QurAlis™

Driving scientific breakthroughs into powerful precision medicines for ALS and other neurodegenerative diseases

September 2026

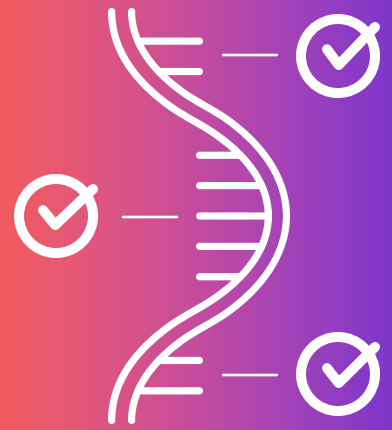
Advancing precision therapeutics for neurodegenerative disease

Technological breakthroughs

Human disease models supportive of developing precision therapies

Novel FlexASO® technology to tune potency, safety, and dosing frequency

AI/ML and large data sets accelerating novel target & hit identification



Disease-modifying RNA therapies

RNA restoration oligonucleotides targets

Diseases caused by mis-splicing (e.g., ALS, SMA, FTD, Fragile X, PSP)

Deep layer tissue penetration providing access to previously challenging brain regions

Previously undruggable targets for large indications and underserved markets

Seasoned executive team with strong track record of execution across clinical & preclinical pipeline

Kasper Roet, PhD
CEO & CO-FOUNDER

Harvard Medical School
Johnson & Johnson

Jason Brown, MBA
CFO & COO

Karuna Therapeutics
PureTech — Giving Life to Science
Novartis

Manoj Malhotra MD
CMO

AbbVie
Ovid Therapeutics
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Hagen Cramer, PhD
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Wave Life Sciences
Avecia
Ridgeway Biosystems Inc.

Dan Elbaum, PhD
CSO

Retrophin
Pfizer
Amgen

Guzide Adhikari, PhD
SVP CMC OPS & STRATEGY

Translate BIO
Takeda
Shire

Investors

sanofi ventures
EQT Life Sciences
Dementia Discovery Fund
mission BIOCAPITAL
Dolby Family Ventures
MP Healthcare Venture Management, Inc. — Mitsubishi Tanabe Pharma Group
Mitsui Global Investment
DROIA ventures
Polaris Innovation Fund
Lilly
ALS Investment Fund
inkef capital
Mass General Brigham Ventures
Amgen

Robust precision neuroscience pipeline

Program	MOA	Indication(s)	Upcoming Milestone(s)	Discovery	IND-Enabling	Ph1 Safety / PoM	Proof of Concept	Registration Studies
QRL-201	**STMN2**	**ALS**	**ANQUR OLE ongoing; pivotal Ph2b initiation expected 2027**					
QRL-101	Kv7.2/7.3	DEE / ALS / Pain	Topline of MAD in SDD microgranule formulation					
QRL-204	UNC13A	ALS / FTD	In partnership with Lilly					
QRL-203	STMN2	ALS / FTD	FlexASO® next-gen candidate					
QRL-TBA	FMR1	Fragile X	DC nomination 2026					
QRL-TBA	Tau	PSP	DC nomination 2027					

Amyotrophic lateral sclerosis (ALS); development candidate (DC); Developmental and Epileptic Encephalopathy (DEE); Frontotemporal dementia (FTD); Multiple Ascending Dose (MAD); Open Label Extension (OLE); Progressive Supranuclear Palsy (PSP); Proof of Mechanism (POM); Spray-Dried Dispersion (SDD)

QRL-201:

A next-generation treatment for ALS

ALS is a devastating neurodegenerative disease with significant unmet medical need

220,000+

global prevalence (est.)

2-3 Months

The survival benefit of current approved therapies (riluzole, edaravone)

