0.17	0.58±0.1	3
AD01942	0.57±0.4	0.55±0.31	0.61±0.32	3
AD01943	0.85±0.2	1.75±1.02	1.21±0.3	3
AD01944	1.32±0.42	1.56±0.78	1.8±1.2	3
AD01945	1.33±0.21	1.67±0.7	1.48±0.34	3
AD01946	0.46±0.12	0.54±0.32	0.45±0.08	3
AD01947	0.4±0.14	0.64±0.38	0.68±0.17	3
AD01948	0.66±0.21	0.77±0.29	0.94±0.69	3
AD01949	0.73±0.29	0.68±0.17	0.55±0.08	3
AD01950	0.45±0.17	0.55±0.21	0.59±0.38	3

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Table 15 provides experimental results of in vivo studies using various HTT RNAi agents to inhibit HTT expression (fused to HTT target sequence comprising nucleotides 5722-8716 Of SEQ ID NO: 1) . The duplex sequences used correspond to those shown in Table 3.

Duplex AD#	remaining percent relative to D8 (Mean ± SD)			Dosage mg/kg
	D15	D22	D29	
AD01473	0.56±0.27	0.58±0.13	0.37±0.29	3
AD01951	0.12±0.03	0.18±0.09	0.1±0.02	3
AD01952	0.16±0.02	0.25±0.1	0.19±0.09	3
AD01953	0.25±0.17	0.38±0.35	0.19±0.15	3
AD01954	0.17±0.03	0.2±0.18	0.14±0.08	3
AD01955	0.58±0.26	0.95±0.31	0.73±0.52	3
AD01956	0.38±0.05	0.51±0.17	0.31±0.15	3
AD01957	0.45±0.22	0.4±0.15	0.35±0.09	3

AD01958	0.25±0.06	0.29±0.17	0.32±0.09	3
AD01959	0.29±0.07	0.32±0.15	0.34±0.13	3
AD01960	0.35±0.14	0.46±0.22	0.18±0.07	3
AD01961	0.28±0.09	0.36±0.04	0.24±0.04	3

Example 7 *In Vivo* testing of HTT siRNA Duplexes

- At day 1, female C57BL/6J mice (4 in each group) were infected by intravenous administration of a solution of adeno-associated virus 8 (AAV8) vector encoding human HTT (fused to HTT target sequence SEQ ID NO: 7) and luciferase gene. On day 8, mice were subcutaneously administered a single 10 mg/kg of HTT siRNA agents or saline solution. Plasma samples were collected on day 8 (pre-dosing plasma sample), day 15, day 22, for quantification of HTT inhibition by luciferase assay. The results are shown in Tables 16.
- Table 16 provides experimental results of *in vivo* studies using various HTT RNAi agents to inhibit HTT expression (fused to HTT target sequence SEQ ID NO: 7). The duplex sequences used correspond to those shown in Table 3A.

Duplex AD#	remaining percent relative to D8 (Mean ± SD)		Dosage mg/kg
	D15	D22	
AD01638	0.36±0.11	0.53±0.39	10
AD01639	0.94±0.1	1.06±0.36	10
AD01640	0.55±0.19	0.9±0.35	10
AD01641	0.95±0.95	2.03±2.99	10
AD01642	1.12±0.48	1.09±0.35	10

Example 8. *In Vitro* Screening of HTT siRNA Duplexes

- Huh7 cells were trypsinized and adjusted to appropriate density, mixed with the complexes of psiCHECK(TM)-2 (fused to HTT target sequence comprising nucleotides of SEQ ID NO: 7) and Lipofectamine 2000 (Invitrogen-11668-019) and seeded into 96-well plates on day 1. On day 2, cells were then transfected with test siRNAs or a control siRNA using Lipofectamine RNAiMax (Invitrogen -13778-150) following the protocol according to manufacturer's recommendation. The siRNAs were tested at three concentrations (10 nM, 1 nM and 0.1 nM) in triplicate. On day 3, the inhibition of HTT mRNA expression was analyzed by Dual-Glo® luciferase assay.

The calculation formula was showed as followed.

- Ratio of sample well= (sample Renilla luminescence-background blank)/ (sample Fireflyluminescence-background blank)

Ratio of no compound control well= (control Renilla luminescence-background blank)/
(control sample Fireflyluminescence-background blank)

% inhibition= 100-(Ratio of sample well/ the average Ratio of no compound control)
×100%

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Table 17 provides experimental results of *in vitro* studies using various HTT RNAi agents to inhibit HTT expression. The duplex sequences used correspond to those shown in Table 2A.

	Inhibition%		
	10nM	1nM	0.1nM
	MEAN±SD		
AV03373	81.07±1.53	46.41±3.99	2.75±17.17
AV03374	74.55±1.12	29.18±7.40	-1.56±3.09
AV03375	65.34±1.64	23.77±6.67	2.06±0.59
AV03376	79.28±3.42	37.19±8.74	4.18±14.44
AV03377	79.59±0.12	66.62±3.00	10.64±8.10
AV03378	64.39±4.87	9.62±6.40	-4.62±6.60
AV03379	72.56±1.30	16.67±1.08	-13.42±0.45
AV03380	66.38±1.10	7.80±5.61	-13.00±15.55
AV03381	69.64±0.63	28.13±0.92	5.27±5.31
AV03382	60.19±1.11	20.33±5.58	9.72±2.94
AV03383	31.72±13.67	6.56±0.72	1.81±1.70
AV03384	59.81±5.99	33.30±4.67	1.97±2.50
AV03385	51.72±8.32	20.59±9.42	-3.31±12.38
AV03386	58.35±6.33	19.95±4.61	-0.56±2.39
AV03387	66.93±4.11	15.94±0.25	7.43±11.62
AV03388	72.27±2.47	25.07±4.03	-17.97±3.55
AV03389	79.77±3.99	41.88±7.63	-12.71±24.86
AV03390	73.00±3.23	24.61±1.05	-22.24±2.32
AV03391	82.15±1.06	58.90±6.35	10.67±4.37
AV03392	73.80±0.86	53.03±3.54	4.79±9.38
AV03393	64.34±4.75	29.43±4.67	-7.47±5.97
AV03394	50.84±4.26	8.46±4.16	-3.98±11.43
AV03395	68.09±1.36	35.60±5.28	6.81±5.29
AV03396	72.41±2.92	23.00±3.02	-13.32±10.23
AV03397	58.60±0.38	18.54±5.58	-0.22±22.86
AV03398	51.51±4.17	7.12±12.27	-15.24±5.78
AV03399	39.20±12.78	1.95±6.07	-5.66±13.37
AV03400	54.00±1.72	11.40±4.39	-1.73±19.12
AV03401	63.47±5.48	20.15±1.93	-2.66±0.63
AV03402	62.31±0.61	16.76±9.67	0.68±7.99
AV03403	64.40±2.71	21.35±3.60	10.16±2.56
AV03404	67.22±0.16	14.05±7.69	-26.68±2.75
AV03405	53.29±4.87	-7.93±5.17	-31.84±8.27

