QurAlis Announces Topline Data From its Phase 1 Clinical Trial of QRL-101 Evaluating Biomarkers of ALS and Epilepsy in Healthy Volunteers

Results demonstrated statistically significant effects on biomarkers that predict ALS disease progression and severity

Evidence of brain penetration, target engagement, and potential anti-seizure effects demonstrated through biomarkers for TMS-EMG and EEG

Safety and tolerability profile consistent with previously reported results for QRL-101

QurAlis intends to advance QRL-101 into proof-of-concept studies as a potentially best-in-class treatment for both ALS and epilepsy

CAMBRIDGE, Mass., *March 12, 2025* – QurAlis Corporation ("QurAlis"), a clinical-stage biotechnology company driving scientific breakthroughs into powerful precision medicines that have the potential to alter the trajectory of neurodegenerative and neurological diseases, today announced positive topline data from QurAlis' Phase 1 proof-of-mechanism (PoM) clinical trial of QRL-101 in healthy volunteers evaluating biomarkers related to amyotrophic lateral sclerosis (ALS) and epilepsy.

Topline results demonstrated a dose-dependent, statistically significant decrease in motor nerve excitability threshold tracking (mNETT) strength-duration time constant (SDTC), the co-primary endpoint of the trial related to ALS. SDTC is a well-established electrophysiological biomarker of peripheral motor excitability related to ALS, where elevation of SDTC has been clinically shown to predict faster disease progression and mortality. The decrease in SDTC observed with QRL-101 in this study was approximately 50% greater than previously reported for the Kv7 potassium channel opener ezogabine in a single-dose study in people with ALS. Additional observations for multiple secondary and exploratory endpoints related to motor nerve excitability were also significantly impacted.

The clinical trial demonstrated a statistically significant impact on multiple secondary and exploratory endpoints related to epilepsy. These included transcranial magnetic stimulation electromyography (TMS-EMG) intracortical facilitation which indicates effective inhibition of cortical excitability, as well as significant increases in electroencephalography (EEG) spectral power in beta and gamma spectral bands further demonstrating cortical target engagement and brain penetration. There was no statistically significant impact on the slower delta and theta EEG bands, which suggests a low potential for GABA-A receptor activation and sedation. The study did not reach statistical significance on the co-primary endpoint of TMS-EMG motor evoked potential (MEP) amplitude, another measure of corticospinal excitability.

Results also demonstrated that the safety and tolerability profile of QRL-101 was consistent with previously reported study results evaluating QRL-101 to date. There were no serious adverse events or discontinuations due to adverse events reported observed in the study.

"We are excited by these topline data from our biomarker study in healthy participants which suggest that QRL-101 has the potential to provide a therapeutic effect for both ALS and epilepsy," said Kasper Roet, Ph.D., CEO and co-founder of QurAlis. "Loss of Kv7.2/7.3 function from the mis-splicing of the KCNQ2 gene leading to hyperexcitability-induced neurodegeneration was one of the first genetic breakthroughs from human ALS motor neuron stem cell models made by our founders at Harvard. QurAlis was started

to develop a best-in-class Kv7 ion channel opener for the treatment of hyperexcitability-induced disease progression in ALS, which occurs in about half of all people living with ALS. Elevated SDTC has been clinically linked to faster disease progression and mortality, underscoring the need for an effective treatment for this population."

Dr. Roet continued, "The decrease in SDTC observed with QRL-101 in this study was approximately 50% greater than previously reported for the Kv7 opener ezogabine in a single-dose study in people with ALS. QRL-101 has the potential to be a promising therapeutic, especially considering the encouraging results from a previous study with ezogabine in ALS patients showing positive effects on both SDTC and the disease progression biomarker compound muscle action potential (CMAP). Further, based on the strong clinical validation of Kv7.2/7.3 ion channel openers in seizure reduction, the TMS-EMG intracortical facilitation together with the EEG data from this study suggest QRL-101 may have the potential to reduce both frequency and severity of seizures in people living with epilepsy without causing sedation. We are encouraged by these results and look forward to advancing the clinical program for QRL-101 in both ALS and epilepsy so that we can fulfill our mission of bringing much-needed precision medicine options to patients."

Kv7.2/7.3 is a voltage-gated potassium channel whose role is crucial for the regulation of both neuronal excitability and membrane potential. QRL-101 is a potentially best-in-class selective Kv7.2/7.3 ion channel opener for the treatment of hyperexcitability-induced disease progression in ALS, which occurs in both sporadic and genetic forms of ALS, with the majority caused by the mis-splicing of the KCNQ2 gene in the pre-mRNA. Kv7 is also a clinically validated target to regulate the hyperexcitable state in epilepsy. *In vivo* and *in vitro* studies have demonstrated that QRL-101 is more potent in threshold track studies and exhibits the potential for fewer clinical adverse events that ezogabine, a less selective, first-generation, Kv7.2/7.3 channel opener.

The Phase 1 PoM study (QRL-101-05, NCT06681441) was a randomized, double-blind, placebo-controlled, three-way crossover trial. The study was conducted at the Centre for Human Drug Research, an early-phase Contract Research Organization based in Leiden, The Netherlands. The study evaluated two dose levels of QRL-101 versus placebo in healthy volunteers, assessing:

- **Co-primary endpoints:**
    - Motor nerve excitability (mNETT SDTC; ALS biomarker)
    - Cortical excitability (TMS-EMG MEP amplitude; epilepsy biomarker)
- **Secondary endpoints:**
    - Additional TMS-EMG cortical excitability measures
    - Resting-state pharmaco-EEG
    - Safety, tolerability, and pharmacokinetics (PK)

Additional QRL-101 clinical trials include:

- QRL-101-01 (NCT05667779) was a first-in-human, single-ascending dose clinical trial in 88 healthy participants. In this clinical trial, QRL-101 was shown to be well tolerated. The study completed in late 2023 and results from QRL-101-01 supported a tolerable dose range for subsequent studies.
- QRL-101-03 (NCT06532396) is a randomized, double-blind, placebo-controlled, multiple-ascending dose clinical trial evaluating the safety, tolerability, and PK of QRL-101 in up to 60 healthy participants.

- QRL-101-04 (NCT06714396) is a Phase 1 PoM single-dose, placebo-controlled clinical trial designed to evaluate the safety and tolerability of QRL-101 in people living with ALS. QRL-101-04 is expected to enroll approximately 12 participants with ALS and will evaluate the impact of QRL-101 on mNETT.
- QRL-101-06 is a Phase 1 randomized, open-label, single dose, cross-over study to evaluate the PK of three formulations of QRL-101 in a fasted condition or in the presence of a high fat meal in healthy participants.

More information about the QRL-101 clinical trials can be found at www.clinicaltrials.gov.

About QurAlis Corporation

At QurAlis, we are neuro pioneers on a quest to cure, boldly seeking to translate scientific breakthroughs into powerful precision medicines. We work collaboratively with a relentless pursuit of knowledge, precise attention to craft, and compassion to discover and develop medicines that have the potential to transform the lives of people living with neurodegenerative and neurological diseases. QurAlis is the leader in development of precision therapies for amyotrophic lateral sclerosis (ALS). In addition to ALS, QurAlis is advancing a robust precision medicine pipeline to bring effective disease-modifying therapeutics to patients suffering from severe diseases defined by genetics and clinical biomarkers. For more information, please visit www.quralis.com or follow us on X @QurAlisCo or LinkedIn.

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