+25%

Increase in prevalence expected by 2040

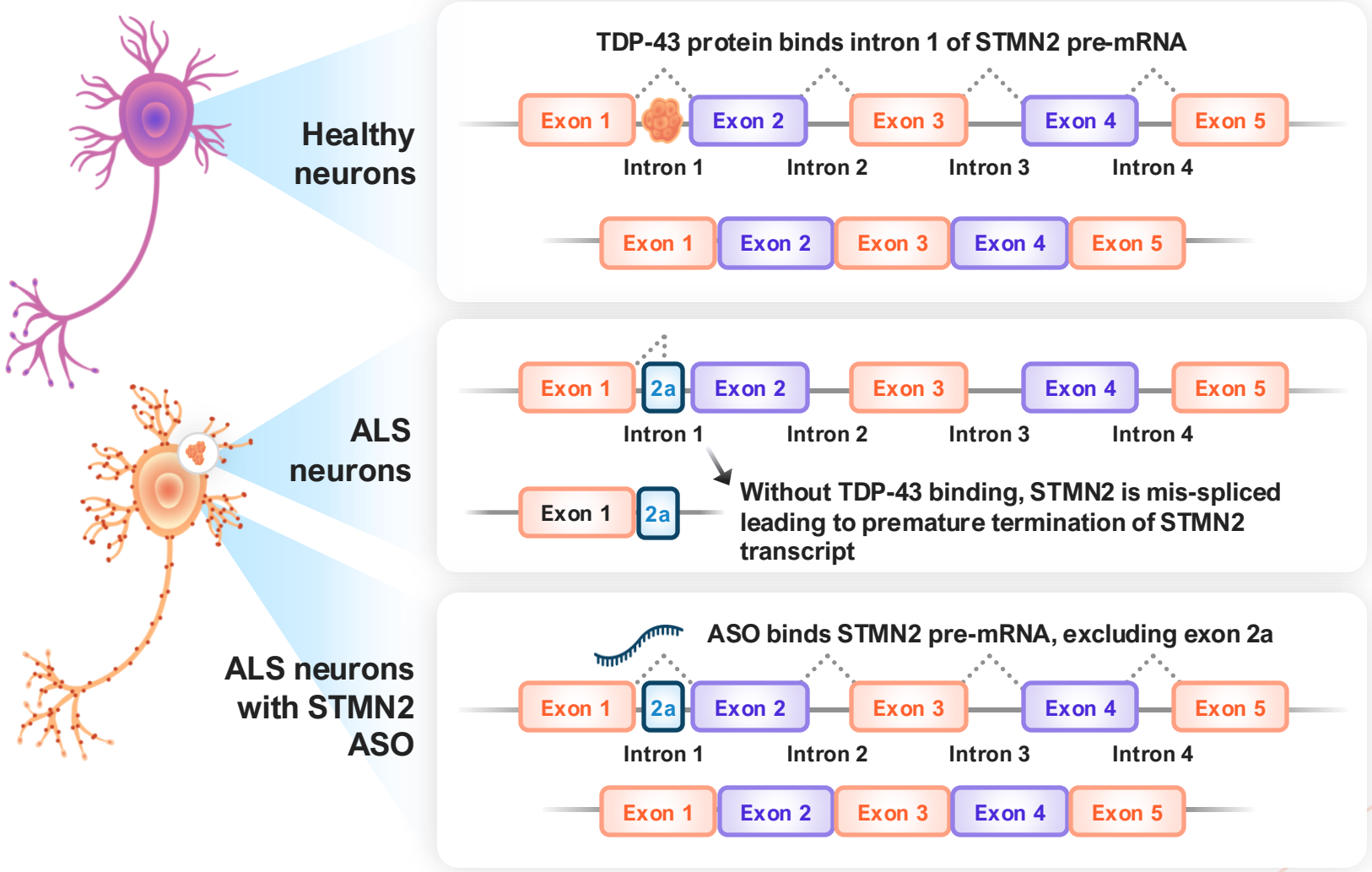
every 90 min

Someone is diagnosed with, and dies from ALS

~97% **The percent of ALS population with TDP-43 pathology who do not benefit from genetic therapies targeting familiar variants (SOD-1, FUS)**

QRL-201 is designed to restore Stathmin-2 (STMN2)

STMN2 is a motor-neuron survival protein silenced by TDP-43-driven mis-splicing in sporadic ALS



In QurAlis' ANQUR study, QRL-201 restored STMN2 to healthy levels in patient tissue and showed a meaningful slowing of functional decline

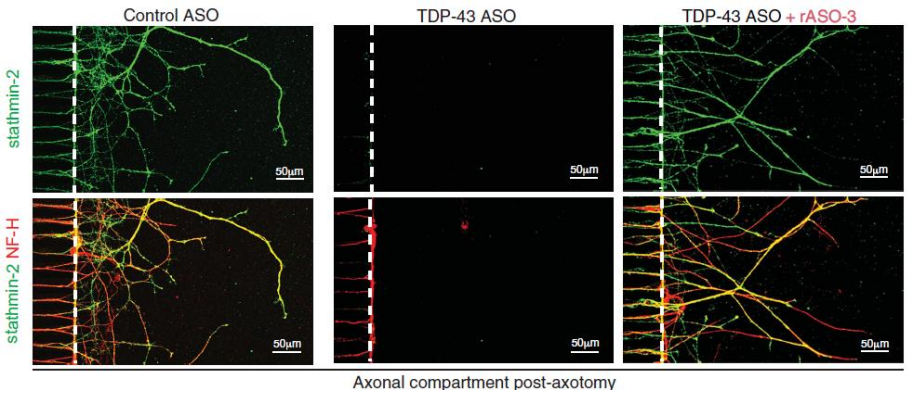
Restoration of STMN2 is a promising therapeutic strategy for the treatment of ALS

STMN2 loss is a validated, mechanistic driver of ALS neurodegeneration

Breakthrough discovery: TDP-43 pathology directly causes STMN2 loss

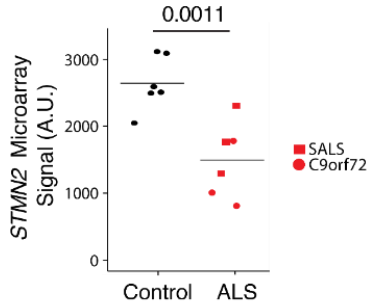
Loss of TDP-43 from the nucleus (ALS hallmark) leads to loss of STMN2

TDP-43 loss causes loss of axons; rescue by restoring STMN2 levels



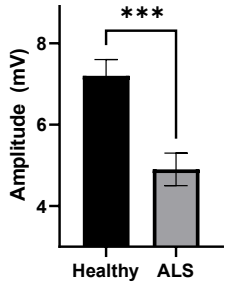
STMN2 is downregulated in ALS patients

Microarray Laser Capture Motor neuron (Highley et al 2014)