AV03406	63.82±2.37	21.05±12.81	-11.88±18.40
AV03407	58.96±3.62	-12.66±2.81	-11.33±1.93
AV03408	27.18±4.88	3.59±0.19	-3.84±1.40
AV03409	73.61±0.93	32.34±2.12	-0.19±2.46
AV03410	78.78±0.09	62.41±1.36	20.47±7.76
AV03411	81.39±0.82	58.74±4.78	14.06±3.40
AV03412	31.52±1.60	-4.10±5.47	-25.52±17.87
AV03413	42.19±3.90	-7.03±1.43	-16.42±10.01
AV03414	33.62±5.40	-5.09±4.33	-21.54±0.35
AV03415	53.17±3.09	29.24±17.43	0.57±7.31
AV03416	44.99±2.16	2.00±2.64	-12.65±3.55
AV03417	68.34±3.24	38.07±6.55	14.21±10.15
AV03418	71.64±2.86	54.72±0.17	15.35±2.88
AV03419	60.50±3.21	30.68±15.20	10.53±5.88
AV03420	58.42±0.63	33.42±1.61	-7.51±9.33
AV03421	53.07±5.08	11.23±1.41	-15.72±5.73
AV03422	25.36±0.80	-14.30±8.99	-22.15±6.24
AV03423	45.09±5.45	14.43±6.11	-38.99±19.60
AV03424	-8.47±6.26	-13.14±0.12	-1.09±6.38
AV03425	60.62±0.72	19.14±3.15	-7.18±4.87
AV03426	52.47±0.05	19.46±2.43	-15.38±7.83
AV03427	29.88±3.93	-5.26±0.76	-14.03±1.31
AV03428	57.12±1.53	23.03±5.96	-2.36±1.11
AV03429	51.07±0.91	24.34±2.33	-8.65±0.81
AV03430	46.09±1.48	4.50±2.54	-20.06±12.06
AV03431	63.94±0.92	32.61±0.90	0.93±0.62
AV03432	43.00±0.09	5.17±7.16	-29.40±22.93
AV03433	66.42±4.64	54.54±2.10	15.30±4.16
AV03434	64.90±4.77	41.29±5.24	-10.97±2.80
AV03435	59.27±0.84	37.15±5.98	0.58±3.89
AV03436	58.39±3.23	33.79±1.72	-4.74±19.25
AV03437	58.72±0.48	24.08±6.07	-24.96±0.47
AV03438	52.05±6.15	18.19±0.16	-22.89±3.54
AV03439	58.51±2.27	-1.07±6.52	-8.83±3.12
AV03440	60.24±1.96	10.92±8.13	-12.39±3.41
AV03441	67.21±0.63	33.72±1.43	-5.07±0.58
AV03442	63.23±1.52	38.70±2.38	1.14±1.26
AV03443	69.07±0.33	58.99±3.49	10.04±2.38
AV03444	52.20±2.51	15.26±1.99	-26.73±1.55
AV03445	51.58±6.91	27.90±7.25	-15.62±9.78
AV03446	35.64±6.25	-9.80±13.55	-23.46±6.18
AV03447	43.88±0.08	15.00±13.14	-3.63±13.89
AV03448	58.18±4.80	49.35±0.21	18.22±10.83
AV03449	25.08±14.03	-16.27±23.40	-12.34±13.00
AV03450	30.82±1.50	4.04±15.66	-14.69±5.59
AV03451	-6.05±7.14	-16.27±4.62	-4.16±0.94

AV03452	35.09±6.56	-21.65±6.18	-26.81±13.48
AV03453	54.86±2.61	8.41±1.82	-19.18±9.74
AV03454	48.48±1.44	1.23±14.37	-22.37±18.53
AV03455	3.21±7.22	-11.05±3.87	-20.33±8.43
AV03456	8.94±4.02	-8.63±15.58	-14.44±6.94
AV03457	45.89±0.79	-8.70±1.34	-17.14±4.31
AV03458	31.41±1.93	2.07±2.03	-20.79±10.56
AV03459	40.04±10.24	19.43±3.48	-8.57±5.23
AV03460	30.90±2.68	-12.00±4.05	-28.44±17.40
AV03461	35.07±7.16	6.21±15.65	-19.86±24.19
AV03462	22.74±0.41	-18.30±2.22	-33.67±14.32
AV03463	51.90±1.23	16.88±3.19	-6.81±4.30
AV03464	52.20±2.99	41.10±4.00	21.61±0.88
AV03465	30.71±4.08	-0.91±11.56	-10.76±1.18
AV03466	58.44±4.78	35.53±6.04	7.62±4.70
AV03467	51.12±3.69	23.29±1.68	-3.30±8.84

Example 9 *In Vivo* testing of HTT siRNA Duplexes

- At day 1, female C57BL/6J mice (4 in each group) were infected by intravenous administration of a solution of adeno-associated virus 8 (AAV8) vector encoding human HTT (fused to HTT target sequence SEQ ID NO: 7) and luciferase gene. On day 8, mice were subcutaneously administered a single 10 mg/kg of HTT siRNA agents or saline solution. Plasma samples were collected on day 8 (pre-dosing plasma sample), day 15, day 22, for quantification of HTT inhibition by luciferase assay. The results are shown in Tables 18 and table19.
- Table 18 provides experimental results of *in vivo* studies using various HTT RNAi agents to inhibit HTT expression (fused to HTT target sequence SEQ ID NO: 7). The duplex sequences used correspond to those shown in Table 3A.

Duplex AD#	remaining percent relative to D8 (Mean ± SEM)		Dosage mg/kg
	D15	D22	
Saline	1±0.36	1±0.29	/
AD01491	0.71±0.65	0.32±0.17	10
AD01644	0.84±0.67	1.06±1.05	10
AD01645	0.66±0.31	0.58±0.23	10
AD01647	0.43±0.09	0.64±0.31	10
AD01648	0.63±0.41	0.49±0.29	10
AD01649	0.91±0.28	0.74±0.46	10
AD01650	1.18±0.29	1.22±0.23	10
AD01651	1.04±0.32	0.84±0.22	10
AD01652	0.87±0.48	0.62±0.37	10

AD01653	0.83±0.54	0.96±0.42	10
AD01654	0.77±0.22	1.01±0.54	10
AD01655	0.61±0.19	0.65±0.18	10
AD01656	1.1±0.68	0.7±0.33	10
AD01657	0.57±0.28	0.73±0.31	10
AD01658	1.39±0.36	0.87±0.28	10
AD01659	0.61±0.33	1.04±0.34	10
AD01660	0.6±0.28	0.57±0.25	10
AD01661	0.58±0.33	0.66±0.15	10
AD01662	0.65±0.22	0.84±0.31	10
AD01663	0.64±0.45	0.57±0.1	10
AD01664	1.12±0.84	0.6±0.3	10
AD01665	0.55±0.36	0.35±0.15	10
AD01666	1.04±0.69	0.59±0.27	10
AD01667	0.84±0.39	0.68±0.5	10

Table 19 provides experimental results of in vivo studies using various HTT RNAi agents to inhibit HTT expression (fused to HTT target sequence SEQ ID NO: 7). The duplex sequences used correspond to those shown in Table 3A.

Duplex AD#	remaining percent relative to D8 (Mean ±SEM)		Dosage mg/kg
	D15	D22	
Saline	1±0.28	1±0.38	/
AD01643	0.35±0.07	0.21±0.03	10
AD01646	0.26±0.06	0.27±0.06	10
AD02260	0.32±0.03	0.3±0.06	10
AD02261	0.26±0.07	0.19±0.05	10
AD02262	0.36±0.12	0.58±0.16	10
AD02263	0.36±0.08	0.25±0.08	10
AD02264	0.34±0.09	0.23±0.08	10
AD02265	0.42±0.07	0.29±0.02	10
AD02266	0.38±0.08	0.3±0.03	10
AD02267	0.16±0.04	0.18±0.05	10
AD02268	0.23±0.01	0.25±0.02	10
AD02269	0.4±0.09	0.16±0.03	10
AD02270	0.61±0.07	0.34±0.09	10
AD02271	0.36±0.06	0.31±0.08	10
AD02272	0.41±0.17	0.26±0.02	10

AD02273	0.42±0.06	0.42±0.16	10
AD02274	0.32±0.04	0.24±0.06	10
AD02275	0.33±0.08	0.23±0.04	10
AD02276	0.45±0.15	0.44±0.08	10

Equivalents

Although several embodiments of the present invention have been described and illustrated herein, those of ordinary skill in the art will readily envision a variety of other means and/or structures for performing the functions and/or obtaining the results and/or one or more of the advantages described herein, and each of such variations and/or modifications is deemed to be within the scope of the present invention. More generally, those skilled in the art will readily appreciate that all parameters, dimensions, materials, and configurations described herein are meant to be exemplary and that the actual parameters, dimensions, materials, and/or configurations will depend upon the specific application or applications for which the teachings of the present invention is/are used. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. It is, therefore, to be understood that the foregoing embodiments are presented by way of example only and that, within the scope of the appended claims and equivalents thereto; the invention may be practiced otherwise than as specifically described and claimed. The present invention is directed to each individual feature, system, article, material, and/or method described herein. In addition, any combination of two or more such features, systems, articles, materials, and/or methods, if such features, systems, articles, materials, and/or methods are not mutually inconsistent, is included within the scope of the present invention.

