

Quralis™

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

June 2026

Driving scientific breakthroughs into powerful precision medicines for genetic targets

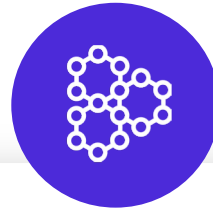


Groundbreaking science

Next-gen precision medicines developed by leveraging **human disease models** pioneered by QurAlis founders

Proprietary FlexASO® platform enables precise RNA restoration in genetic diseases resulting from mis-splicing targets

Multiple candidates advanced to clinical stage based on QurAlis' technology platform



First & best-in-class programs

QRL-201 ANQR results demonstrate **meaningful impact on disease progression & biomarkers** in sporadic ALS

QRL-201 expected to initiate pivotal study in sporadic ALS in 2027

Expansion to **additional CNS indications** where FlexASO® technology can be applied to breakthrough genetics & biology



World-class team to execute

Seasoned executive team responsible for development of multiple approved medicines

Strong track record of execution across clinical & preclinical pipeline

UNC13A partnership with Lilly highlights value of FlexASO® platform

QurAlis' expertise and technologies enable two distinct franchises

Pursuing treatment for CNS disorders with innovative biology and proven modalities

RNA Restoration

(antisense oligonucleotide, "ASO")

- Potential to develop first-in-class and best-in-class medicines utilizing FlexASO[®] platform
 - Two active ASO candidates currently in clinical trials (QRL-201, QRL-204)
- Specifically addresses mis-splicing targets which underly biology of neurodegenerative diseases including:
 - TDP-43-opathies
 - Tau-opathies
 - Fragile X syndrome
- Multiple candidates generated to date with reproduceable path to IND and Proof of Concept (PoC)

Ion Channel Recovery

(small molecule)

- Kv7.2/7.3 potassium channel is a commercially or clinically validated target for multiple high unmet need indications, including:
 - Epilepsy (focal, generalized, DEEs, etc.)
 - Pain (acute, neuropathic, etc.)
 - >50% of ALS
 - Mood disorders
- QRL-101, a highly selective Kv7.2/7.3 opener, is well positioned as potential best-in-class therapeutic:
 - Developed in partnership with Eli Lilly; full global rights licensed to QurAlis
 - High selectivity results in lack of burdensome side effects associated with first-generation Kv7 compounds
 - Formulations optimized for different indications

Advancing precision neuroscience pipeline across multiple clinical and preclinical programs

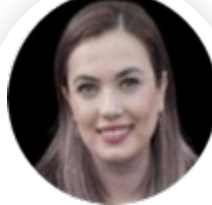
Program	MOA	Indication	Upcoming Milestone(s)	Discovery	IND-Enabling	Ph1 Safety / PoM ¹	Proof of Concept	Registration Studies
QRL-201	STMN2	ALS	ANQUR OLE on-going, pivotal study initiation expected 2027 ⁴	▶				
QRL-101	Kv7.2/7.3	DEEs ²	KCNQ2 PoC ³ initiation H1 2027 ⁴	▶				
		ALS	PoC ³ planning under way	▶				
QRL-204	UNC13A	Pain	PoM ¹ study initiation H2 2026 ⁴	▶				
		ALS / FTD	In partnership with <i>Lilly</i>	▶				
QRL-TBA	FMR1	Fragile X	DC ⁵ nomination 2026	▶				
QRL-TBA	Undis.	PSP	DC ⁵ nomination 2026	▶				

1. PoM = Proof of Mechanism; 2. DEE = Developmental and Epileptic Encephalopathy; 3. PoC = Proof of Concept; 4. Pending Series C funding; 5. DC = development candidate

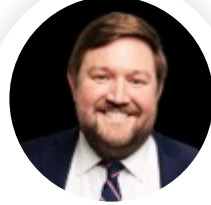
Pioneers with unrelenting commitment to patients



