QurAlis to Present Data Showing Link Between TDP-43 Pathology and Role of UNC13A in Neuronal Biology Related to ALS and Other Neurodegenerative Diseases

Results showed TDP-43 pathology drives loss of synaptic UNC13A function; UNC13A is an essential regulator of neurotransmitter release at synapses

UNC13A mis-splicing is critical genetic alteration in neurodegenerative diseases, occurring in 58 percent of all ALS patients and up to half of all frontotemporal dementia cases

CAMBRIDGE, Mass., *September 6, 2023* – QurAlis Corporation, a clinical-stage biotechnology company developing breakthrough precision medicines for amyotrophic lateral sclerosis (ALS) and other neurodegenerative diseases with genetically validated targets, today announced it will present preclinical data showing that TDP-43 (TAR DNA-binding protein 43) pathology drives loss of synaptic UNC13A function in neurodegenerative diseases including ALS and frontotemporal dementia (FTD). Data also showed that an UNC13A splice-switching antisense oligonucleotide (ASO) prevented cryptic exon inclusion in UNC13A transcripts, increased UNC13A protein levels, and normalized localization of UNC13A protein at the synapse.

"UNC13A is a genetically validated target in ALS and FTD and our results showed that TDP-43 pathology drives loss of synaptic UNC13A function. At QurAlis, we hypothesize that ameliorating UNC13A mis-splicing using a splice-switching ASO can alleviate symptoms of ALS, FTD, and ALS/FTD spectrum disorder associated with synaptic dysfunction that underlies clinical manifestation and disease progression," said Daniel Elbaum, Ph.D., chief scientific officer of QurAlis. "We recently launched our newest program that targets UNC13A mis-splicing and look forward to advancing this program along with our other programs targeting neurodegenerative diseases so that we can make a real difference in patients' lives."

QurAlis will present these data in a poster presentation at the 1st Biennial Conference on TDP-43 Function and Dysfunction in Disease in Trieste, Italy on Thursday, September 7, 2023.

About UNC13A

UNC13A is an essential regulator of neurotransmitter release at synapses. In ALS and FTD, the loss of TDP-43 causes the mis-splicing of certain pre-mRNA transcripts resulting in expression of a cryptic exon-containing transcript that interferes with appropriate protein generation. An exon is a segment of a DNA or RNA molecule containing information coding for a protein or peptide sequence.

UNC13A is one of a number of pre-mRNAs that becomes mis-spliced due to loss of TDP-43 in disease. Fifty-eight percent of ALS patients and up to half of FTD patients carry a single nuclear polymorphism in the UNC13A gene or show TDP-43 pathology which greatly exacerbates UNC13A mis-splicing leading to loss of function of the UNC13A protein. There are currently no cures for ALS or FTD. Limited therapeutic options are available for ALS and FTD patients who are in desperate need for effective therapies.

Incorporating its proprietary FlexASO™ Splice Modulator Platform, QurAlis' antisense oligonucleotides (ASOs) correct this mis-splicing, restore UNC13A protein production, and reduce cryptic exons that may contribute to disease progression.

The QurAlis FlexASO Splice Modulator Platform was developed to generate splice-switching ASOs with improved potency and an increased therapeutic index. In addition to UNC13A, QurAlis is currently exploring this ASO technology for multiple other disease targets.

About QurAlis Corporation

QurAlis is trailblazing the path to conquering amyotrophic lateral sclerosis (ALS) and other neurodegenerative diseases with genetically validated targets with next-generation precision medicines. QurAlis' proprietary platforms and unique biomarkers enable the design and development of drugs that act directly on disease-causing genetic alterations. Founded by an internationally recognized team of neurodegenerative biologists from Harvard Medical School and Harvard University, QurAlis is advancing a deep pipeline of antisense oligonucleotides and small molecule programs including addressing sub-forms of ALS that account for the majority of ALS patients. For more information, please visit www.quralis.com or follow us on Twitter @QurAlisCo.

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