All definitions, as defined and used herein, should be understood to control over dictionary definitions, definitions in documents incorporated by reference, and/or ordinary meanings of the defined terms.

The indefinite articles “a” and “an,” as used herein in the specification and in the claims, unless clearly indicated to the contrary, should be understood to mean “at least one.”

The phrase “and/or,” as used herein in the specification and in the claims, should be understood to mean “either or both” of the elements so conjoined, i.e., elements that are conjunctively present in some cases and disjunctively present in other cases. Other elements may optionally be present other than the elements specifically identified by the “and/or” clause, whether related or unrelated to those elements specifically identified, unless clearly indicated to the contrary.

All references, patents and patent applications and publications that are cited or referred to in this application are incorporated herein in their entirety herein by reference.

Claims

1. A double-stranded ribonucleic acid (dsRNA) agent for inhibiting expression of HTT, wherein the dsRNA agent including a sense strand and an antisense strand, wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO: 1, 3, 5, or 7 and the antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of SEQ ID NO:2,4,6,or 8, wherein the sense strand and the antisense strand can be partially, substantially, or fully complementary to each other.
2. The dsRNA agent of claim 1, wherein the dsRNA agent includes a sense strand and an antisense strand, wherein the sense strand comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides that differ by 0, 1, 2, or 3 nucleotides from any one of the nucleotide sequences of nucleotides 4394-4524, 6503-6633, 2327-2457, 1892-2022, 3141-3271, 7517-7647, 1503-1633, 2062-2192, 6570-6700, 393-523, 394-524, 395-525, 396-526, 397-527, 398-528, 399-529, 400-530, 401-531, 403-533, 404-534, 410-540, 426-556, 428-558, 432-562, 435-565, 436-566, 438-568, 440-570, 446-576, 448-578, 481-611, 490-620, 491-621, 522-652, 590-720, 600-730, 602-732, 605-735, 608-738, 609-739, 610-740, 614-744, 618-748, 619-749, 621-751, 833-963, 834-964, 836-966, 844-974, 854-984, 890-1020, 905-1035, 1160-1290, 1161-1291, 1200-1330, 1206-1336, 1208-1338, 1213-1343, 1214-1344, 1218-1348, 1391-1521, 1394-1524, 1457-1587, 1501-1631, 1864-1994, 1871-2001, 1872-2002, 1874-2004, 2070-2200, 2196-2326, 2200-2330, 2204-2334, 2206-2336, 2207-2337, 2320-2450, 2321-2451, 2330-2460, 2332-2462, 2334-2464, 2340-2470, 2390-2520, 2395-2525, 2397-2527, 2399-2529, 2527-2657, 2561-2691, 2592-2722, 2595-2725, 2630-2760, 2658-2788, 2706-2836, 2797-2927, 2828-2958, 2858-2988, 2864-2994, 2867-2997, 2878-3008, 2880-3010, 3006-3136, 3009-3139, 3090-3220, 3134-3264, 3157-3287, 3195-3325, 3202-3332, 3213-3343, 3214-3344, 3217-3347, 3219-3349, 3248-3378, 3249-3379, 3250-3380, 3301-3431, 3393-3523, 3766-3896, 3785-3915, 3797-3927, 3799-3929, 3816-3946, 3817-3947, 3827-3957, 3828-3958, 3835-3965, 3845-3975, 3852-3982, 4030-4160, 4058-4188, 4060-4190, 4063-4193, 4064-4194, 4075-4205, 4076-4206, 4083-4213, 4365-4495, 4371-4501, 4377-4507, 4380-4510, 4382-4512, 4389-4519, 4394-4524, 4398-4528, 4400-4530, 4402-4532, 4404-4534, 4410-4540, 4412-4542, 4413-4543, 4415-4545, 4416-4546, 4433-4563, 4472-4602, 4475-4605, 4507-4637, 4508-4638, 4516-4646, 4520-4650, 4527-4657, 4542-4672, 4545-4675, 4549-4679, 4553-4683, 4555-4685, 4627-4757, 4628-4758, 4631-4761, 4647-4777, 4648-4778, 4650-4780, 4651-4781, 4653-4783, 4654-4784, 4656-4786, 4660-4790, 4667-4797, 4670-4800, 4673-4803, 4674-4804, 4683-4813, 4688-4818, 4689-4819, 4783-4913, 4797-4927, 4852-4982, 4883-5013, 4889-5019, 4973-5103, 5004-5134, 5008-5138, 5010-5140, 5029-

5159, 5030-5160, 5096-5226, 5135-5265, 5175-5305, 5188-5318, 5199-5329, 5202-5332, 5207-5337, 5211-5341, 5337-5467, 5347-5477, 5348-5478, 5357-5487, 5362-5492, 5381-5511, 5383-5513, 5384-5514, 5394-5524, 5398-5528, 5436-5566, 5440-5570, 5441-5571, 5471-5601, 5475-5605, 5731-5861, 5732-5862, 5787-5917, 5794-5924, 5804-5934, 5833-5963, 5837-5967, 5838-5968, 5842-5972, 5844-5974, 5846-5976, 5848-5978, 5858-5988, 5885-6015, 5888-6018, 5891-6021, 5895-6025, 5900-6030, 6010-6140, 6048-6178, 6198-6328, 6200-6330, 6245-6375, 6291-6421, 6337-6467, 6438-6568, 6463-6593, 6510-6640, 6516-6646, 6591-6721, 6593-6723, 6743-6873, 7170-7300, 7217-7347, 7263-7393, 7466-7596, 7467-7597, 7470-7600, 7473-7603, 7519-7649, 7520-7650, 7521-7651, 7802-7932, 7803-7933, 7809-7939, 7810-7940, 7811-7941, 7814-7944, 8142-8272, 8695-8825, 8696-8826, 8747-8877, 9012-9142, 9015-9145, 9110-9240, 9185-9315, 9398-9528, 9422-9552, 9523-9653, 9525-9655, 9526-9656, 9527-9657, 9534-9664, 10094-10224, 10107-10237, 4389-4519, 24-154, 898-1028, 1238-1368, 1206-1336, 5097-5227, 4399-4529, 5186-5316, 6006-6136, 6162-6292, 6570-6700, 9528-9658, 9118-9248, 8949-9079, 402-429, 431-457, 440-473, of SEQ ID NO: 1, and the antisense strand comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the corresponding nucleotide sequence of SEQ ID NO:2, wherein the sense strand and the antisense strand can be partially, substantially, or fully complementary to each other.