Kasper Roet,
PhD
CEO
Co-founder



Guzide Adhikari,
PhD
SVP CMC
Operations &
Strategy



Jason Brown,
MBA
CFO & COO



Hagen Cramer,
PhD
CTO



Dan Elbaum,
PhD
CSO



Manoj Malhotra
MD
CMO



Vikas Sharma,
PhD
CBO



Supported and recognized by investors, pharma, and industry



Investors



EQT
Life Sciences

sanofi ventures



DROIA ventures



Dementia
Discovery
Fund

inkef capital



MP Healthcare Venture Management, Inc.
Mitsubishi Tanabe Pharma Group



ALEXANDRIA



Awards



FIERCE 15
2020 WINNER



THE
TERMEER
FOUNDATION



Collaborators



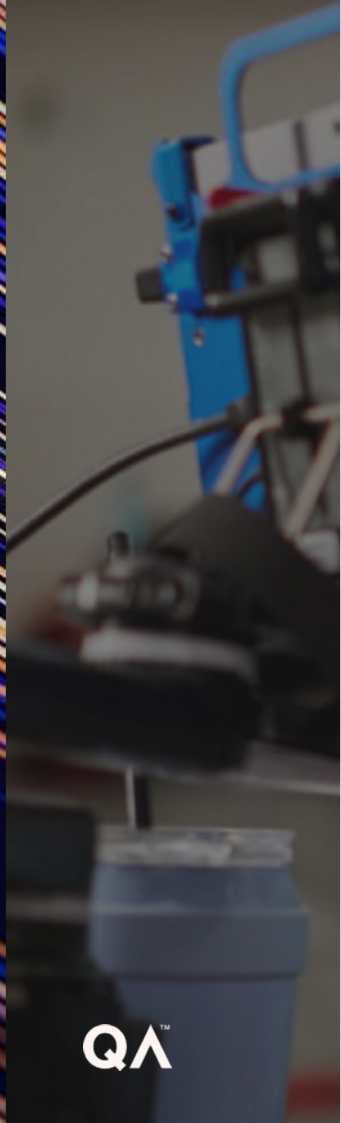
*QRL-101 in-license
QRL-204 out-license*



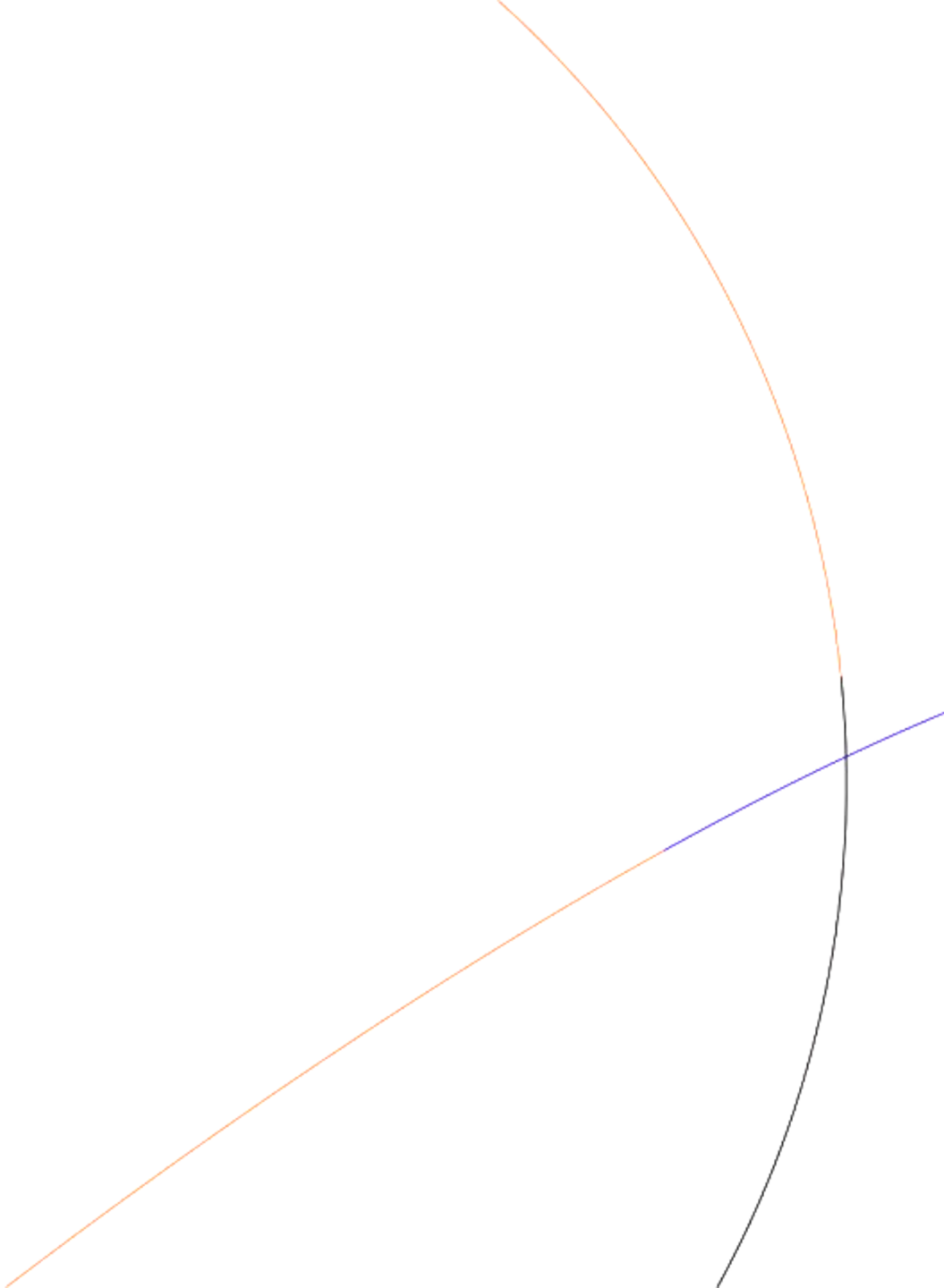
UMass Chan
MEDICAL SCHOOL

Fragile X

RNA STM



QA™



QurAlis is pioneering novel genetic treatments for ALS

ALS is a devastating neurodegenerative disease with significant unmet medical need

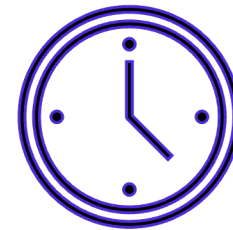


220,000+
global prevalence (est.)

