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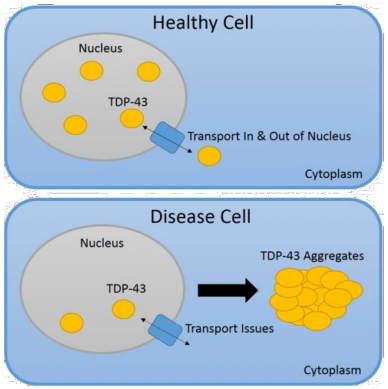
QRL-201-01 ANQUR
A multi-center, randomized, double-blind, placebo-controlled, multiple-ascending dose study to evaluate the safety and tolerability of QRL-201 in amyotrophic lateral sclerosis

QRL-201 Clinical Program Overview

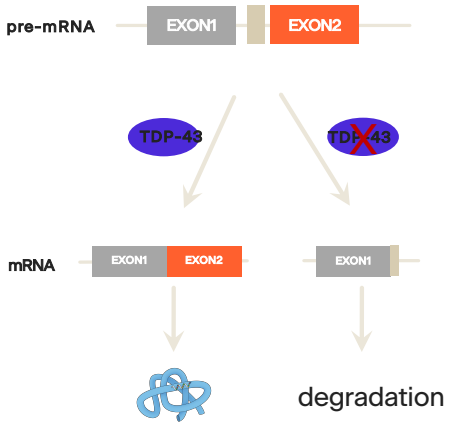
- Phase 1 ANQUR clinical trial – first-in-human global, multi-center, randomized, double-blind, placebo-controlled multiple-ascending dose (MAD) study of QRL-201 vs. placebo in participants living with ALS (NCT05633459)
  - **First-ever clinical trial to evaluate a therapy that potentially rescues STMN2 expression in people living with ALS**
  - Study primary objective: determine safety and tolerability of multiple doses of QRL-201 in people living with ALS
- Study has received regulatory authorization in Canada, the United Kingdom, and the European Union
- Cohort 2 is in progress

STMN2: A Genetic Target for the Sporadic ALS Population

QURALIS THERAPEUTIC STRATEGY

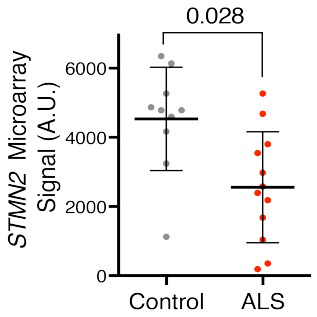


QurAlis niche



TDP-43 regulation of *STMN2*

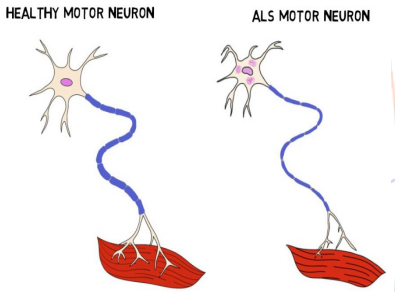
Loss of full length *STMN2*



Rabin et al., 2009

Cryptic splicing-ASO approach to restore STMN2

Axonal degeneration and impaired repair



Rescue of axonal stability and repair

Nat. Neurosci. Feb 2019, Eggan ALS One 2020, Li et al., 2009, Morii et al., 2006, Shin et al., 2012, Shin et al., 2014, Xu et al., 2010

QRL-201 Clinical Program Overview (cont.)

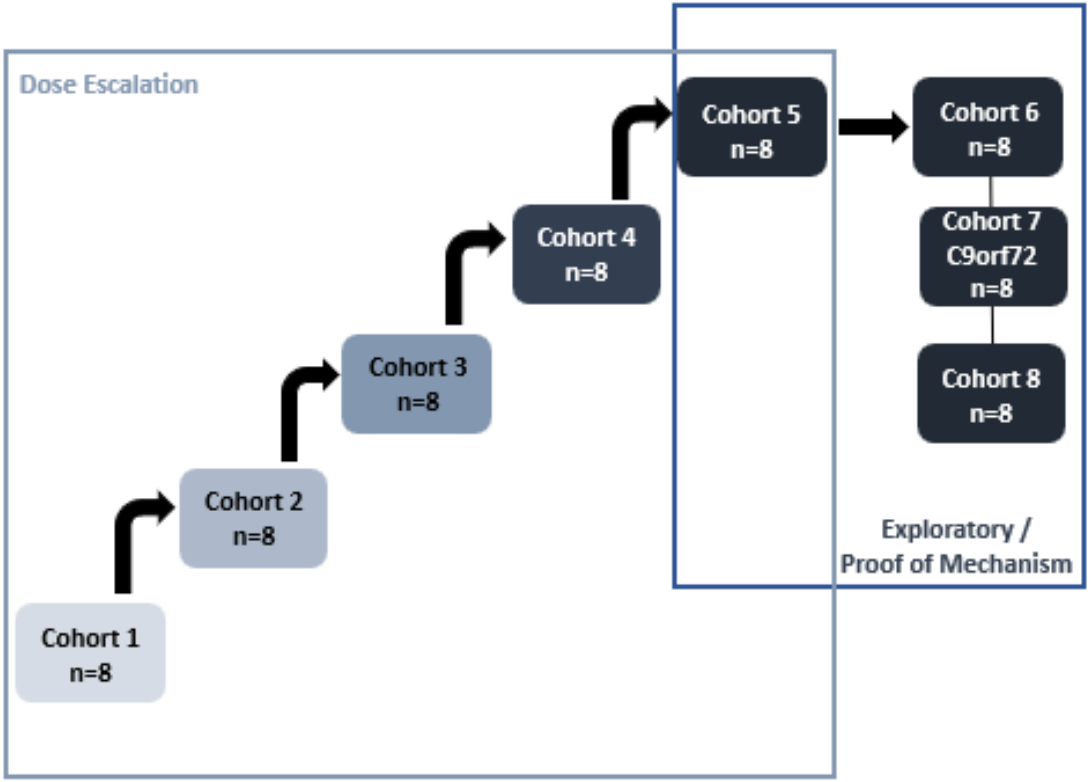
QRL-201	•Splice switching ASO against STMN2 pathology
Function/MoA	•Correct *STMN2* mis-splicing & restoration of STMN2 protein
Route of Administration	•Intrathecal injection
Dosing Regimen	•3 loading doses •Monthly dosing thereafter
Placebo	•Supplied; artificial CSF •Same route of administration and regimen as QRL-201