3. The dsRNA agent of claim 2, wherein the sense strand comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides that differ by 0, 1, 2, or 3 nucleotides from any one of the nucleotide sequences of nucleotides 4399-4419, 6508-6528, 2332-2352, 1897-1917, 3146-3166, 7522-7542, 1508-1528, 2067-2087, 6575-6595, 398-418, 399-419, 400-420, 401-421, 402-422, 403-423, 404-424, 405-425, 406-426, 408-428, 409-429, 402-429, 415-435, 431-451, 433-453, 437-457, 431-457, 440-460, 441-461, 443-463, 445-465, 451-471, 453-473, 440-473, 486-506, 495-515, 496-516, 527-547, 595-615, 605-625, 607-627, 610-630, 613-633, 614-634, 615-635, 619-639, 623-643, 624-644, 626-646, 838-858, 839-859, 841-861, 849-869, 859-879, 895-915, 910-930, 1165-1185, 1166-1186, 1205-1225, 1211-1231, 1213-1233, 1218-1238, 1219-1239, 1223-1243, 1396-1416, 1399-1419, 1462-1482, 1506-1526, 1869-1889, 1876-1896, 1877-1897, 1879-1899, 2075-2095, 2201-2221, 2205-2225, 2209-2229, 2211-2231, 2212-2232, 2325-2345, 2326-2346, 2335-2355, 2337-2357, 2339-2359, 2345-2365, 2395-2415, 2400-2420, 2402-2422, 2404-2424, 2532-2552, 2566-2586, 2597-2617, 2600-2620, 2635-2655, 2663-2683, 2711-2731, 2802-2822, 2833-2853, 2863-2883, 2869-2889, 2872-2892, 2883-2903, 2885-2905, 3011-3031, 3014-3034, 3095-3115, 3139-3159, 3162-3182, 3200-3220, 3207-3227, 3218-3238, 3219-3239, 3222-3242, 3224-3244, 3253-3273, 3254-3274, 3255-3275, 3306-3326, 3398-3418, 3771-

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 10 4677-4695, 4680-4698, 4681-4699, 4690-4708, 4695-4713, 4696-4714, 4790-4808,
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 5364-5382, 5369-5387, 5388-5406, 5390-5408, 5391-5409, 5401-5419, 5405-5423,
 15 5443-5461, 5447-5465, 5448-5466, 5478-5496, 5482-5500, 5738-5756, 5739-5757,
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 5902-5920, 5907-5925, 6017-6035, 6055-6073, 6205-6223, 6207-6225, 6252-6270,
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 20 6600-6618, 6750-6768, 7177-7195, 7224-7242, 7270-7288, 7473-7491, 7474-7492,
 7477-7495, 7480-7498, 7526-7544, 7527-7545, 7528-7546, 7809-7827, 7810-7828,
 7816-7834, 7817-7835, 7818-7836, 7821-7839, 8149-8167, 8702-8720, 8703-8721,
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 9530-9548, 9532-9550, 9533-9551, 9534-9552, 9541-9559, 10101-10119, 10114-
 25 10132, 4396-4414, 31-49, 905-923, 1245-1263, 1213-1231, 5104-5122, 4406-4424,
 5193-5211, 6013-6031, 6169-6187, 6577-6595, 9535-9553, 9125-9143, 8956-8974, of
 SEQ ID NO: 1, and the antisense strand comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous
 nucleotides differing by 0, 1, 2, or 3 nucleotides from the corresponding nucleotide sequence of
 SEQ ID NO:2.

30

4. The dsRNA agent of claim 1, wherein the dsRNA agent includes a sense strand and an
 antisense strand, wherein the sense strand comprises at least 15, 16, 17, 18, 19, 20 or 21
 contiguous nucleotides that differ by 0, 1, 2, or 3 nucleotides from any one of the nucleotide
 sequences of nucleotides 23-53, 18-48, 31-61, 1-29, 6-36, 17-47, 23-53, 25-55, 26-
 35 56, 27-57, 28-58, 29-59, 30-60, 31-61, 35-65, 52-82, 56-86, 57-87, 68-98, 74-
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281-311, 282-312, 303-333, 307-337, 309-339, 311-341, 368-398, 372-402, 378-408, 383-413, 145-175, 2-32, 142-172, 120-150, 772-802, 918-948, 920-950, 921-951, 994-1024, 1010-1040, 1040-1070, 1047-1077, 1066-1096, 1078-1108, 1084-1114, 1092-1122, 1116-1146, 1118-1148, 1129-1159, 1164-1194, 1189-1219, 1192-1222, 1195-1225, 1226-1256, 1242-1272, 1251-1281, 1312-1342, 1319-1349, 1321-1351, 1401-1431, 1402-1432, 1434-1464, 1435-1465, 1461-1491, 1462-1492, 1480-1510, 1507-1537, 1597-1627, 1608-1638, 1610-1640, 1651-1681, 1696-1726, 1721-1751, 1727-1757, 1732-1762, 1734-1764, 1735-1765, 1779-1809, 1780-1810, 1781-1811, 1819-1849, 1865-1895, 1870-1900, 1874-1904, 1877-1907, 1891-1921, 1901-1931, 1928-1958, 1946-1976, 1948-1978, 1952-1982, 1958-1988, 1959-1989, 1961-1991, 1963-1993, 2025-2055, 2026-2056, 2046-2076, 2047-2077, 2051-2081, 2052-2082, 2061-2091, 2066-2096, 2074-2104, 2080-2110, 2081-2111, 2086-2116, 2097-2127, 2099-2129, 2150-2180, 2165-2195, 2170-2200, 2172-2202, 2522-2552, 2535-2565, 2544-2574, 2550-2580, 2600-2630, 2604-2634, 2651-2681, 2674-2704, 2676-2706, 2686-2716, 2753-2783, 3054-3084, 3056-3086, 3066-3096, 3070-3100, 3071-3101, 1645-1675, 1656-1686, 1062-1092, 591-621, 1040-1070, 628-658, 818-848, 1190-1220, 1191-1221, 1193-1223, 1194-1224, 1199-1229, 1216-1246, 1222-1252, 1225-1255, 1228-1258, 1229-1259, 1230-1260, 1237-1267, 1323-1353, 1324-1354, 1388-1418, 1389-1419, 1399-1429, 1400-1430, 1403-1433, 1406-1436, 1411-1441, 1422-1452, 1423-1453, 1424-1454, 1427-1457, 1432-1462, 1433-1463, 1439-1469, 1736-1766, 1754-1784, 1766-1796, 1769-1799, 1771-1801, 1772-1802, 1774-1804, 1775-1805, 1778-1808, 1783-1813, 1792-1822, 1794-1824, 1816-1846, 1817-1847, 1826-1856, 1829-1859, 1834-1864, 1840-1870, 1859-1889, 1860-1890, 1861-1891, 1863-1893, 2068-2098, 2073-2103, 2076-2106, 2077-2107, 2079-2109, 2082-2112, 2083-2113, 2084-2114, 2085-2115, 2087-2117, 2090-2120, 2091-2121, 2092-2122, of SEQ ID NO: 7, and the antisense strand comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the corresponding nucleotide sequence of SEQ ID NO:8, wherein the sense strand and the antisense strand can be partially, substantially, or fully complementary to each other.

30

5. The dsRNA agent of claim 1, wherein the dsRNA agent includes a sense strand and an antisense strand, wherein the sense strand comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides that differ by 0, 1, 2, or 3 nucleotides from any one of the nucleotide sequences of nucleotides 28-48, 23-43, 36-56, 4-24, 11-31, 22-42, 28-48, 30-50, 31-51, 32-52, 33-53, 34-54, 35-55, 36-56, 40-60, 57-77, 61-81, 62-82, 73-93, 79-99, 89-109, 91-111, 101-121, 102-122, 106-126, 111-131, 113-133, 120-140, 131-151, 133-153, 136-156, 139-159, 145-165, 150-170, 151-171, 152-172, 153-173, 154-174, 155-175, 157-177, 158-178, 160-180, 161-181, 163-183, 165-185, 169-189, 175-195, 179-199, 180-200, 181-201, 182-202, 183-203,

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- 184-204, 188-208, 286-306, 287-307, 308-328, 312-332, 314-334, 316-336, 373-393, 377-397, 383-403, 388-408, 150-170, 7-27, 147-167, 125-145, 777-797, 923-943, 925-945, 926-946, 999-1019, 1015-1035, 1045-1065, 1052-1072, 1071-1091, 1083-1103, 1089-1109, 1097-1117, 1121-1141, 1123-1143, 1134-1154,
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 10 1235-1253, 1236-1254, 1237-1255, 1244-1262, 1330-1348, 1331-1349, 1395-1413,
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 15 1836-1854, 1841-1859, 1847-1865, 1866-1884, 1867-1885, 1868-1886, 1870-1888,
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 2091-2109, 2092-2110, 2094-2112, 2097-2115, 2098-2116, 2099-2117, 144-162,
 149-167, of SEQ ID NO: 7, and the antisense strand comprises at least 15, 16, 17, 18, 19, 20 or
 21 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the corresponding
 20 nucleotide sequence of SEQ ID NO: 8, wherein the sense strand and the antisense strand can be
 partially, substantially, or fully complementary to each other.