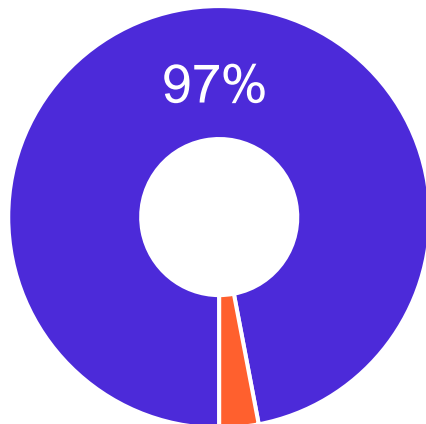
2-3
months

Current approved therapies (riluzole, edaravone) only provide modest survival benefit

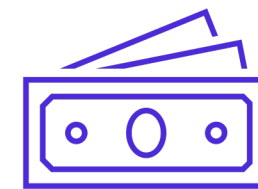
+25% Increase in prevalence expected by 2040



Every **90** Minutes someone is diagnosed with ALS, and someone passes away from it



■ TDP-43 pathology (sporadic, C9orf72)
■ Non-TDP-43 pathology (SOD-1, FUS)



\$250,000

Estimated annual out-of-pocket cost for care

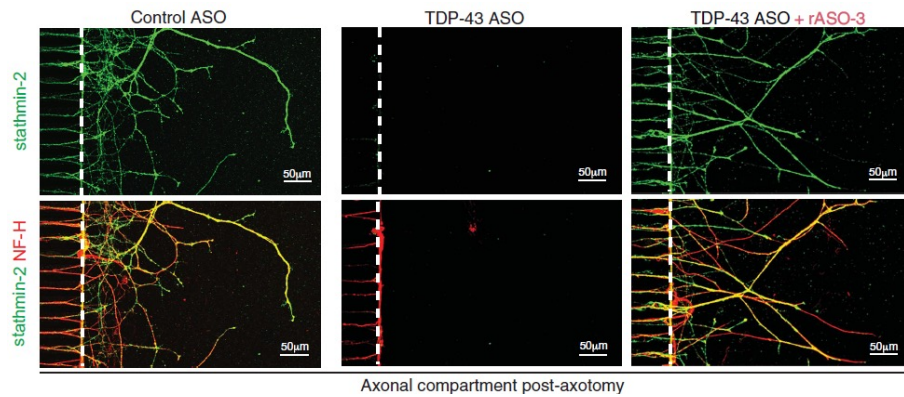
Restoration of STMN2 levels by ASO is a promising therapeutic strategy for the majority of ALS patients

QRL-201 restores full-length STMN2 and protects neurons from degeneration phenotypes

Breakthrough discovery shows TDP-43 driven neurodegenerative phenotypes caused by STMN2 loss

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

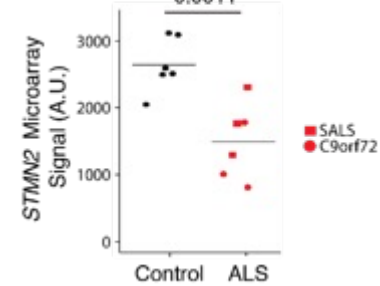
TDP-43 loss causes loss of axons; rescue by restoring STMN2 levels



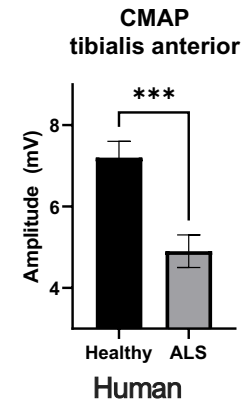
- Melamed Z, López-Erauskin J, Baughn MW, et al. Premature polyadenylation-mediated loss of stathmin-2 is a hallmark of TDP-43-dependent neurodegeneration. *Nat Neurosci*. 2019;22(2):180-190. doi:10.1038/s41593-018-0293-z
- Klim, J.R., Williams, L.A., Limone, F. et al. ALS-implicated protein TDP-43 sustains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

STMN2 is downregulated in ALS patients

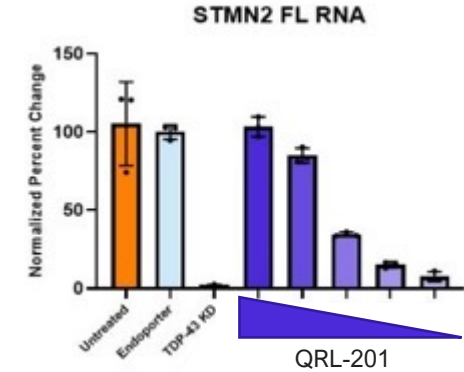
Microarray Laser Capture Motor neuron (Highley et al 2014)



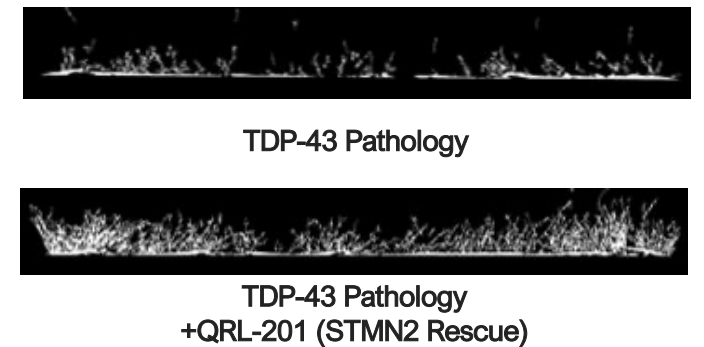
Loss of STMN2 leads to denervation of muscles