Loss of STMN2 leads to denervation of muscles

CMAP tibialis anterior



Human

Restoring STMN2 is a compelling therapeutic strategy

- **Not a bystander effect:** TDP-43 pathology, the defining hallmark present in the majority of ALS, directly causes STMN2 loss
- **Confirmed in human patients:** STMN2 downregulation is measured directly in ALS motor neurons, not just in preclinical models
- **Mechanistically clear path to benefit:** STMN2 loss produces a measurable functional cascade, from axon loss to muscle denervation, giving a direct, testable link between restoring STMN2 and clinical benefit
- **Broad patient relevance:** because TDP-43 pathology spans sporadic and most genetic forms of ALS, this mechanism applies to the majority of patients, not a narrow subtype

1. Melamed Z, López-Erauskin J, Baughn MW, et al. Premature polyadenylation-mediated loss of stathmin-2 is a hallmark of TDP-43-dependent neurodegeneration. *Nat Neurosci.* 2019;22(2):180-190. doi:10.1038/s41593-018-0293-z
2. Klim, J.R., Williams, L.A., Limone, F. et al. ALS-implicated protein TDP-43 sustains levels of STMN2, a mediator of motor neuron growth and repair. *Nat Neurosci* 22, 167–179 (2019). https://doi.org/10.1038/s41593-018-0300-4
3. Baughn, M. W., et al. (2023). "Mechanism of STMN2 cryptic splice-polyadenylation and its correction for TDP-43 proteinopathies." *Science* 379(6637): 1140-1149.
4. Krus et al., 2022 *Cell Rep* Jun 28;39(13):111001. doi: 10.1016/j.celrep.2022.111001

STMN2 has the potential to treat the majority of ALS patients

Approved genetic therapies reach a narrow slice of ALS patients; STMN2 restoration reaches nearly all ALS patients

Genetically targeted therapies, today

~3%

SOD1 and FUS-driven ALS: a narrow genetic subset of ~2K[1] patients (estimated globally) addressable by gene-targeted therapies.

~$0.4B theoretical combined US & EU market at current list prices

STMN2

the mechanism that scales

ALS addressable with STMN2 restoration

~97%

TDP-43 pathology drives STMN2 loss across sporadic and *C9orf72* ALS: ~58K[1] patients, for the first time reachable by a single mechanism-based approach.

~$10B theoretical combined US & EU market at current list prices

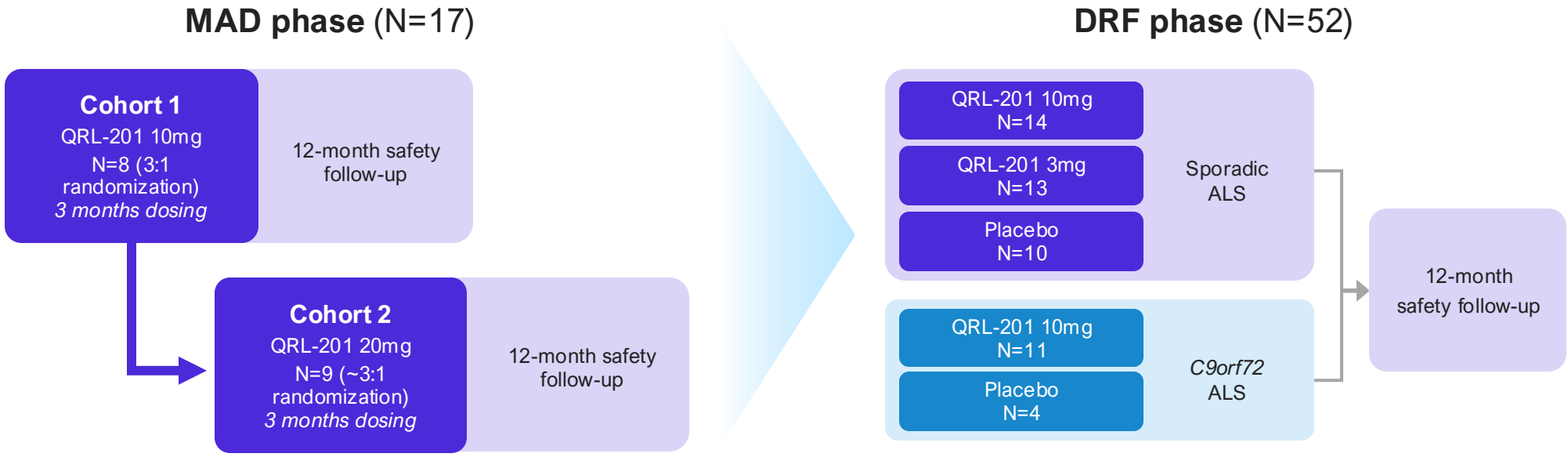
STMN2 loss is a convergent, mechanism-based driver of ALS, not a rare mutation. Restoring it is the first approach with the potential to reach the majority of patients, not just a genetically defined niche.

