Claims

1. An oligonucleotide comprising 10 to 25 nucleotides, wherein the sequence of nucleotides of the oligonucleotide is at least 80 to 90 % complementary to a corresponding region of a LRRK2 nucleic acid sequence and wherein at least one nucleotide is modified and the modification selected from a modified sugar and optionally a modified internucleoside linkage.

2. The oligonucleotide according to claim 1, wherein the LRRK2 nucleic acid is mRNA of leucine-rich repeat kinase 2 (LRRK2) of SEQ ID NO.1 and/or pre-mRNA of LRRK2 of SEQ ID NO.2 and/or a fragment thereof.

3. The oligonucleotide according to claim 1 or 2, wherein the modification is selected from the group consisting of LNA, ENA, cET, a 2'Fluoro modified nucleotide, a 2´O-Methyl modified nucleotide, a 2´O-Methoxy modified nucleotide, a FANA and a combination thereof, and/or wherein the modification is located in a sequence of at least 3 nucleotides or at least 5 nucleotides of the 5´-end and/or 3´-end of the oligonucleotide, and/or wherein the modification is located in a sequence of 5 nucleotides of the 5´-end and/or 3´-end of the oligonucleotide.

4. The oligonucleotide according to any one of claims 1 to 3, wherein the oligonucleotide comprises 10 to 25 nucleotides and at least one nucleotide having a bridged nucleic acid modification selected from the group consisting of LNA, ENA, cET, a 2'Fluoro modified nucleotide, a 2´O-Methyl modified nucleotide, a 2´O-Methoxy modified nucleotide, a FANA and a combination thereof, wherein said modification is located in a sequence of 5 nucleotides of the 5´-end and/or 3´-end of the oligonucleotide and wherein the oligonucleotide hybridizes with a transcript or an mRNA of leucine-rich repeat kinase 2 (LRRK2) of SEQ ID NO.1 and/or with pre-mRNA of LRRK2 of SEQ ID NO.2 and/or a fragment thereof.

5. The oligonucleotide according to any one of claims 1 to 4, wherein the oligonucleotide hybridizes outside a hybridizing active region or within a hybridizing active region of position 27001 to 27500, position 102001 to 102500, position 80501 to 81000, position 24501 to 25000, position 114001 to 114500, position 92001 to 92500, position 99501 to 100000, position 67001 to 67500, position 15001 to 15500, position 24001 to 24500,

position 26501 to 27000, position 79501 to 80000, position 87001 to 87500, position 120501 to 121000, position 142001 to 142500, position 135001 to 135500, position 71001 to 71500, position 140501 to 141000 or a combination thereof.

6. The oligonucleotide according to any one of claims 1 to 5, wherein the oligonucleotide comprises SEQ ID NO.69, SEQ ID NO.210, SEQ ID NO.164, SEQ ID NO.254, SEQ ID NO.222, SEQ ID NO.186, SEQ ID NO.204, SEQ ID NO.142, SEQ ID NO.209, SEQ ID NO.255, SEQ ID NO.45, SEQ ID NO.46, SEQ ID NO.60, SEQ ID NO.66, SEQ ID NO.162, SEQ ID NO.171, SEQ ID NO.224, SEQ ID NO.241, SEQ ID NO.250, SEQ ID NO.149, SEQ ID NO.256, SEQ ID NO.239, or a combination thereof.

7. The oligonucleotide according to any one of claims 1 to 6, wherein the oligonucleotide is selected from the group consisting of