QRL-201 restores STMN2



QRL-201 restores neuronal processes



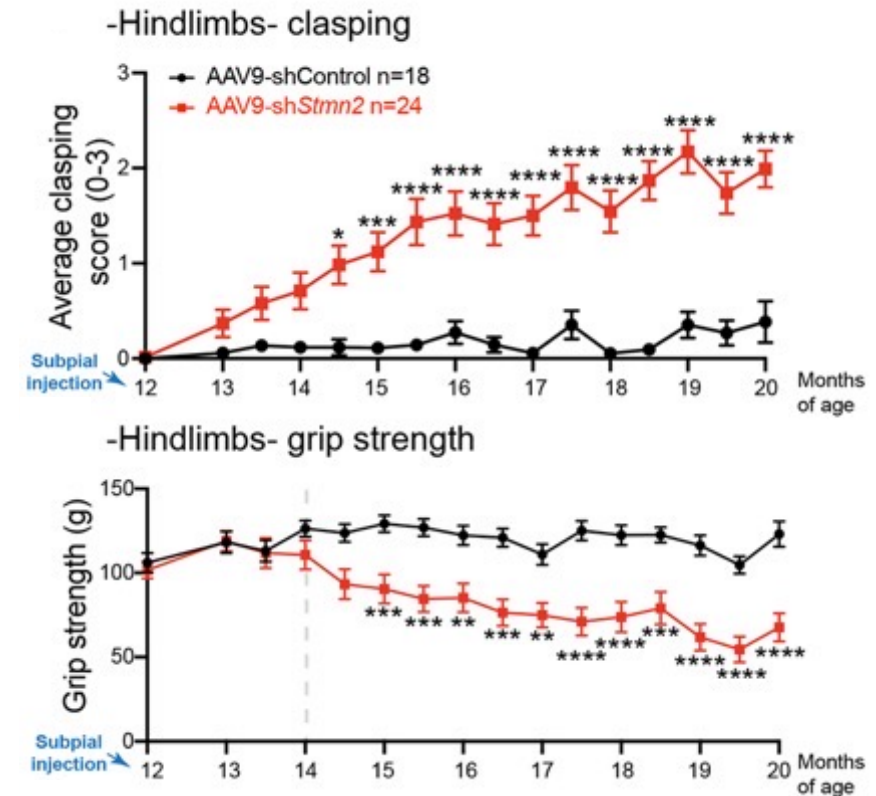
QRL-201: STMN2-targeting ASO for treatment of sporadic ALS

Preclinical biology is well established; ANQUR results provide human validation

- STMN2 is most strongly down-regulated by TDP-43 mis-localization
- Restoration of STMN2 pre-mRNA mis-splicing through ASO treatment restores neuronal processes, Golgi outposts, and protects neuronal activity in human motor neurons
- QurAlis has developed QRL-201 and QRL-203 to restore STMN2 levels in TDP-43-opathies (ALS, TDP-FTD)
- Two approved ASO therapies for motor neuron diseases (Spinraza[®] for SMA and Qalsody[®] for SOD-1 ALS) demonstrate that an ASO therapy strategy to modulate gene expression is technologically feasible



Loss of STMN2 leads to loss of muscle innervation and paralysis in preclinical models



Lopez-Erauskin, Jone, et al. "Stathmin-2 loss leads to neurofilament-dependent axonal collapse driving motor and sensory denervation." *Nature neuroscience* 27.1 (2024): 34-47.

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

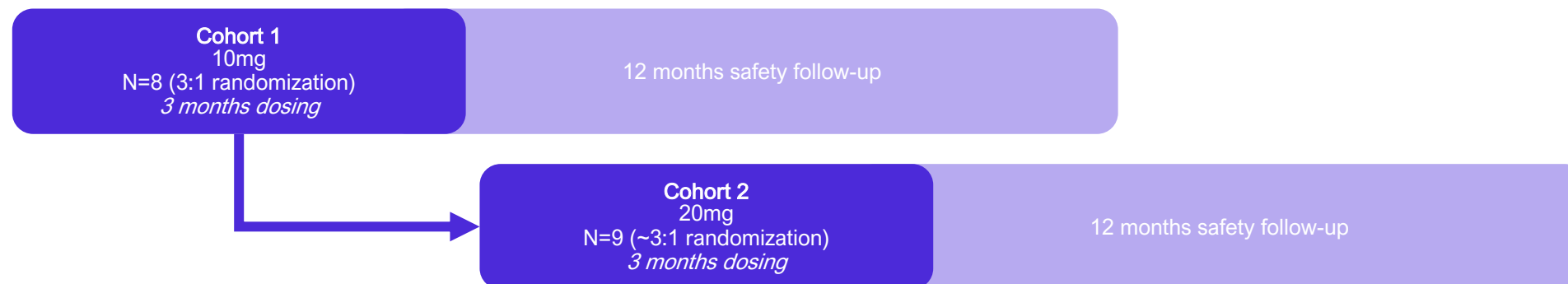
ANQUR MAD overview: randomized, double-blind, placebo-controlled study evaluating QRL-201 in ALS patients

