QurAlis Announces First Patient Dosed With QRL-201, a First-in-Class STATHMIN-2 Precision Therapy for ALS

First patient dosed in Canada in Phase 1 ANQUR study – the first-ever clinical trial to evaluate a therapy that rescues STATHMIN-2 expression in ALS patients

STATHMIN-2 is a well-validated protein important for neural repair and axonal stability, the expression of which is significantly decreased in nearly all ALS patients

CAMBRIDGE, Mass., *April 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 that the first patient has been dosed in its Phase 1 clinical trial of QRL-201 for the treatment of ALS (ANQUR). QRL-201 is a first-in-class therapeutic product candidate aiming to restore STATHMIN-2 (STMN2) expression in ALS patients. ANQUR is the first-ever study to evaluate a therapy that rescues STMN2 expression in ALS patients.

"STATHMIN-2 is a well-validated protein important for neural repair and axonal stability and is the most significantly regulated gene by TDP-43 exclusively in humans. Its expression is significantly decreased in nearly all ALS patients and it is the most consistently decreased gene over all sporadic ALS patient data sets. QRL-201 rescues STMN2 loss of function in QurAlis ALS patient-derived motor neuron disease models in the presence of TDP-43 pathology," said Angela Genge, M.D., FRCP(C), chief medical officer of QurAlis. "QRL-201 recently entered the clinic in Canada and we are pleased to dose our first patient. We look forward to advancing the ANQUR clinical trial of QRL-201 for the treatment of ALS so that we can make a meaningful difference in patients' lives."

The first participant in the ANQUR study was dosed at University of Montréal Hospital Centre (CHUM) by Geneviève Matte, M.D.C.M., FRCP(C), assistant clinical professor, Department of Neurosciences, University of Montréal; ALS clinic director, CHUM; principal investigator, University of Montréal Hospital Research Centre (CRCHUM); and an ANQUR study investigator.

"ALS is a serious neurodegenerative disease with limited treatment options. There is great need for therapies that could slow disease progression and improve outcomes. This study has the potential to show QRL-201 could be such a therapy that could potentially benefit ALS patients who have a loss of STMN2 due to TDP-43 pathology," said Merit Cudkowicz, M.D., M.Sc., director of the Sean M. Healey & AMG Center for ALS, chief of neurology at Massachusetts General Hospital, director and the Julieanne Dorn Professor of Neurology at Harvard Medical School, and member of QurAlis' Clinical Advisory Board.

ANQUR (NCT05633459) is a first-in-human global, multi-center, randomized, double-blind, placebo-controlled multiple-ascending dose Phase 1 clinical trial designed to evaluate the safety, tolerability, and pharmacokinetics of QRL-201 versus placebo in patients with ALS. The primary

objective of the study is to determine the safety and tolerability of multiple doses of QRL-201 in people living with ALS. The ANQUR clinical trial is expected to include 64 study participants with ALS across sites in Canada, the U.S., the United Kingdom, Belgium, the Netherlands, Italy, Germany, and Ireland.

Visit www.clinicaltrials.gov for more information about the ANQUR study.

About STATHMIN-2 and TDP-43
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. STATHMIN-2 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.

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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