[1]Based on literature review of SOD1 and FUS (1%-3% of total) prevalence in US, UK, DE, FR, ES, IT
[2]Based GlobalData prevalence estimates in US, UK, DE, FR, ES, IT less SOD-1 and FUS segment
[3]Pricing analogs based on monthly list price of ~$15k (excluding loading) for Qalsody® and Radicava® in United States

ANQUR proof-of-concept Phase 1/2 design overview

Progressed from MAD to DRF phase based on positive PK & tolerability in MAD cohorts

AnQur



ANQUR open-label extension ongoing; pivotal trial planning underway with study expected to initiate in 2027

Multiple Ascending Dose (MAD), Dose Range Findings (DRF)

ANQUR study validates QRL-201 as a first- and best-in-class ASO to treat sporadic ALS

A Favorable safety and tolerability profile

- QRL-201 was generally safe and well tolerated across evaluated doses, with no dose-limiting toxicities observed

B Favorable CSF pharmacokinetics

- CSF exposure exceeded predicted efficacy thresholds with a long half-life, supporting durable target coverage
- PK profile supports durable exposure with less frequent dosing
- Relatively homogeneous distribution observed across spinal cord and motor cortex tissue

C Clear evidence of target engagement

- Statistically significant ~2-4x increase of STMN2
- Statistically significant improvement of STMN2/cryptic STMN2 ratio in tissue

D Statistical significance on key registrational endpoint (ALSFRS-R)

- 50% Decrease of ALSFRS-R progression in 10mg dose

E Meaningful effects on efficacy biomarkers

- CSF pNfH shows early and durable reductions consistent with improved axonal integrity
- CSF NfL decreases meaningfully
- Plasma NfL demonstrates directionally consistent reductions, particularly in the ex-high baseline NfL population, supporting translational coherence

Preliminary data pending QC review

A QRL-201 demonstrated favorable safety & tolerability profile[1]

Data Safety Monitoring Board agreed to continue the study without modifications during all phases, and as recently as May 2026

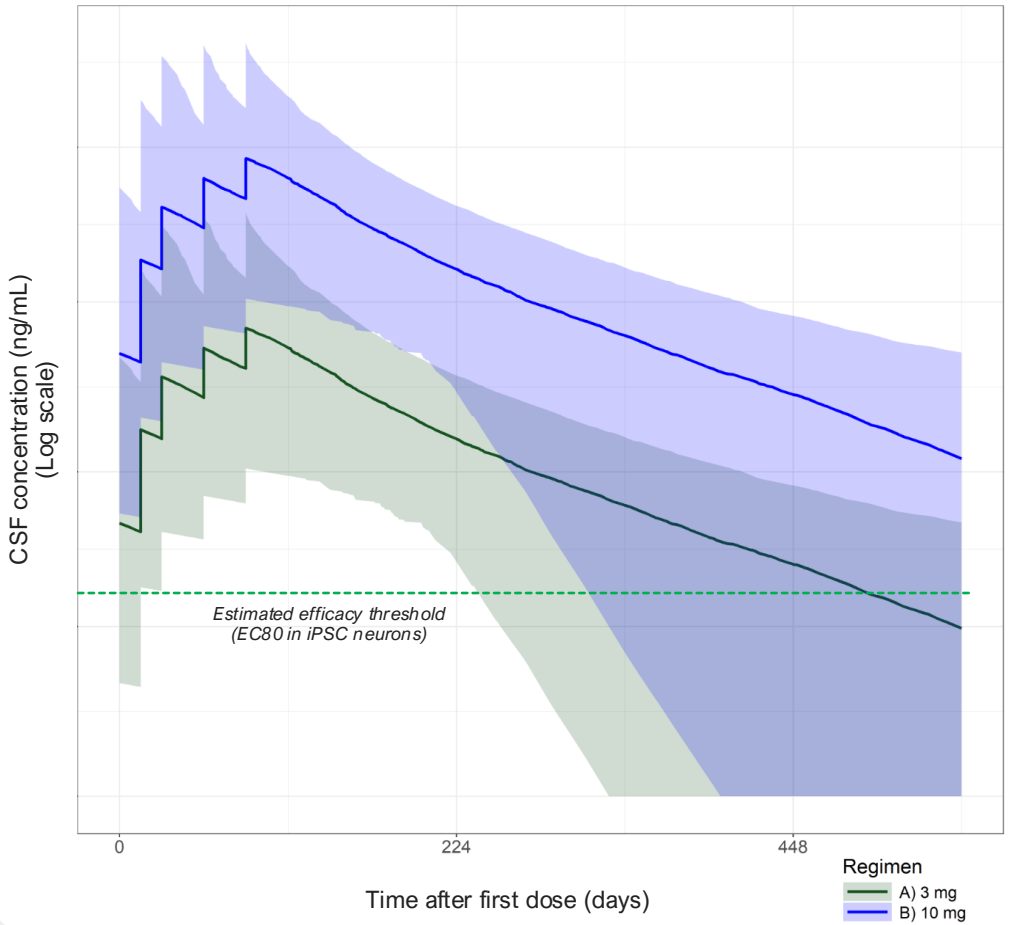
Safety Population (MAD+DRF) *N (%)*	**3mg (N=13)**	**10mg (N=31)**	**20mg (N=7)**	**Placebo (N=18)**
Any Adverse Event (AE)	13 (100%)	31 (100%)	7 (100%)	18 (100%)
Treatment Emergent Aes (TEAEs)	13 (100%)	31 (100%)	7 (100%)	18 (100%)
TEAEs related to study drug	3 (23%)	10 (32%)	2 (29%)	2 (11%)
AEs of Special Interest (AESIs)	-	5 (16%)[2]	-	2 (11%)[2]

There was one (1) TEAE leading to discontinuation and one (1) TESAE related to study drug reported in the study, both in the MAD phase, for which the dose groups cannot be disclosed until the study is unblinded