QRL-201

AnQur

CSF PK and half-life observed in MAD cohorts supported expansion into DRF¹ phase

Dose escalation phase



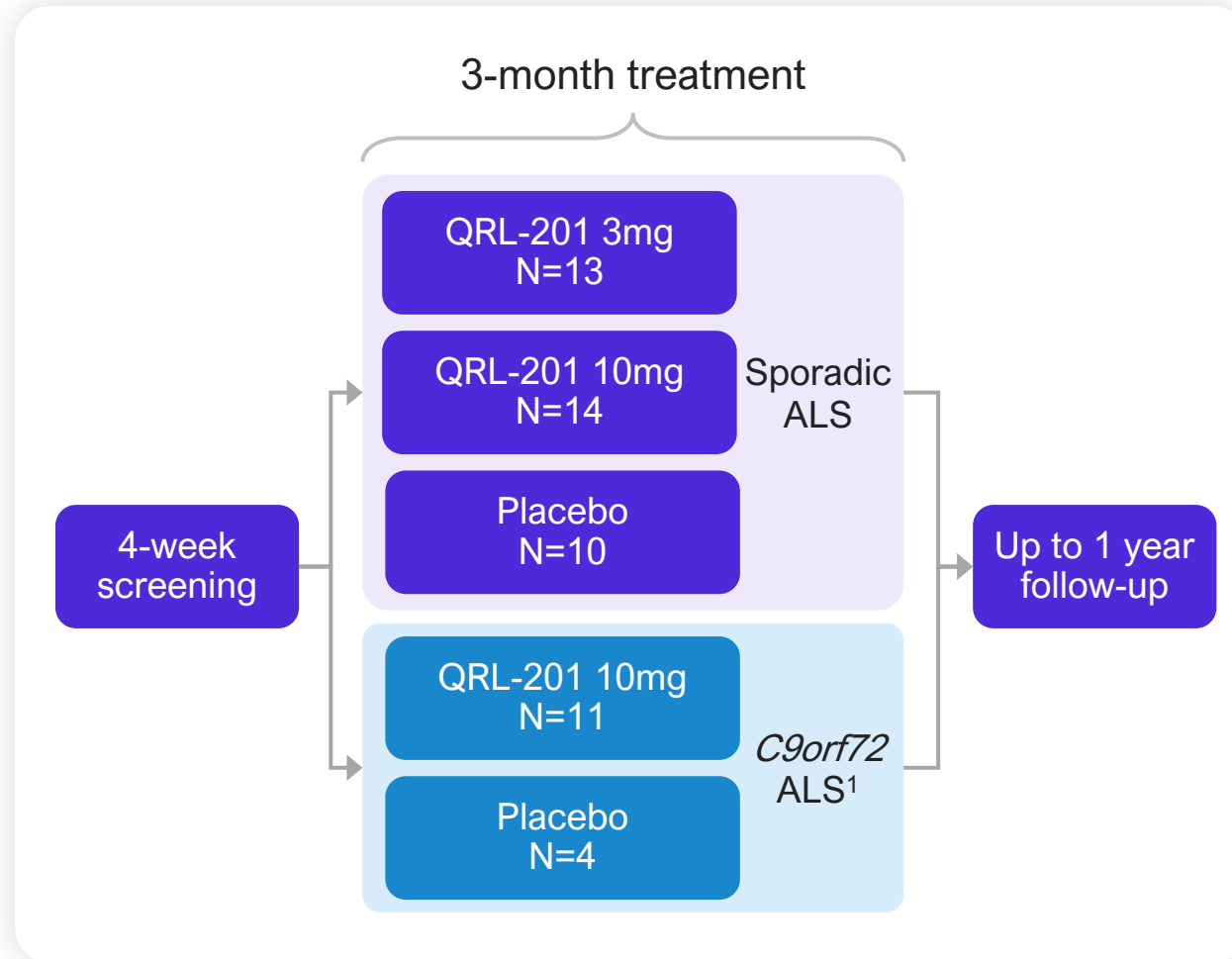
Dose escalation results

- Total of 17 patients (randomized ~3:1) dosed with QRL-201
- DSMB recommended continuing with dosing after both cohorts
- Cohort 1 patients were ~33 months from symptom onset. Inclusion criteria updated to enroll patients who are <24 months onset after Cohort 1
- PK estimated to have significantly exceeded estimated efficacy threshold for >9 months for majority of patients
- Half-life estimated to exceed 100 days, providing opportunity for lower dosing frequency
- Protocol amended to evaluate two dose levels with larger number of patients rather than continuing with escalation

¹DRF = Dose Range Finding

ANQUR study progressed to dose range-finding phase, focused on signal detection and safety

Data to support future development path



¹ *C9orf72* patients are a homogeneous population with consistently decreased STMN2 levels