6. The dsRNA agent of claim 1, wherein said antisense strand comprises a region of
 complementarity to a HTT RNA transcript which comprises at least 15 contiguous nucleotides
 25 differing by no more than 1, 2, or 3 nucleotides from any one of the antisense sequences listed
 in any one of Tables 1-3, Tables 1A-3A.

7. The dsRNA agent of claim 1, wherein said antisense strand comprises a region of
 complementarity to a HTT RNA transcript which comprises at least 15 contiguous nucleotides
 30 from any one of the antisense sequences listed in any one of Tables 1-3, Tables 1A-3A.

8. The dsRNA agent of any one of claims 1-7, wherein the dsRNA agent comprises a sense
 strand and an antisense strand, nucleotide positions 2 to 18 in the antisense strand comprising a
 region of complementarity to a HTT RNA transcript, wherein the region of complementarity
 35 comprises at least 15, 16, 17, 18, 19, 20 or 21 contiguous nucleotides that differ by 0, 1, 2, or 3
 nucleotides from one of the antisense sequences listed in one of Tables 1-3, Tables 1A-3A, and
 optionally comprising a targeting ligand.

9. The dsRNA agent of any one of claims 1-8, wherein the region of complementarity to a HTT RNA transcript comprises at least 15, 16, 17, 18, or 19 contiguous nucleotides that differ by no more than 3 nucleotides from one of the antisense sequences listed in one of Tables 1-3, Tables 1A-3A.

5

10. The dsRNA agent of any one of claims 1-9, wherein the antisense strand of dsRNA is substantially or fully complementary to any one of a target region of SEQ ID NO: 1, and preferably the dsRNA agent comprises an antisense strand sequence set forth in any one of Tables 1-3; wherein the antisense strand of dsRNA is substantially or fully complementary to
10 any one of a target region of SEQ ID NO: 7, and preferably the dsRNA agent comprises an antisense strand sequence set forth in any one of Tables 1A-3A.

11. The dsRNA agent of any one of claims 1-10, wherein the sense strand sequence is at least substantially complementary to or fully complementary to the antisense strand sequence in the
15 dsRNA agent, preferably, wherein the dsRNA agent comprises a sense strand sequence set forth in any one of Tables 1-3, Tables 1A-3A.

12. The dsRNA agent of any one of claims 1-11, wherein the dsRNA agent comprises the sequences set forth as a duplex sequence in any of Tables 1-3, Tables 1A-3A.

20

13. The dsRNA of any one of claims 1-12, wherein the dsRNA agent comprises at least one modified nucleotide.

14. The dsRNA agent of any one of claims 1-13, wherein all or substantially all of the nucleotides
25 of the sense strand and/or the antisense strand are modified nucleotides.

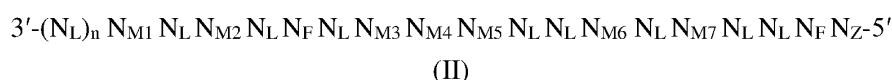
15. A double-stranded ribonucleic acid (dsRNA) agent for inhibiting expression of HTT, wherein the dsRNA agent including a sense strand and an antisense strand, wherein the sense strand is complementary to the antisense strand, wherein the antisense strand comprises a region
30 complementary to part of a HTT RNA transcript, wherein each strand is about 15 to about 30 nucleotides in length, wherein the sense strand comprises sequence may be represented by formula (I):



wherein:

35 each N'_F represents a 2'-fluoro-modified nucleotide; each N'_{N1} and N'_{N2} independently represents a modified or unmodified nucleotide; each N'_L independently represents a modified or unmodified nucleotide but not a 2'-fluoro-modified nucleotide, and m' and n' are each independently an integer of 0 to 7.

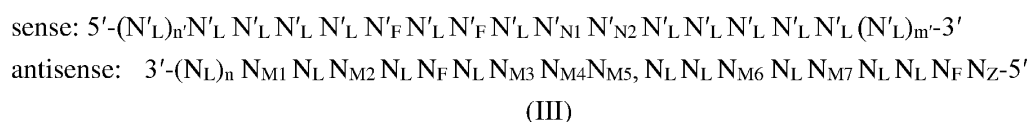
16. A double-stranded ribonucleic acid (dsRNA) agent for inhibiting expression of HTT is provided, wherein the dsRNA agent including a sense strand and an antisense strand, wherein the sense strand is complementary to the antisense strand, wherein the antisense strand comprises a region complementary to part of a HTT RNA transcript, wherein each strand is about 18 to about 30 nucleotides in length, wherein the antisense strand comprises sequence may be represented by formula (II):



wherein:

- each N_F represents a 2'-fluoro-modified nucleotide; each N_{M1} , N_{M2} , N_{M3} , N_{M4} , N_{M5} , N_{M6} , and N_{M7} independently represents a modified or unmodified nucleotide; each N_L and /or N_Z independently represents a modified or unmodified nucleotide but not a 2'-fluoro-modified nucleotide, and n is an integer of 0 to 7.

17. A double-stranded ribonucleic acid (dsRNA) agent for inhibiting expression of HTT is provided, wherein the dsRNA agent including a sense strand and an antisense strand, wherein the sense strand and the antisense strand form a dsRNA duplex, wherein said sense strand is complementary to the antisense strand, wherein said antisense strand comprises a region of complementarity to a HTT RNA transcript, wherein the region of complementarity comprises at least 15 contiguous nucleotides, wherein the dsRNA comprises duplex represented by formula (III):



wherein:

- each strand is about 18 to about 30 nucleotides in length;
- each N_F and N'_F independently represents a 2'-fluoro-modified nucleotide; N_{M1} , N_{M2} , N_{M3} , N_{M4} , N_{M5} , N'_{N1} , and N'_{N2} each independently represents a modified or unmodified nucleotide; N'_{N1} and N'_{N2} include only one 2'-Fluorine modified nucleotides; N_{M1} , N_{M2} , N_{M3} , N_{M4} , N_{M5} , N_{M6} , and N_{M7} have only three 2'-fluoro-modified nucleotides; each N_Z , N_L and N'_L independently represents a modified or unmodified nucleotide but not a 2'-fluoro-modified nucleotide, and m' , n' and n are each independently an integer of 0 to 7.

18. The dsRNA agent of any one of claims 1-17, wherein the one or more modified nucleotides are independently selected from the group consisting of: a 2'-O-methyl nucleotide, a 2'-Fluoro nucleotide, a 2'-deoxy nucleotide, a 2'3'-seco nucleotide mimic, a locked nucleotide, an unlocked nucleic acid nucleotide (UNA), a glycol nucleic acid nucleotide (GNA), a 2'-F-Arabino nucleotide, a 2'-methoxyethyl nucleotide, an abasic nucleotide, an ribitol, inverted

nucleotide, an inverted abasic nucleotide, an isomannide nucleotide, an inverted 2'-Ome nucleotide, an inverted 2'-deoxy nucleotide, a 2'-amino-modified nucleotide, a 2'-alkyl-modified nucleotide, a mopholino nucleotide, a 3'-OMe nucleotide, a nucleotide comprising a 5'-phosphorothioate group, a nucleotide comprising phosphate mimic, a terminal nucleotide
 5 linked to a cholesteryl derivative or dodecanoic acid bisdecylamide group, a 2'-amino-modified nucleotide, a phosphoramidate, or a non-natural base comprising nucleotide.

19. The dsRNA agent of any one of claims 1-18, comprises an E-vinylphosphonate nucleotide at the 5' end of the antisense strand.
 10

20. The dsRNA agent of any one of claims 1-19, wherein the dsRNA agent comprises at least one phosphorothioate internucleoside linkage.

21. The dsRNA agent of any one of claims 1-19 wherein the sense strand comprises at least one
 15 phosphorothioate internucleoside linkage.

22. The dsRNA agent of any one of claims 1-19, wherein the antisense strand comprises at least one phosphorothioate internucleoside linkage.