QRL-201-01 Study Design

Cohorts 1-5: sporadic ALS*
Dose Escalating MAD
*C9orf72 (+) pts may be enrolled in Cohorts 1-5

Cohort 7: C9orf72 ALS / Cohort 6 & 8: sporadic ALS
Exploratory, biomarker cohorts – dosing at maximum tolerated dose

Cohort 1-8: n = 64*
Cohorts randomized 6:2 (QRL-201 : placebo)
Sentinel Participants randomized 1:1 (QRL-201 : placebo)
***replacement participants at QurAlis' discretion**



*Protocol V3.0 11-May-2023
ClinicalTrials.gov ID: NCT05633459

QRL-201-01 Study Design (cont.)

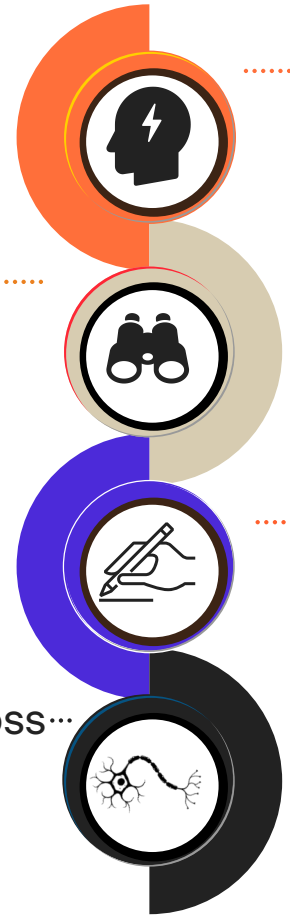
OBJECTIVES	ENDPOINTS
PRIMARY: To determine the safety and tolerability of multiple doses of QRL-201	Incidence of AEs and SAEs associated with QRL-201
SECONDARY: To determine the plasma PK profile of QRL-201 after multiple doses	Multiple dose PK

KEY INCLUSION CRITERIA*	KEY EXCLUSION CRITERIA*
• Male or female participants aged 18 to 80 years diagnosed with ALS • ALS symptom onset within 24 months • Slow vital capacity >50% • Clinical evidence of lower motor neuron involvement • Not pregnant and not nursing • Willing and able to practice effective contraception • Able to tolerate lumbar puncture • If on approved therapies for the treatment of ALS during the course of the study, must be on a stable dose (at the Sponsor's discretion)	• Pathogenic variant, likely pathogenic variant, or variant of uncertain significance in the superoxide dismutase 1 (SOD1) and/or fused in sarcoma (FUS) genes • Currently enrolled in any other clinical study involving either an investigational product (IP) or off-label use of a drug or device • Prior exposure to stem cell or gene therapy products • Any contraindication to intrathecal drug administration • Abnormal laboratory values deemed clinically significant by the Investigator • Significant infection, or known inflammatory process

*Additional I/E criteria may apply

Comprehensive Biomarkers and Phenotypic Assessments to Measure Activity

AnQur



Electrophysiology

- Established NMJ innervation measurements (STMN2 MOA/efficacy)
- Motor excitability recordings (CMAP, M-Scan)

Target Engagement

- STMN2 levels

Clinical Measurements

- ALSFRS-R
- ROADS
- SVC
- HHD
- Ventilation assistance-free survival
- Time to event measures

Biomarkers of Neuronal Loss

- NfL and other exploratory biomarkers

Summary

- QurAlis' mission is to bring breakthrough precision medicine technology to people living with ALS. QRL-201-01 is designed to evaluate the safety and tolerability of multiple doses of QRL-201 in people living with ALS and explore the hypothesis that restoration of STMN2 is a suitable disease modifying approach in ALS.

- QRL-201 is an investigational ASO for the recovery of STMN2 expression and function in ALS patients, even in the continued presence of TDP-43 pathology.

- To investigate QRL-201, QurAlis has designed a first in human study evaluating the safety and tolerability of multiple doses of QRL-201 in people living with ALS.

- This study is expected to enroll 64 study participants, at up to 16 sites, across North America and Europe. Enrollment began in early 2023. Refer to www.clinicaltrials.gov for further details and updates: **NCT05633459**