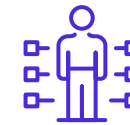
Design

Randomized, double-blind, placebo-controlled



Population

37 sporadic ALS patients
15 *C9orf72* ALS patients



Key entry criteria

Symptom onset within 24 months of screening
Slow vital capacity >50%
Clinical evidence of low motor neuron involvement
Stable dose of current treatment during study



Endpoints

Safety & tolerability
Preliminary efficacy
Biomarker panel

A QRL-201 demonstrated favorable safety & tolerability profile

Data Safety Monitoring Board (DSMB) agreed to continue the study without modifications during all phases, and as recently as December 2025

Parameter <i>N (%)</i>	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: (4) Pleocytosis and (1) Dysaesthesia

Pharmacokinetics & target engagement are supportive of biomarker and clinical efficacy observations

B

Pharmacokinetics (PK)

- ✓ Dose-proportional uptake observed in CSF¹
- ✓ 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

C

Target Engagement

- Autopsy samples were obtained from the MAD phase of the study²
- mRNA tissue analysis was performed using validated assays and compared to natural history ALS patient controls, dosing with QRL-201 showed:
 - ✓ Statistically significant increase of STMN2 full length levels in spinal cord above estimated therapeutic target
 - ✓ Statistically significant improvement of the ratio of full length STMN2 full to cryptic STMN2 levels in the spinal cord (splice correction)
 - ✓ No measurable cryptic STMN2 levels in the motor cortex

¹ CSF = Cerebrospinal fluid

² Patient samples were obtained within 6 months after their last dose

Clinically meaningful effects on both functional endpoints and neurofilament biomarkers

		QRL-201 Impact	
		3mg Dose	10mg Dose
Endpoint	Significance		
D ALSFRS-R	Captures whether the biologic effect translates to slowed disease progression and is the registrational endpoint in ALS	36% Effect vs Placebo at 8.5mo	50% (p<0.05) Effect vs Placebo at 8.5mo
E	pNfH (CSF)	~46% (p<0.0001) Decrease from Baseline at 6.5mo	~5% Decrease from Baseline at 6.5mo
	NfL (CSF)	~33% (p<0.05) ¹ Decrease from Baseline at 6.5mo <i>(Excl. single injury outlier)</i>	~14% Decrease from Baseline at 6.5mo
	NfL (Plasma)	~22% Decrease from Baseline at 11mo ²	~24% Decrease from Baseline at 11mo ²

Consistency across CSF pNfH, CSF NfL, and plasma NfL provides a coherent biomarker framework supporting QRL-201's observed clinical signal

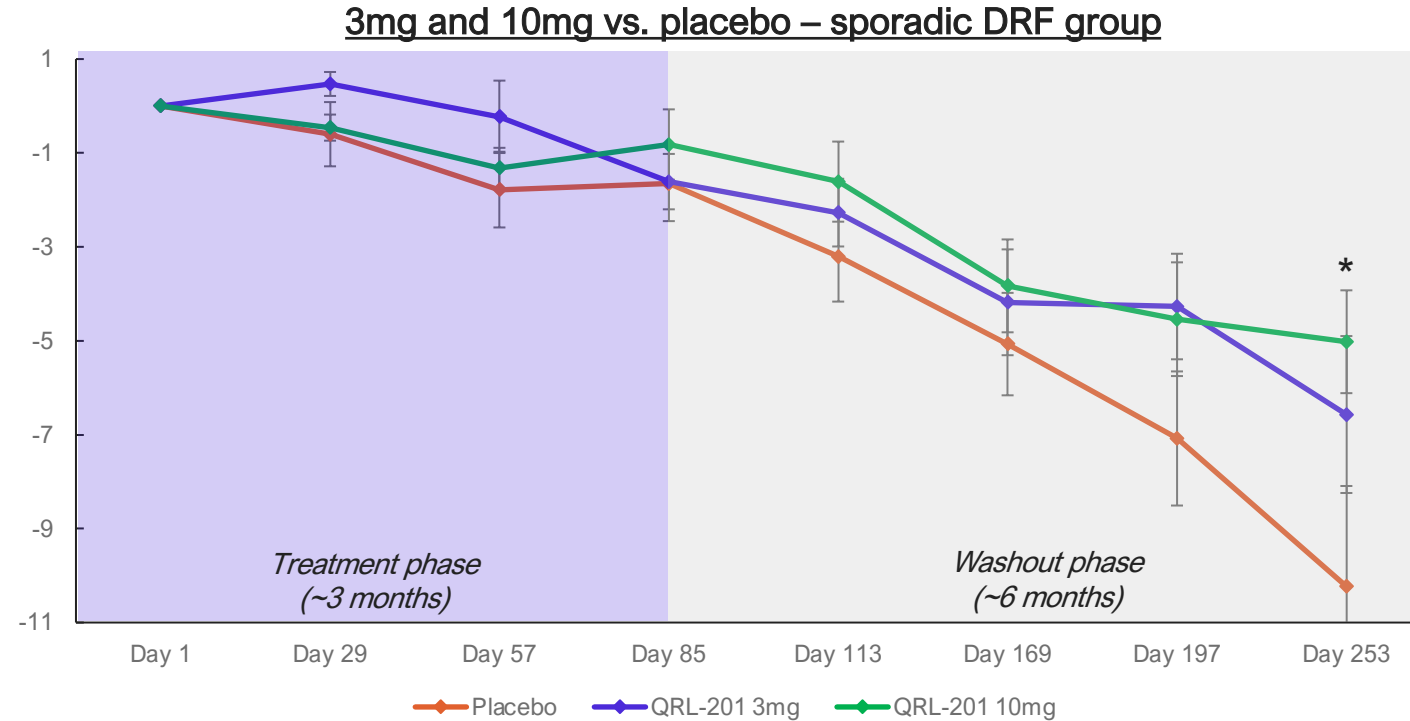


¹ Non-QCed post-hoc analysis (t-test)