20 23. The dsRNA agent of any one of claims 1-19, wherein the sense strand comprises 1, 2, 3, 4, 5, or 6 phosphorothioate internucleoside linkages.

24. The dsRNA agent of any one of claims 1-19, wherein the antisense strand comprises 1, 2, 3, 4, 5, or 6 phosphorothioate internucleoside linkages.
 25

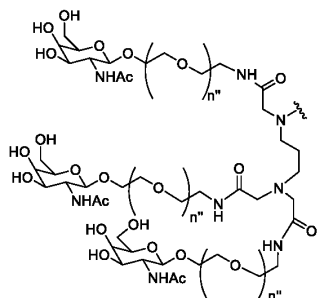
25. The dsRNA agent of any one of claims 1-24, wherein the modified sense strand is a modified sense strand sequence set forth in one of Tables 2-3, Tables 2A-3A.

26. The dsRNA agent of any one of claims 1-24, wherein the modified antisense strand is a
 30 modified antisense strand sequence set forth in one of Tables 2-3, Tables 2A-3A.

27. The dsRNA agent of any one of claims 1-26, wherein the sense strand is complementary or substantially complementary to the antisense strand, and the region of complementarity is between 16 and 23 nucleotides in length.
 35

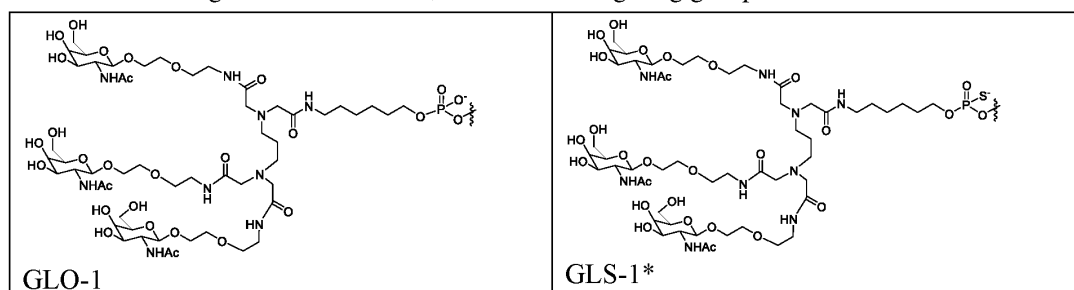
28. The dsRNA agent of any one of claims 1-27, wherein the region of complementarity is 19-21 nucleotides in length.

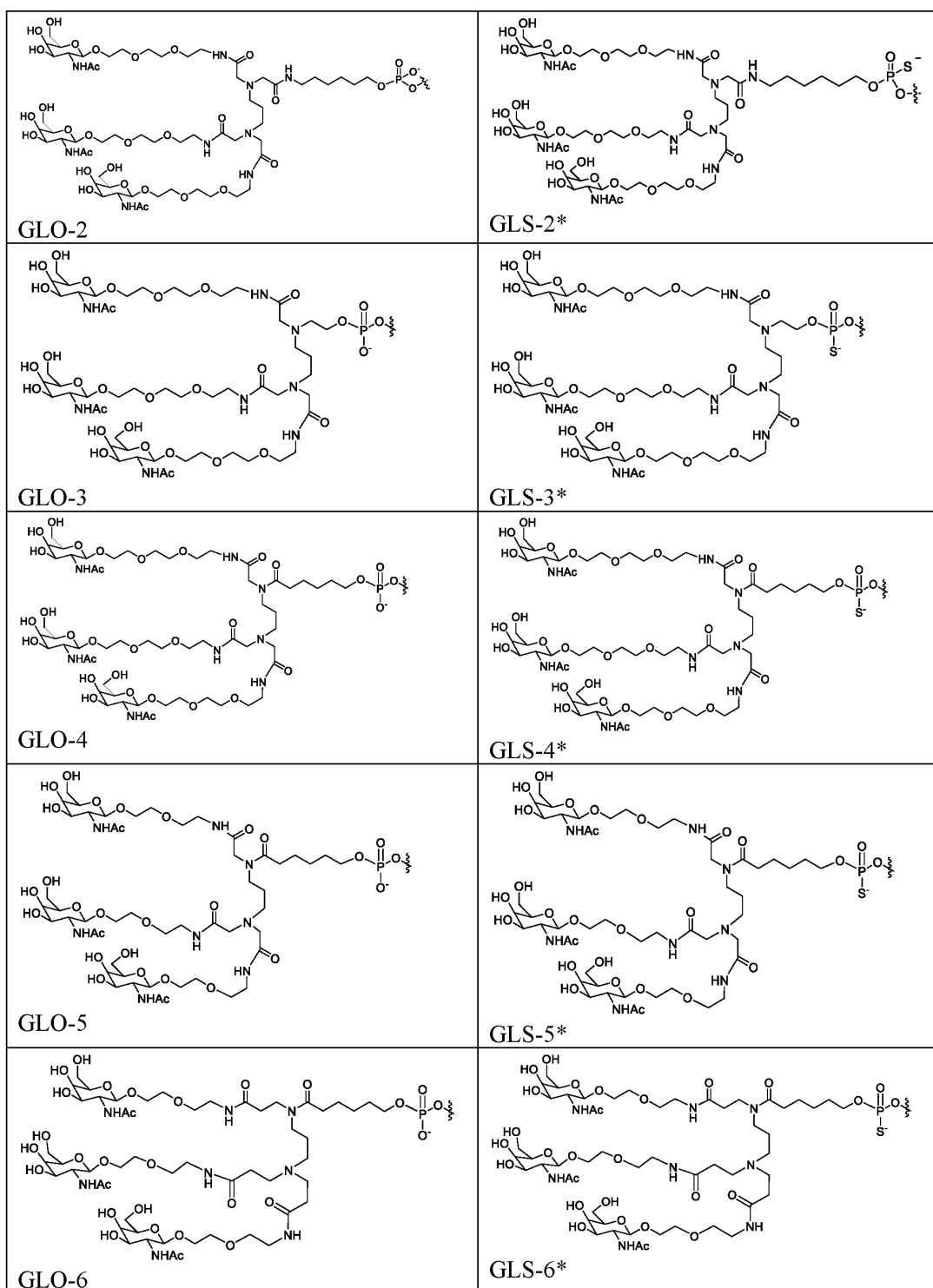
29. The dsRNA agent of any one of claims 1-28, wherein each strand is no more than 30 nucleotides in length.
30. The dsRNA agent of any one of claims 1-28, wherein each strand is no more than 25 nucleotides in length.
31. The dsRNA agent of any one of claims 1-28, wherein each strand is no more than 23 nucleotides in length.
32. The dsRNA agent of any one of claims 1-31, wherein the dsRNA agent comprises at least one modified nucleotide and further comprises one or more targeting groups or linking groups.
33. The dsRNA agent of claim 32, wherein the one or more targeting groups or linking groups are conjugated to the sense strand.
34. The dsRNA agent of claim 32 or 33, wherein the targeting group or linking group comprises N-acetyl-galactosamine (GalNAc).
35. The dsRNA agent of claim 32-34, wherein the targeting group has a structure:

