

ANTISENSE OLIGOMERS FOR TREATMENT OF NON-SENSE MEDIATED RNA DECAY BASED CONDITIONS AND DISEASES

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 63/381,640, filed October 31, 2022, which is incorporated herein by reference in its entirety.

BACKGROUND

[0002] Alternative splicing events in genes can lead to non-productive mRNA transcripts which in turn can lead to aberrant protein expression, and therapeutic agents which can target the alternative splicing events in genes can modulate the expression level of functional proteins in patients and/or inhibit aberrant protein expression. Such therapeutic agents can be used to treat a condition or disease caused by protein deficiency.

SUMMARY

[0002a] Provided herein, in some aspects, is a use of a therapeutic agent in preparing a medicament for treating or reducing the likelihood of developing a disease or condition in a subject in need thereof by modulating expression of a target protein in a cell of the subject, the use comprising: contacting the cell of the subject with the therapeutic agent or a vector encoding the therapeutic agent, wherein the cell comprises a pre-mRNA that is transcribed from a target gene and that encodes the target protein, the pre-mRNA comprising an alternatively-spliced coding exon (ASCE), wherein an alternative processed mRNA that is produced by splicing out of the ASCE during processing of the pre-mRNA undergoes non-sense mediated RNA decay, wherein the therapeutic agent promotes inclusion of the ASCE during the processing of the pre-mRNA, thereby increasing a level of a processed mRNA that is processed from the pre-mRNA and that comprises the ASCE

[0003] Provided herein, in some aspects, is a method of modulating expression of a target protein in a cell comprising a pre-mRNA that is transcribed from a target gene and that encodes the target protein, the pre-mRNA comprising an alternatively-spliced coding exon (ASCE), wherein an alternative processed mRNA that is produced by splicing out of the ASCE during processing of the pre-mRNA undergoes non-sense mediated RNA decay, the method comprising contacting a therapeutic agent or a vector encoding the therapeutic agent to the cell, wherein the therapeutic agent promotes inclusion of the ASCE during the processing of the pre-mRNA, thereby increasing a level of a processed mRNA that is processed from the pre-mRNA and comprises the ASCE.

[0004] Provided herein, in some aspects, is a method of treating or reducing the likelihood of developing a disease or condition in a subject in need thereof by modulating expression of a target protein in a cell of the subject, the method comprising: contacting the cell of the subject with a therapeutic agent or a vector encoding the therapeutic agent, wherein the cell comprises a pre-mRNA that is transcribed from a target gene and that encodes the target protein, the pre-mRNA comprising an alternatively-spliced coding exon (ASCE), wherein an alternative processed mRNA that is produced by splicing out of the ASCE during processing of the pre-mRNA undergoes non-sense mediated RNA decay, wherein the therapeutic agent promotes inclusion of the ASCE during the processing of the pre-mRNA, thereby increasing a level of a processed mRNA that is processed from the pre-mRNA and comprises the ASCE.

[0005] In some embodiments, the expression of the target protein is increased in the cell.