² Data from 4 patients in 3mg group, 4 patients in 10mg group at this timepoint

ALSFRS-R Total Score sporadic ALS

10mg has statistically significant effect at Day 253 (~8.5 months) with consistent slowing of functional decline for both dose groups



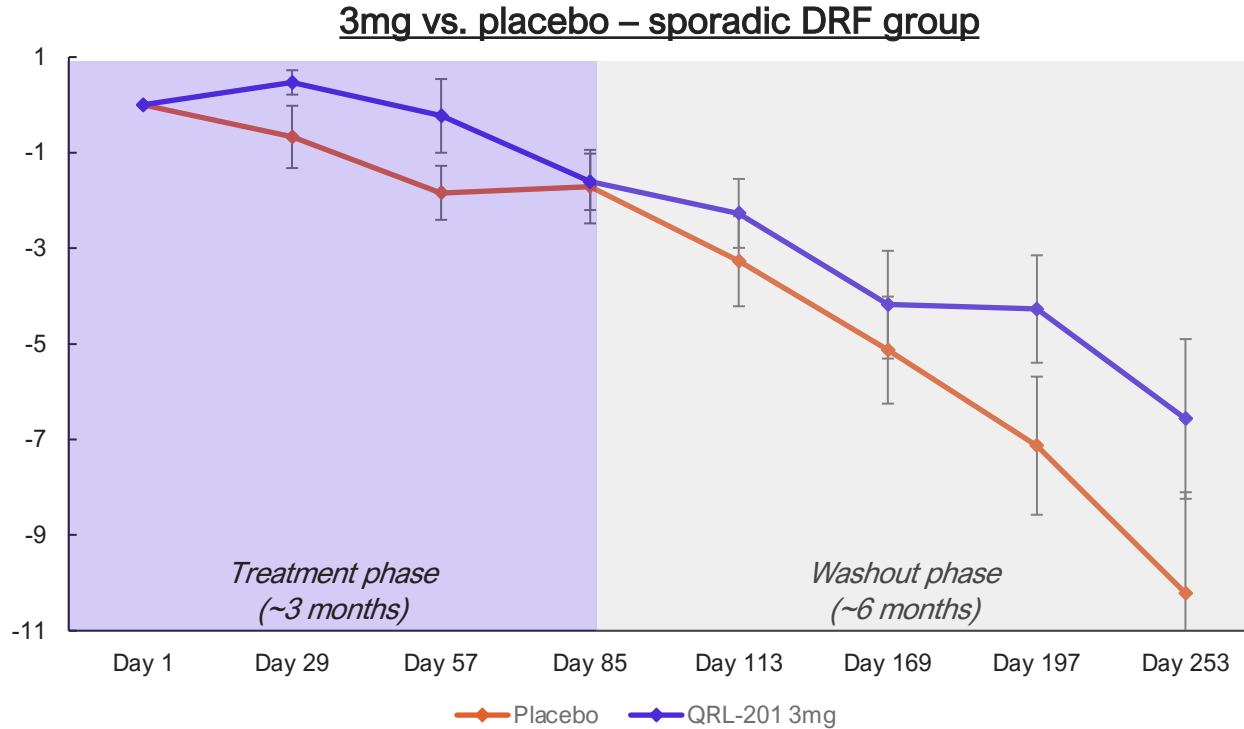
QRL-201 3mg	13	13	13	13	12	12	12	10
QRL-201 10mg	14	13	14	14	14	14	14	13
Placebo	10	10	10	10	10	8	6	6

Discontinuation (death, disease progression, other):	<u>3mg</u>	<u>10mg</u>	<u>Placebo</u>
	15%	7%	40%