[1] Includes data from Multiple Ascending Dose (MAD) and Dose Range Finding (DRF) phases as of data cut-off date (2/28/2026)

[2] Reported AESIs as follows: (6) Pleocytosis and (1) Dysaethesia

B Pharmacokinetics (PK) & target engagement are supportive of biomarker and clinical efficacy observations



Pharmacokinetics (PK)

- ✓ Dose-proportional uptake observed in CSF[1]
- ✓ Half-life estimated to exceed 100 days, providing opportunity for less frequent dosing in future studies
- ✓ All doses tested were well in excess of estimated efficacy threshold. Low-dose PK median concentration after last dose is estimated to be 6-fold above estimated efficacy threshold
- ✓ Autopsy sample analysis indicated relatively homogeneous tissue distribution of QRL-201 throughout spinal cord and motor cortex

[1] CSF = Cerebrospinal fluid

C Statistically significant increase of STMN2 levels of ≥2-fold in tissue compared to natural history ALS patients

STMN2 is down-regulated 2-fold in ALS patients; targeting 2-fold up-regulation (healthy individuals)

Sample	Fold Increase Relative to ALS NH[1]	FL: Cryptic Ratio *(dCT T-statistic)*
Motor cortex	1.2 - 1.2	<LOD
Brain stem	2.0 - 4.6	2.6 - 14.0
Cervical spinal cord	3.7 - 9.6	(0.4) - 3.1
Thoracic spinal cord	2.3 - 5.7	1.2 - 1.7
Lumbar spinal cord	2.0 - 3.0	8.0 - 10.8

*Values in **blue** indicate 95% confidence in difference from ALS Natural History mean*
*Values in **green** indicate 80% confidence in difference from ALS Natural History mean*

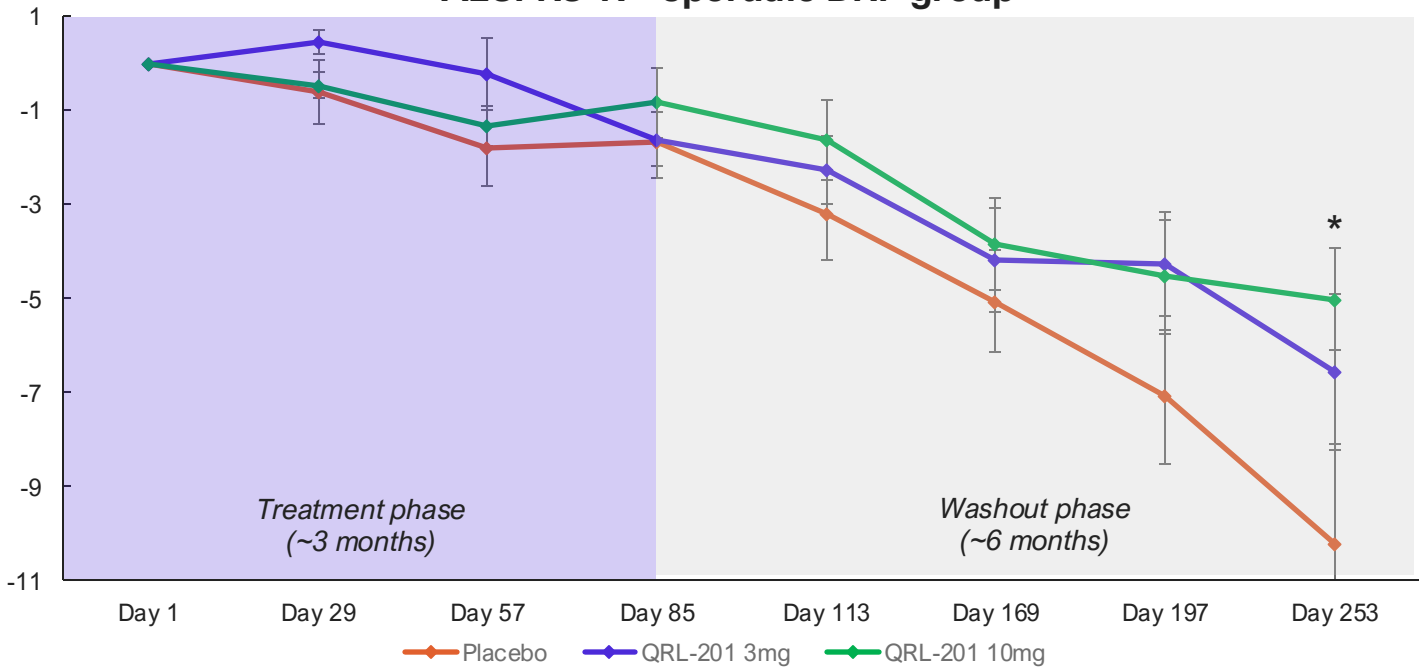
- Autopsy samples were obtained from the MAD phase of the study[2] and mRNA tissue analysis was performed using validated assays and compared to natural history ALS patient controls
- **≥2-fold increase of full length STMN2 levels in tissue**, especially robust in brain stem and spinal cord regions; **stat. sig. increase in most regions**
- The improvement in STMN2/cryptic STMN2 splicing is **most robust in the lumbar spinal cord**, as well as the **brain stem, and cervical spinal cord**
- No quantifiable cryptic STMN2 in the motor cortex, and consequently the ratio could not be calculated

[1] Sample comparison to ALS natural history samples analyzed by the same lab & validated methods
[2] Patient samples were obtained within 6 months after their last dose
Data not QCed

