QurAlis' FlexASOs Show High Potency and Improved Safety Over Standard ASOs

Company's FlexASO programs targeting STATHMIN-2 and UNC13A showed three-fold potency, two-fold biodistribution improvement, improved safety, and greatly reduced off-target activity over standard ASOs

QurAlis' FlexASO™ Splice Modulator Platform designed to improve ASO performance, correct mis-splicing to restore synapse function, optimize distribution to deeper brain regions, and improve disease outcomes

Data to be showcased in an oral presentation at 3rd Annual Oligonucleotides for CNS Summit

CAMBRIDGE, Mass., *June 8, 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 new preclinical data showing the potential of the company's antisense oligonucleotides (ASOs) generated from its proprietary FlexASO™ Splice Modulator Platform. Data from two of QurAlis' FlexASO programs targeting rescue of STATHMIN-2 (STMN2) and UNC13A showed up to three-fold improvement over standard ASOs in both potency and biodistribution, and significantly reduced off-target effects, often from approximately 50 to 0, in human motor neurons. In addition, QurAlis' FlexASOs were not associated with cytokine or chemokine production. Observations from both programs therefore indicate that FlexASO™ technology results in a higher therapeutic index than observed with traditional ASO.

"QurAlis' FlexASO platform is based on unique and novel insights. We designed the platform to improve ASO performance, correct mis-splicing, and optimize distribution to deeper brain regions with the goal of identifying novel precision-medicine candidates for serious neurodegenerative diseases like sporadic ALS and frontotemporal dementia," said Kasper Roet, Ph.D., CEO and co-founder of QurAlis. "These new preclinical data showed that our ASOs targeting restoration of STMN2 and UNC13A exhibited significantly higher potency, greater biodistribution, and reduced off-target activity over standard ASOs. We are excited by these promising data and look forward to continue advancing our programs so that we can fulfill our mission of bringing transformative disease-modifying therapies to patients with significant neurodegenerative diseases in desperate need of options."

QurAlis will present these data in an oral presentation at the 3rd Annual Oligonucleotides for CNS Summit being held June 7-8, 2023 in Boston, MA. Daniel Elbaum, Ph.D., chief scientific officer of QurAlis, will present on June 8, 2023 at 8:00 AM ET, in a talk entitled, "Recent Advances in the Development of Splice Switching Oligonucleotides for CNS Diseases."

The QurAlis FlexASO Splice Modulator Platform was developed to generate splice-switching ASOs with improved potency and an increased therapeutic index. In addition to STMN2 and UNC13A, QurAlis is currently exploring this ASO technology for multiple other disease targets.

About STATHMIN-2, TDP-43, and UNC13A

STATHMIN-2 (STMN2) is a well-validated protein important for neural repair and axonal stability, the expression of which is significantly decreased in nearly all ALS patients. Also known as SCG-10, STMN2 is a protein essential for the stabilization of microtubules which form an important component of the cytoskeleton of cells and axons. STMN2 is highly expressed in human motor neurons, the cells that primarily degenerate in patients suffering from ALS. In animal models, STMN2 deletion was found to cause axonal degeneration and loss of muscle innervation, which is the primary functional deficit that leads to paralysis in ALS patients.

Using human neuronal stem cell models from ALS patients, QurAlis co-founder and former Harvard professor Kevin Eggan, Ph.D., discovered in 2019 that the expression of STMN2 is regulated by TDP-43. The Eggan Lab showed that loss of normal TDP-43 function leads to a highly significant decrease in expression of STMN2 and an impairment in neuronal repair which could be rescued by restoring STMN2 levels. These results were published in *Nature Neuroscience*.

In addition to nearly all ALS patients, TDP-43 pathology is also associated with approximately 50 percent of patients with frontotemporal degeneration (FTD), the second most common form of dementia; about a third of Alzheimer's Disease patients; and up to seven percent of Parkinson's disease patients.

UNC13A is an essential regulator of neurotransmitter release at synapses. In ALS and FTD, TDP-43 accumulates in the cytoplasm and no longer maintains its normal function controlling RNA metabolism in the nucleus. Due to its loss, certain pre-mRNA transcripts are mis-spliced resulting in expression of a cryptic exon-containing transcript that interferes with appropriate protein generation. UNC13A is a pre-mRNA that is 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 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.

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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