QurAlis' ANQUR Clinical Trial of QRL-201 in ALS Advances to Dose Range-Finding (DRF) Phase With First Participant Dosed

PK data analysis in dose-escalation phase indicated exposures of QRL-201 met or exceeded the targeted therapeutic range prompting advancement to the DRF phase

ANQUR protocol amended to include additional biomarkers and cohort of participants with C9orf72-related ALS; Company to present update at 35th International Symposium on ALS/MND

CAMBRIDGE, Mass., *November 19, 2024* – QurAlis Corporation, a clinical-stage biotechnology company driving scientific breakthroughs into powerful precision medicines that have the potential to alter the trajectory of amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD), and other neurodegenerative and neurological diseases, today announced that the Phase 1 ANQUR clinical trial evaluating QRL-201 for the treatment of ALS has successfully completed the dose-escalation phase, based on pharmacokinetic (PK) data analysis from Cohorts 1 and 2, indicating cerebrospinal fluid (CSF) exposure levels of QRL-201 met or exceeded the targeted therapeutic range. QRL-201 is a first-in-class precision therapeutic product candidate that has the potential to restore STATHMIN-2 (STMN2) expression in ALS patients with the aim to modify disease progression and improve outcomes.

The ANQUR clinical trial (QRL-201-01; NCT05633459) has advanced to the dose range-finding (DRF) phase which will evaluate two doses of QRL-201 and include additional biomarkers. The study design will now also include a cohort of participants with C9orf72-related ALS in addition to participants with sporadic ALS. Based on previous expression analysis, patients with C9orf72-related ALS show consistent mis-splicing of STMN2. The ANQUR clinical trial is currently active in Canada, the United Kingdom (UK), and the European Union (EU). Cohorts 1 and 2 have successfully completed dosing and an amendment to the DRF study design has been approved in Canada and the UK, with anticipated approval from the EU in the near future. The first participant in the DRF phase has been dosed in Canada.

"ALS is a devastating, fatal neurodegenerative disease with a large unmet medical need. Our mission is to make a meaningful difference in patients' lives, and we believe QRL-201 could potentially modify disease progression and improve outcomes in ALS patients who have a loss of STMN2 due to TDP-43 pathology," said Kasper Roet, Ph.D., CEO and co-founder of QurAlis. "The PK data analysis from the first two completed cohorts of ANQUR indicated CSF exposures of QRL-201 met or exceeded the targeted therapeutic range. These findings further support our confidence in the potential therapeutic effect of QRL-201 in the treatment of sporadic ALS."

STMN2 is a well-validated protein important for neural repair, axonal stability, and muscle innervation and is the most significantly regulated gene by TDP-43 exclusively in humans. STMN2 is the most consistently decreased gene across multiple ALS RNA expression studies. Loss of nuclear TDP-43 leads to mis-splicing of the pre-mRNA of STMN2, resulting in loss of full-length transcript and protein. QRL-201 rescues STMN2 loss of function in QurAlis' ALS patient-derived motor neuron disease models in the presence of TDP-43 pathology. TDP-43 pathology is associated with nearly all ALS patients, approximately 50 percent of patients with FTD, the second most common form of dementia, and with about a third of Alzheimer's Disease patients. There are currently no cures for ALS or FTD, and there are limited therapeutic options available for ALS and FTD patients who are in desperate need of effective therapies.

"We are pleased that the first participant in Canada has been dosed in the dose range-finding stage of the ANQUR clinical trial," said Doug Williamson, M.D., QurAlis' chief medical officer. "This represents a significant milestone in the QRL-201 program to evaluate a potential transformative breakthrough precision medicine for patients with sporadic ALS."

QurAlis will present an update on the ANQUR clinical trial in a poster presentation at the 35th International Symposium on ALS/MND being held December 6-8, 2024, in Montreal, Canada and virtually. Details of the presentation are as follows:

Title: QRL-201-01 (ANQUR): A multicenter, randomized, double-blind, placebo-controlled multiple ascending dose study to evaluate the safety and tolerability of QRL-201 in amyotrophic lateral sclerosis
Date/Time: Saturday, December 7, 2024 5:00-7:00PM ET
Theme: Clinical Trials and Trial Design
Abstract Number: CLT-11
Session: Poster Session B
Presenter: Emma Bowden, Ph.D., senior vice president, head of clinical development, QurAlis

About the ANQUR Clinical Trial
ANQUR (QRL-201-01; NCT05633459) is the first-ever clinical trial to evaluate a potential therapy to rescue STATHMIN-2 (STMN2) expression in people with amyotrophic lateral sclerosis (ALS). ANQUR is a global, multi-center, randomized, double-blind, placebo-controlled multiple-ascending dose Phase 1 clinical trial designed to evaluate the safety and tolerability of QRL-201 versus placebo in participants with ALS. The primary objective and endpoint of the study is to determine the safety and tolerability of multiple doses of QRL-201. The secondary objective and endpoint is the plasma pharmacokinetic (PK) profile of QRL-201 after multiple doses. ANQUR also intends to evaluate multiple exploratory endpoints including biomarkers of neuronal loss and STMN2 biology (neurofilament levels, STMN2 levels, Chitinase-3-like protein 1, and miRNA profiles), clinical outcome measures (ALSFRS-R, ALSAQ-5, ROADS, King's Staging, SVC, muscle strength, electrophysiology markers of denervation [maximum compound muscle action potential/CMAP and repetitive nerve stimulation/RNS]), and cerebrospinal fluid (CSF) PK profile.

The ANQUR clinical trial is expected to include 64 study participants with ALS across sites in Canada, the European Union (EU), and United Kingdom (UK). Sites participating in the ANQUR clinical trial: Canada – University of Alberta (Edmonton, Alberta) University of Calgary (Calgary, Alberta), Montréal Neurological Institute-Hospital (Montreal, Quebec), and CHUM-Hopital Notre-Dame (Montréal, Quebec); EU – Universitaire Ziekenhuizen Leuven (Leuven, Belgium), Charité Research Organisation (Berlin, Germany), University Hospital Schleswig-Holstein Campus Lübeck (Lübeck, Germany), Universitätsklinikum Ulm (Ulm, Germany), Universitair Medisch Centrum Utrecht (Utrecht, The Netherlands); and UK – St. James Hospital (Dublin, Ireland), Kings College Hospital NHS Foundation Trust (London, England), and The University of Sheffield, Royal Hallamshire Hospital (Sheffield, England).

The ANQUR clinical trial successfully completed the dose-escalation phase, based on PK data analysis from Cohorts 1 and 2, indicating CSF exposure levels of QRL-201 met or exceeded the targeted therapeutic range. The dose range-finding phase will evaluate two doses of QRL-201 and will enroll an additional 48 participants: 32 participants with sporadic ALS and 16 participants with C9orf72-related ALS.

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

About QurAlis Corporation

At QurAlis, we are neuro pioneers on a quest to cure. We work with a relentless pursuit of knowledge, a precise attention to craft, and an optimistic mindset to discover and develop effective precision medicines that have the potential to alter the trajectory of amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD), and other neurodegenerative and neurological diseases. Founded by an internationally recognized team of neurodegenerative biologists from Harvard Medical School and Harvard University, QurAlis is advancing a robust precision medicine pipeline with therapeutic candidates aimed at modifying severe disease pathology in defined patient populations based on both disease-causing genetic mutation(s) and clinical biomarkers. For more information, please visit www.quralis.com or follow us on X @QurAlisCo or LinkedIn.

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