D Consistent slowing of functional decline demonstrated with both doses

10mg group has a 50% slowing of decline (statistically significant) at Day 253 (~8.5 months)

ALSFRS-R – sporadic DRF group



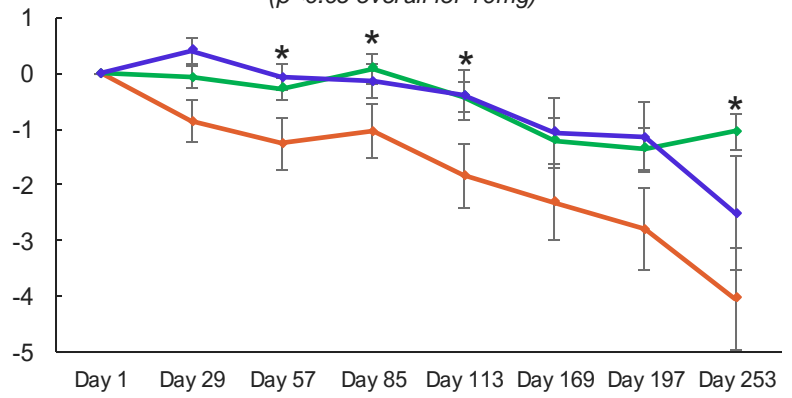
QRL-201 3mg	13	13	13	13	12	12	12	10
QRL-201 10mg	14	13	14	14	14	14	14	13
Placebo	10	10	10	10	10	8	6	6

Discontinuation (death, disease progression, other): **3mg 15%** **10mg 7%** **Placebo 40%**

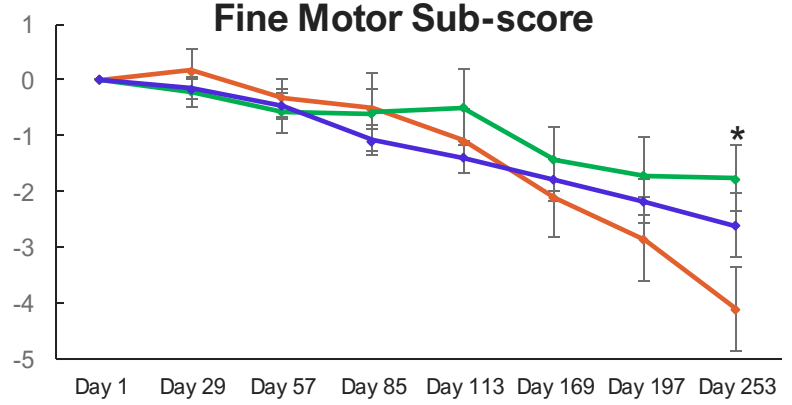
P<0.05 (10mg vs. placebo): *

Gross Motor Sub-score

(p<0.05 overall for 10mg)