+A*+A*+T*A*C*T*A*C*T*A*T*T*T*G*T*T*+T*+C*+C (A57067Hi; SEQ ID NO.69),

+T*+A*+C*A*A*T*A*T*T*T*A*T*G*G*T*T*+C*+T*+C (A57208Hi; SEQ ID NO.210),

+G*+T*+C*A*T*A*A*G*T*T*G*T*C*A*G*+T*+A*+T (A57162Hi; SEQ ID NO.164),

+G*+A*+C*T*T*C*G*T*T*T*A*A*T*A*C*+C*+A*+G (A57252H; SEQ ID NO.254),

+C*+T*+T*T*G*C*T*T*A*T*T*C*G*T*G*+A*+C*+T (A57220Hi; SEQ ID NO.222),

+T*+T*+T*A*T*T*G*C*A*G*T*C*A*T*A*G*+T*+G*+A (A57184Hi; SEQ ID NO.186),

+C*+T*+T*T*G*T*A*A*A*T*G*A*C*G*T*T*+T*+C*+C (A57202Hi; SEQ ID NO.204),

+T*+G*+A*A*A*T*G*T*C*T*A*T*T*A*G*C*+A*+C*+A (A57140Hi, SEQ ID NO.142),

+A*+C*+A*A*T*A*T*T*T*A*T*G*G*T*T*C*+T*+C*+A (A57207Hi; SEQ ID NO.209),

+G*+G*+A*C*T*T*C*G*T*T*T*A*A*T*A*C*+C*+A*+G (A57253H; SEQ ID NO.255),

+C*+G*+G*C*T*A*A*A*T*G*T*T*T*C*A*G*+T*+T*+C (A57043Hi; SEQ ID NO.45),

+T*+C*+G*G*C*T*A*A*A*T*G*T*T*T*C*+A*+G*+T (A57044Hi; SEQ ID NO.46),

+G*+T*+G*T*A*A*C*T*A*A*G*T*G*A*T*+C*+T*+C (A57058Hi; SEQ ID NO.60),

+G*+A*+T*A*T*T*G*A*C*A*A*C*C*T*G*+C*+T*+G (A57064Hi; SEQ ID NO.66),

+T*+G*+T*G*T*T*A*C*C*A*T*A*T*C*C*A*+T*+T*+T (A57160Hi; SEQ ID NO.162),

+C*+T*+G*T*G*A*C*T*T*T*G*C*A*T*C*A*+A*+C*+T (A57169Hi; SEQ ID NO.171),

+C*+A*+A*T*G*T*A*T*A*C*C*A*T*G*C*+A*+G*+T (A57222Hi; SEQ ID NO.224),

+T*+T*+C*C*T*G*A*T*T*A*T*A*C*C*A*T*+A*+T*+G (A57239Hi; SEQ ID NO.241),

+A*+T*+G*C*T*C*T*T*A*T*C*C*A*C*A*A*+T*+C*+C (A57248Hi; SEQ ID NO.250),

+T*+T*+T*G*A*T*C*T*G*T*A*G*T*A*C*A*+T*+A*+C (A57147Hi; SEQ ID NO.149),

+A*+T*+G*G*A*C*T*T*C*G*T*T*T*A*A*T*+A*+C*+C (A57254H; SEQ ID NO.256),

+G*+G*+A*C*A*T*G*T*A*T*C*T*T*A*A*T*+A*+G*+T (A57237Hi; SEQ ID NO.239),

and a combination thereof, wherein + indicates an LNA nucleotide and * indicates a phosphorothioate (PTO) linkage between the nucleotides.

8. The oligonucleotide according to any one of claims 1 to 7, wherein the oligonucleotide has 80 to 99 %, 85 to 98 %, 90 to 95 or 93 % sequence identity to any one of the oligonucleotides of SEQ ID NO.3 – SEQ ID NO.5301, and/or wherein said oligonucleotide comprises at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21 or at least 22 contiguous nucleotides of any one of the oligonucleotides of SEQ ID NO.3 – SEQ ID NO.5301.

9. The oligonucleotide according to any one of claims 1 to 8, wherein the oligonucleotide inhibits the expression of LRRK2, a LRRK2 mRNA, a LRRK2 pre-mRNA or a combination thereof at a nanomolar or micromolar concentration.

10. A pharmaceutical composition comprising an oligonucleotide according to any one of claims 1 to 9 and a pharmaceutically acceptable carrier, excipient, adjuvant, or a combination thereof, optionally further comprising a therapeutically active agent.

11. The oligonucleotide according to any one of claims 1 to 9, or the pharmaceutical composition according to claim 10 for use in preventing and/or treating a human disease such as a neurodegenerative disease.

12. Use of an oligonucleotide according to any one of claims 1 to 9 or a pharmaceutical composition according to claim 10 in the manufacture of a medicament for preventing and/or treating a human disease.

13. The oligonucleotide or the pharmaceutical composition for use according to claim 11 or the use according to claim 12, wherein the pharmaceutically acceptable carrier, excipient, adjuvant, or a combination thereof, or the therapeutically active agent is administrated separately before or after delivery of the oligonucleotide, or is administered simultaneously via different delivery methods.

14. The oligonucleotide or the pharmaceutical composition for use according to claim 11 or 13, or the use according to claim 12, wherein the disease is selected from the group consisting of Parkinson´s disease (PD), Alzheimer´s disease, Huntington´s disease, amyotrophic lateral sclerosis, multiple sclerosis, multiple system atrophy, dementia with Lewy bodies (DLB), pure autonomic failure (PAF), frontotemporal dementia and prion disease.

15. The oligonucleotide or pharmaceutical composition for use according to any one of claims 11, 13 or 14, or the use according to claim 12 or 14, wherein the oligonucleotide and/or the pharmaceutical composition is for local or systemic administration.