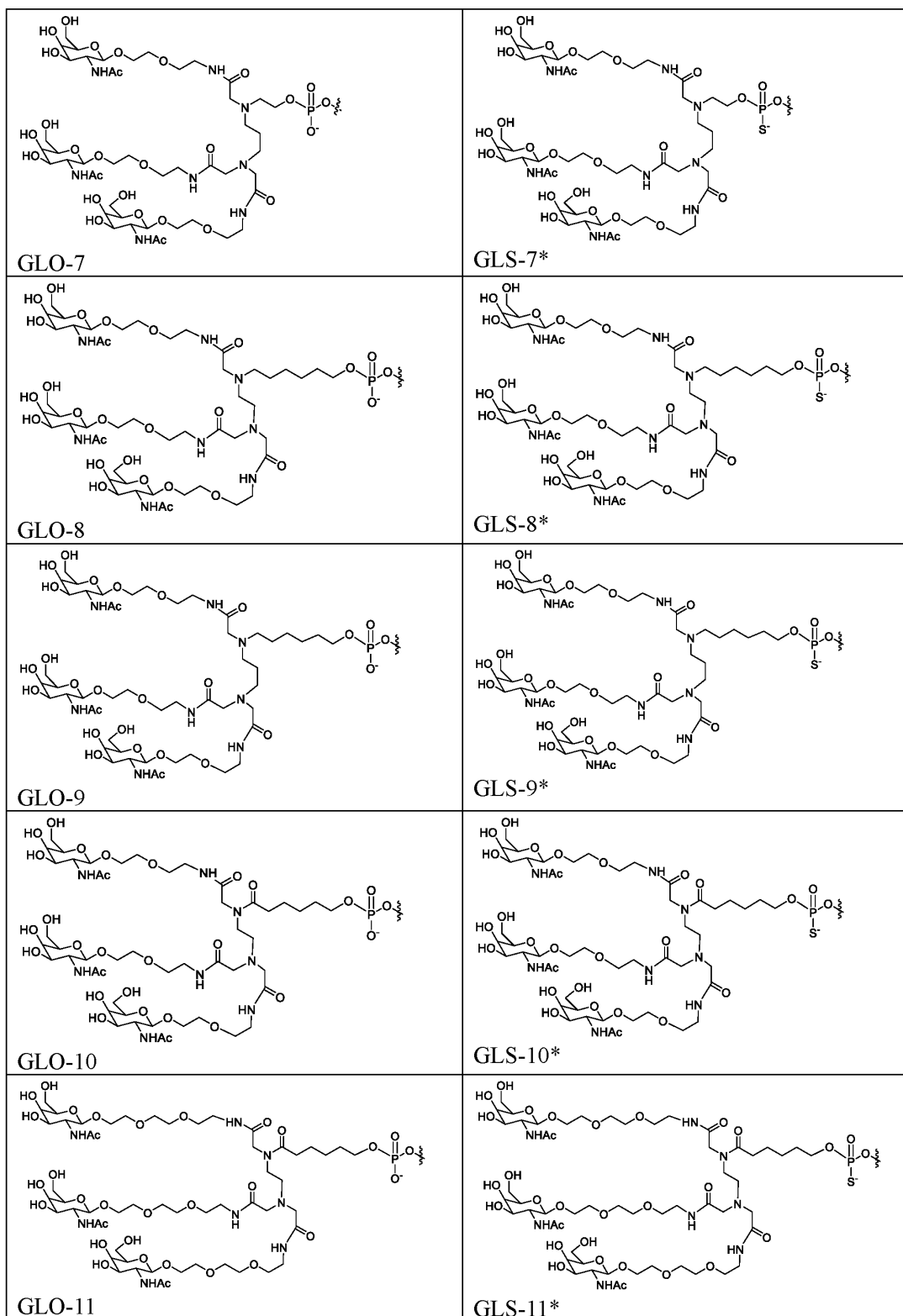


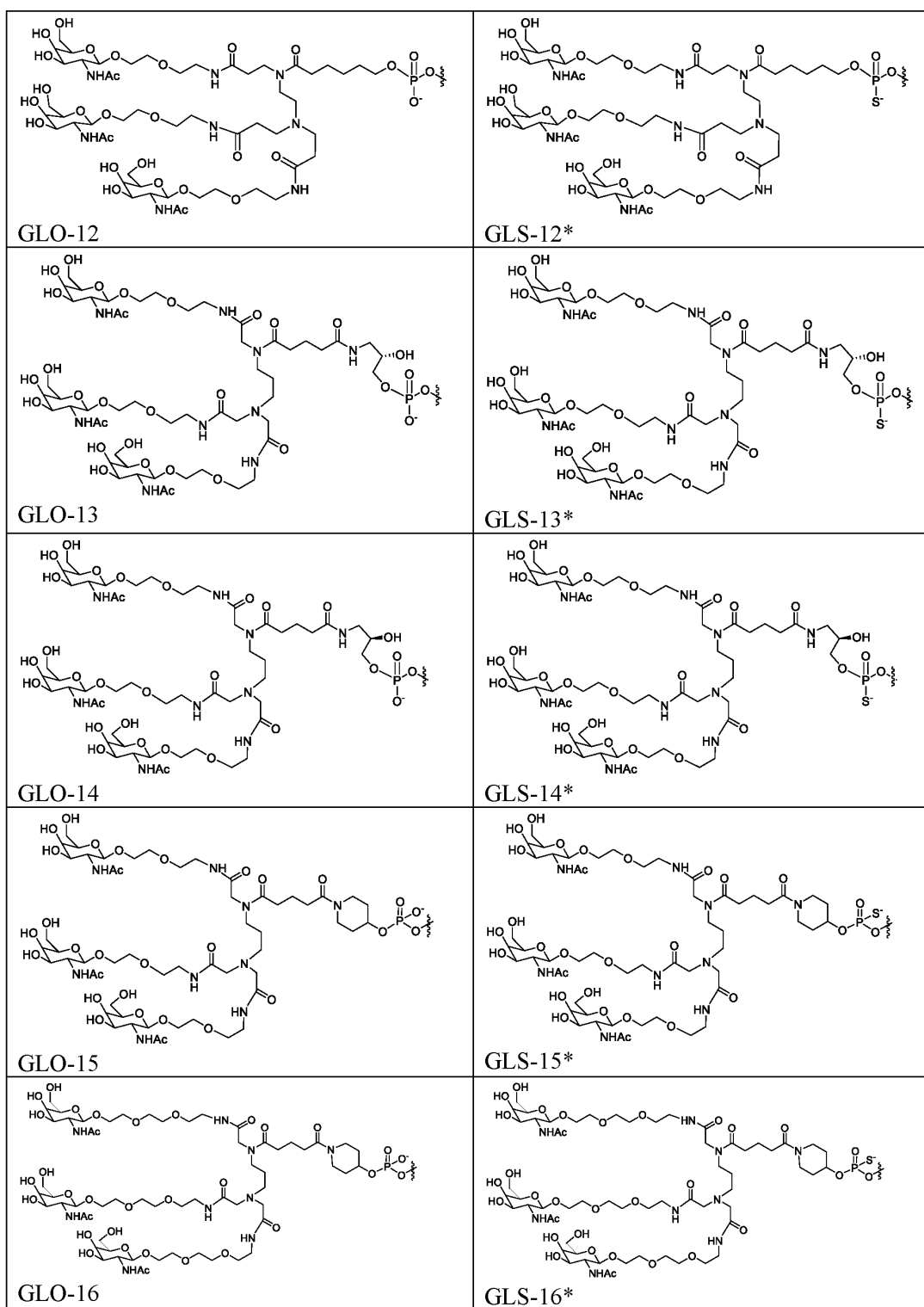
n'' are independently selected from 1 or 2.

36. The dsRNA agent of claim 32-35, wherein the targeting group has a structure:









37. The dsRNA agent of any one of claims 1-36, wherein the dsRNA agent comprises a targeting group that is conjugated to the 5'-terminal end of the sense strand.

38. The dsRNA agent of any one of claims 1-36, wherein the dsRNA agent comprises a targeting group that is conjugated to the 3'-terminal end of the sense strand.

5 39. The dsRNA agent of any one of claims 1-36, wherein the antisense strand comprises one inverted abasic residue at 3'-terminal end.

40. The dsRNA agent of any one of claims 1-36, wherein the sense strand comprises one or two inverted abasic residues or imann residues at 3' or/and 5' terminal end.

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41. The dsRNA agent of any one of claims 1-40, wherein the dsRNA agent each end of the sense strand includes one inverted abasic residue or imann residues at the 5' terminal end of the sense strand, wherein inverted abasic residue or imann residues is linked to an adjacent nucleotide via a phosphorothioate linkage to the 5' terminal end of the nucleotide sequence of the sense strand.