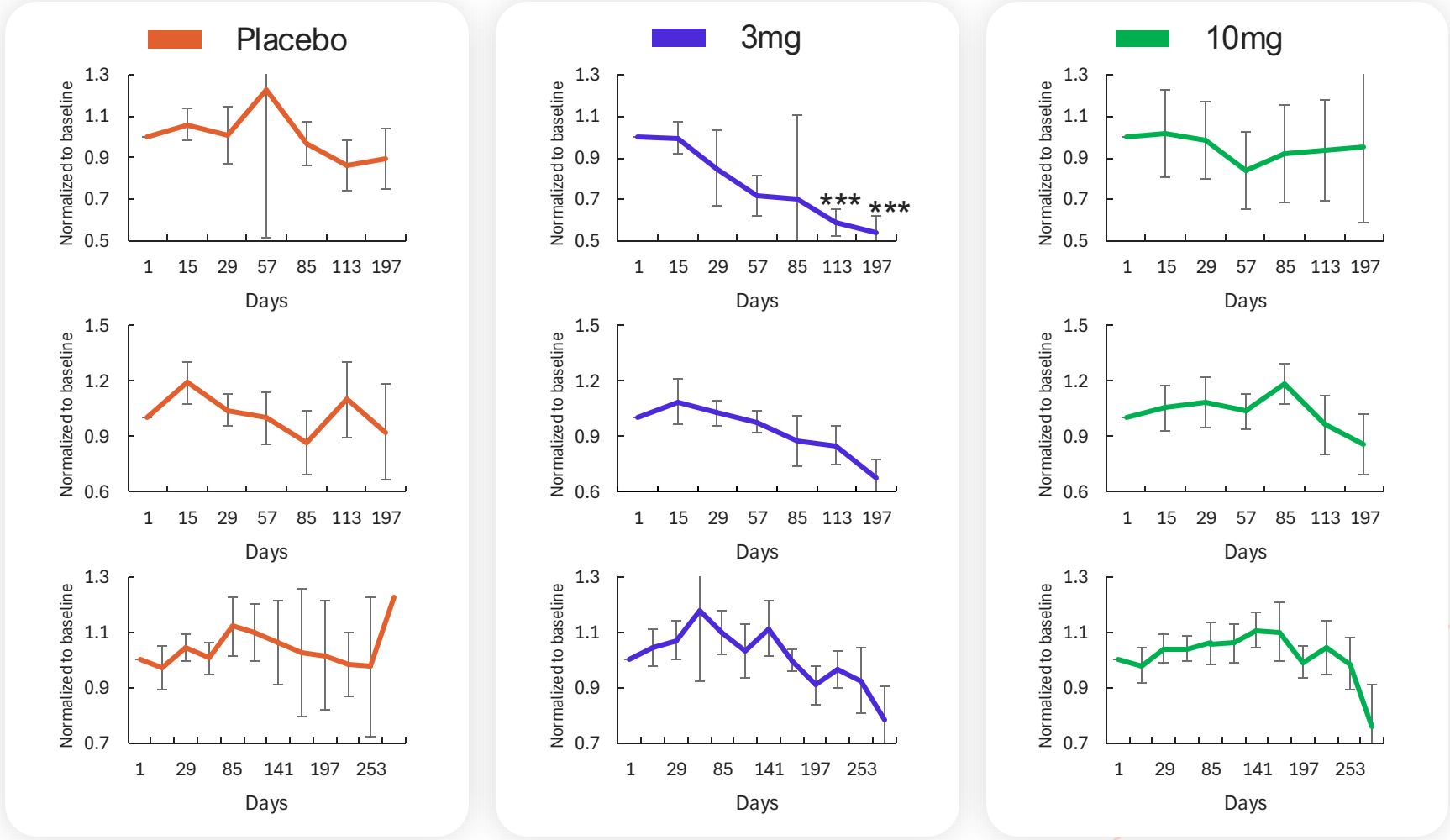
Fine Motor Sub-score



Minimal decline (≤1 point) observed on bulbar and respiratory sub-scores in both treatment and placebo groups

E Baseline reduction seen in biomarkers across both doses

Trend of decrease in NfL CSF and plasma after ~6 months



P<0.0001 vs. baseline: ***
P<0.05 vs. baseline: *
NfL CSF 3mg: patient with injury excluded; p-value based on non-Qced post-hoc analysis (t-test)
Note: Patients with 1 point decrease or less (stable) includes patients with improved functional score

Clinically meaningful effects on both functional endpoints and neurofilament biomarkers

	Endpoint	Significance	TPP	QRL-201 Impact: 3mg Dose	QRL-201 Impact: 10mg Dose
D	ALSFRS-R	The ALS registrational endpoint for functional decline	~20%	36% Effect vs Placebo at 8.5mo	50% (p<0.05) Effect vs Placebo at 8.5mo
E	pNfH (CSF)	Marks axonal degeneration; tracks progression and STMN2 expression	20%-40%[3]	~46% (p<0.0001) Decrease from Baseline at 6.5mo	~5% Decrease from Baseline at 6.5mo
E	NfL (CSF)	Marker of disease activity in select ALS subgroups (e.g., SOD1)		~33% (p<0.05)[1] Decrease from Baseline at 6.5mo *(Excl. single injury outlier)*	~14% Decrease from Baseline at 6.5mo
E	NfL (Plasma)	Peripheral proxy for neuroaxonal injury; lags behind CSF NfL		~22% Decrease from Baseline at 11mo[2]	~24% Decrease from Baseline at 11mo[2]

ANQUR open-label extension ongoing; pivotal trial planning underway with study expected to initiate in 2027

[1] Non-QCed post-hoc analysis (t-test)
[2] Data from 4 patients in 3mg group, 4 patients in 10mg group at this timepoint
[3] Based on KOL feedback

Pipeline Programs

QurAlis' technologies enable pipeline expansion through two different proven modalities

RNA Restoration
(antisense oligonucleotide, "ASO")

- Lead program (QRL-201) for ALS entering late-stage development in 2027 with multiple potential shots-on-goal for approval (ALSFRS-R, survival, neurofilaments)
- FlexASO® platform with multiple candidates in development including QRL-203, the second-generation compound targeting STMN2
- Specifically addresses mis-splicing targets which underly biology of neurodegenerative diseases including: TDP-43-opathies, Tau-opathies and Fragile X syndrome

Ion Channel Recovery
(small molecule)

- Lead program (QRL-101) advancing toward clinic as a selective Kv7.2/7.3 opener well-positioned for best-in-class potential
- Optimized formulations for multiple indications
- Addresses high unmet needs in commercially or clinically validated targets including epilepsy, pain, ALS, and mood disorders
- Developed in partnership with Eli Lilly with full global rights licensed to QurAlis; high selectivity results in favorable tolerability profile

QRL-203 is QurAlis' FlexASO® being developed for ALS

FlexASO® Architecture

- ✓ **Novel backbone design:** proprietary sugar-backbone modification gives the molecule structural flexibility that conventional ASOs lack
- ✓ **Optimized architecture**: ASO length and location of Flex modifications tuned for each specific target
- ✓ **Controlled hybridization**: These modifications additionally reduce off-target hybridization

Therapeutic Advantages

Greater Therapeutic Potency

Enables superior splicing correction, more robust target engagement and functional RNA restoration

Enhanced Precision & Safety

Minimizes off-target effects, toxicity, immune activation, and unintended gene regulation

Prolonged Therapeutic Effects & Less Frequent Dosing

Improved CNS biodistribution, reaches deep degenerative neurons for durable, sustained impact

Ion channel dysfunction seen across wide range of CNS disorders

Kv7.2/3 channel openers have validation across variety of diseases

- **Ezogabine:** previously marketed by GSK for partial-onset seizures
- **Flupirtine:** previously marketed in Europe for 6 different pain indications
- **Kv7.2/3:** demonstrated in epilepsy by azetukalner and other clinical programs

Older generation Kv7 ion channel openers exhibited **safety & adverse event liabilities** due to:

- Non-specific binding
- GABA-A affinity
- Compound-specific adverse events (retinal pigmentation)

- QurAlis' QRL-101 is a **highly selective Kv7.2/3 channel opener**:
  - High affinity to Kv7.2/3
  - Lack of affinity for GABA-A receptors and other Kv7 subtypes
  - Human target engagement observed in Phase 1 studies relevant for epilepsy, pain, and ALS

Robust Phase 1 data package supports future development

QRL-101 has been dosed in 208 subjects to date[1]

Ion Channel Recovery
(small molecule)

Tolerability, Safety, & PK (Liquid Formulation):
HV SAD (N=88) & HV MAD (N=60)

Central & Peripheral Target Engagement:
HV Proof of Mechanism (N=27)

Target Engagement in ALS Patients:
Proof of Mechanism (N=12)

Tolerability, Safety, & PK (SDD formulation):
HV SAD (N=25) & HV MAD (N=48)

Safety, Tolerability & PK Findings

- Generally well tolerated, large majority of AEs were mild & transient
- No treatment-emergent SAEs observed across any study
- New formulation demonstrates a significantly lower peak-to-trough ratio and AEs as compared to liquid formulation

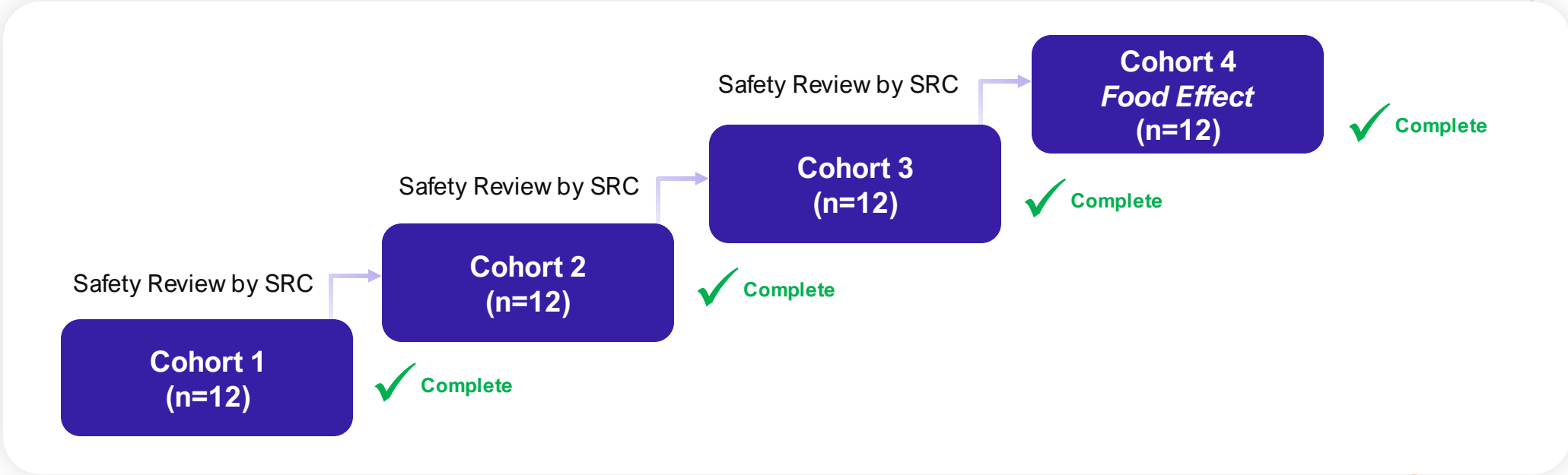
Target Engagement Findings

- **Epilepsy (central):**
  - Statistically significant results on TMS-Evoked Potential
  - Statistically significant Passive EEG high-frequency gamma & beta bands
  - No effect on Passive EEG low-frequency bands associated with sedation
  - Statistically significant reduction in TMS-EMG intracortical facilitation
- **ALS / Pain (peripheral):**
  - Several measures of peripheral nerve excitability demonstrated inhibitory effects, including multiple measures with dose dependent response
  - Consistent results observed in both ALS patients & healthy volunteers

[1]As of Augst 31, 2026
HVs: Healthy Volunteers; SAD: Single Ascending Dose; MAD: Multiple Ascending Dose; PoM: Proof of Mechanism; PK: Pharmacokinetics

QRL-101-08: SDD MAD study design

A randomized, double-blind, placebo-controlled, multiple ascending dose (MAD) study to evaluate the safety, tolerability, and PK of extended-release QRL-101 in healthy participants



Key endpoints

Safety | Tolerability | PK

Topline data expected Q4 2026

bis in die (BID; twice a day); No Observed Adverse Effect Level (NOAEL); placebo (PBO); Safety Review Committee (SRC)

Multiple upcoming catalysts to drive value

Key data readouts and program milestones anticipated across the pipeline through 2027

2H 2026

- ✓ All patients have received first dose in ANQUR open-label extension
- Topline of QRL-101 MAD in SDD microgranule formulation
- Fragile X discovery candidate nomination

2027

- Initiate pivotal study of QRL-201 in ALS
- PSP discovery candidate nomination
- Topline of QRL-201 ANQUR open-label extension

Thank you

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