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42. The dsRNA agent of any one of claims 41, the sense strand further includes targeting group linked to an inverted abasic residue or imann residues at the 5' terminal end of the sense strand, wherein targeting group is linked to an adjacent inverted abasic residue or imann via a phosphorothioate linkage, and optionally targeting group is N-acetyl-galactosamine (GalNAc).

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43. The dsRNA agent of any one of claims 1-42, wherein the dsRNA agent has two blunt ends.

44. The dsRNA agent of any one of claims 1-42, wherein at least one strand comprises a 3' overhang of at least 1 nucleotide.

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45. The dsRNA agent of any one of claims 1-44, wherein at least one strand comprises a 3' overhang of at least 2 nucleotides.

46. The dsRNA agent of any one of claims 1-45 wherein the HTT RNA transcript is SEQ ID
30 NO: 1 and/or SEQ ID NO: 7.

47. A composition comprising a dsRNA agent of any one of claims 1-46.

48. The composition of claim 47, further comprising a pharmaceutically acceptable carrier.

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49. The composition of claim 48, further comprising one or more additional therapeutic agents.

50. The composition of claim 49, wherein the composition is packaged in a kit, container, pack, dispenser, pre-filled syringe, or vial.

51. The composition of any one of claims 45-48, wherein the composition is formulated for subcutaneous administration, is formulated for intrathecally administration, intracerebroventricular (ICV) injection administration, intrastriatal (IS) injection administration,
5 or is formulated for intravenous (IV) administration.

52. A cell comprising a dsRNA agent of any one of claims 1-46, optionally, the cell is a mammalian cell, optionally a human cell, optionally a CNS cell.

10 53. A method of inhibiting the expression of a HTT gene in a cell, the method comprising:
(i) preparing a cell comprising an effective amount of a double-stranded ribonucleic acid (dsRNA) agent of any one of claims 1-46 or a composition of any one of claims 47-51.

54. The method of claim 53, further comprising:
15 (ii) maintaining the cell prepared in claim 53 (i) for a time sufficient to obtain degradation of the mRNA transcript of a HTT gene, thereby inhibiting expression of the HTT gene in the cell.

55. The method of any one of claims 53-54, wherein the cell is in a subject and the dsRNA agent
20 is administered to the subject by subcutaneously, by intracerebroventricular, by intrastriatal, by intrathecally or by intravenous (IV).

56. The method of claim 55, further comprising assessing inhibition of the HTT gene, following the administration of the dsRNA agent to the subject, wherein a means for the assessing
25 comprises:

(i) determining one or more physiological characteristics of a HTT-associated disease or condition in the subject and
(ii) comparing the determined physiological characteristic(s) to a baseline pre-treatment physiological characteristic of the HTT-associated disease or condition and/or to a control
30 physiological characteristic of the HTT-associated disease or condition,
wherein the comparison indicates one or more of a presence or absence of inhibition of expression of the HTT gene in the subject.

57. The method of claim 56, wherein the determined physiological characteristic is one or more
35 of: the HTT mRNA level, the HTT protein level in the subject, or the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease.

58. The method of claim 57, wherein a reduction in one or more of the subject's HTT mRNA level, the HTT protein level in the subject, and/or the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease in the subject.

5 59. A method of inhibiting expression of a HTT gene in a subject, the method comprising administering to the subject an effective amount of a double-stranded ribonucleic acid (dsRNA) agent of any one of claims 1-46 or a composition of any one of claims 47-51.

60. The method of claim 59, wherein the dsRNA agent is administered to the subject by
10 subcutaneously, by intracerebroventricular, by intraatrial, by intrathecally or by intravenous (IV).

61. The method of any one of claims 59-60, further comprising assessing inhibition of the HTT gene, following the administration of the dsRNA agent, wherein a means for the assessing
15 comprises:

(i) determining one or more physiological characteristics of a HTT-associated disease or condition in the subject and

(ii) comparing the determined physiological characteristic(s) to a baseline pre-treatment physiological characteristic of the HTT-associated disease or condition and/or to a control
20 physiological characteristic of the HTT-associated disease or condition,
wherein the comparison indicates one or more of a presence or absence of inhibition of expression of the HTT gene in the subject.

62. The method of claim 61, wherein the determined physiological characteristic is one or more
25 of: the HTT mRNA level, the HTT protein level in the subject, the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease in the subject.

63. The method of claim 62, wherein a reduction in one or more of the subject's HTT mRNA
30 level, the HTT protein level in the subject, and/or reduce the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease in the subject.

64. A method of treating a disease or condition associated with the presence of HTT protein, the
35 method comprising administering to a subject an effective amount of a double-stranded ribonucleic acid (dsRNA) agent of any one of claims 1-46, or a composition of any one of claims 47-51, to inhibit HTT gene expression.

65. The method of claim 64, wherein the disease or condition is one or more of HD (Huntington's disease).

5 66. The method of claim 65, further comprising administering an additional therapeutic regimen to the subject.

67. The method of claim 66, wherein the additional therapeutic regimen comprises: administering to the subject one or more HTT antisense polynucleotides of the invention, administering to the subject a non-HTT dsRNA therapeutic agent, and a behavioral modification
10 in the subject.

68. The method of claim 67, wherein the non-HTT dsRNA therapeutic agent is one of more of: a monoamine inhibitor, e.g., tetrabenazine (Xenazine), deutetrabenazine (Austedo), and reserpine, an anticonvulsant, e.g., valproic acid (Depakote, Depakene, Depacon),
15 and clonazepam (Klonopin), an antipsychotic agent, e.g., risperidone (Risperdal), and haloperidol (Haldol), and an antidepressant, e.g., paroxetine (Paxil).

69. The method of any one of claims 64-68, wherein the dsRNA agent is administered to the subject by subcutaneously, by intracerebroventricular, by intrastriatal, by intrathecally or by
20 intravenous (IV).

70. The method of any one of claims 64-69, further comprising determining an efficacy of the administered double-stranded ribonucleic acid (dsRNA) agent in the subject.

25 71. The method of claim 70, wherein a means of determining an efficacy of the treatment in the subject comprises:

(i) determining one or more physiological characteristics of the HTT-associated disease or condition in the subject and

(ii) comparing the determined physiological characteristic(s) to a baseline pre-treatment
30 physiological characteristic of the HTT-associated disease or condition
wherein the comparison indicates one or more of a presence, absence, and level of efficacy of the administration of the double-stranded ribonucleic acid (dsRNA) agent to the subject.

72. The method of claim 71, wherein the determined physiological characteristic is: the HTT
35 mRNA level, the HTT protein level in the subject, or the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease in the subject.

73. The method of claim 72, wherein a reduction in one or more of the HTT mRNA level, the HTT protein level in the subject, and/or reduce the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease in the subject.

5 74. A method of decreasing a level of HTT protein in a subject compared to a baseline pre-treatment level of HTT protein in the subject, the method comprising administering to the subject an effective amount of a double-stranded ribonucleic acid (dsRNA) agent of any one of claims 1-46, or a composition of any one of claims 47-51, to decrease the level of HTT gene expression.

10 75. The method of claim 74, wherein the dsRNA agent is administered to the subject by subcutaneously, by intracerebroventricular, by intraatrial, by intrathecally or by intravenous (IV).

15 76. A method of altering a physiological characteristic of a HTT-associated disease or condition in a subject compared to a baseline pre-treatment physiological characteristic of the HTT-associated disease or condition in the subject, the method comprising administering to the subject an effective amount of a double-stranded ribonucleic acid (dsRNA) agent of any one of claims 1-46, or a composition of any one of claims 47-51, to alter the physiological characteristic of the HTT-associated disease or condition in the subject.

20 77. The method of claim 76, wherein the dsRNA agent is administered to the subject by subcutaneously, by intracerebroventricular, by intraatrial, by intrathecally or by intravenous (IV).

25 78. The method of any one of claims 76-77, wherein the physiological characteristic is one or more of: the HTT mRNA level, the HTT protein level in the subject, or the level of C9orf72 expanded or levels of the neurotransmitters gamma-aminobutyric acid (GABA) and substance P decrease in the subject.