P<0.05 vs. placebo: *
P<0.10 vs. placebo: #

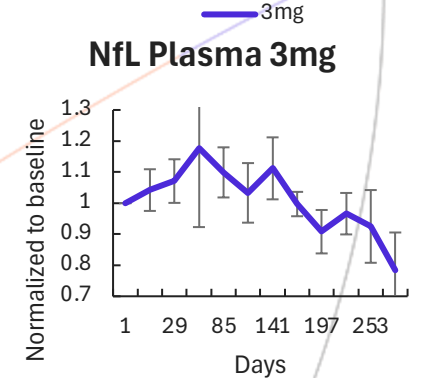
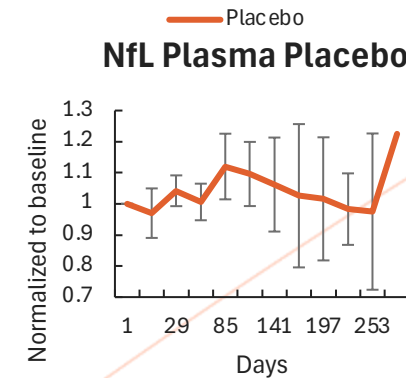
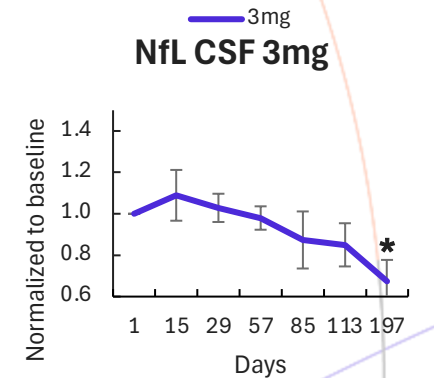
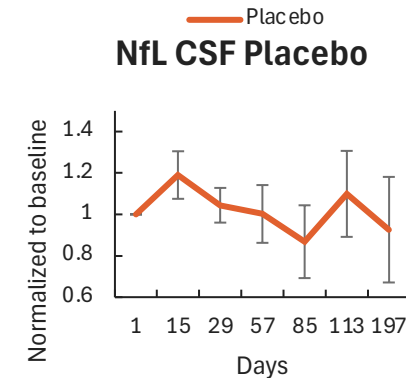
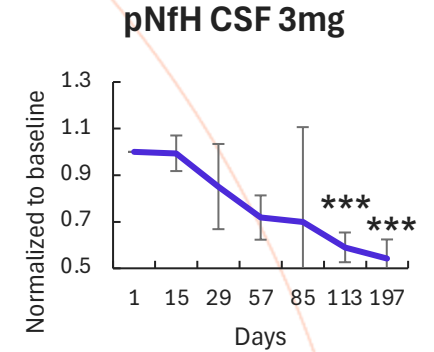
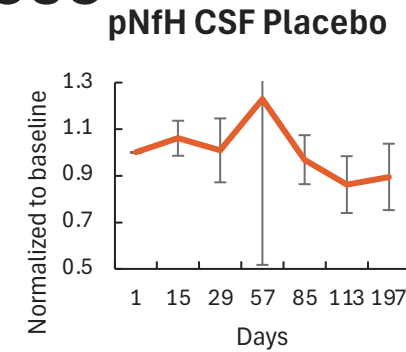
ALSFRS-R Total Score sporadic ALS: 3mg dose

3.66pt (36%) difference with placebo after ~8.5 months
 Reduction of pNfH and NfL from baseline



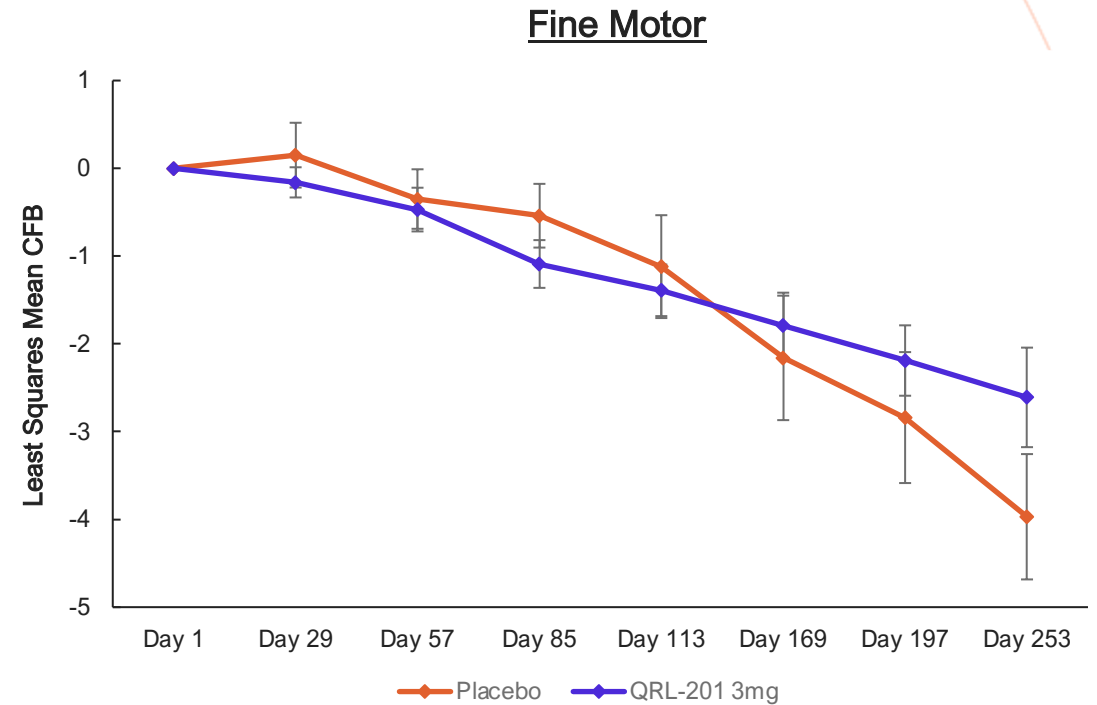
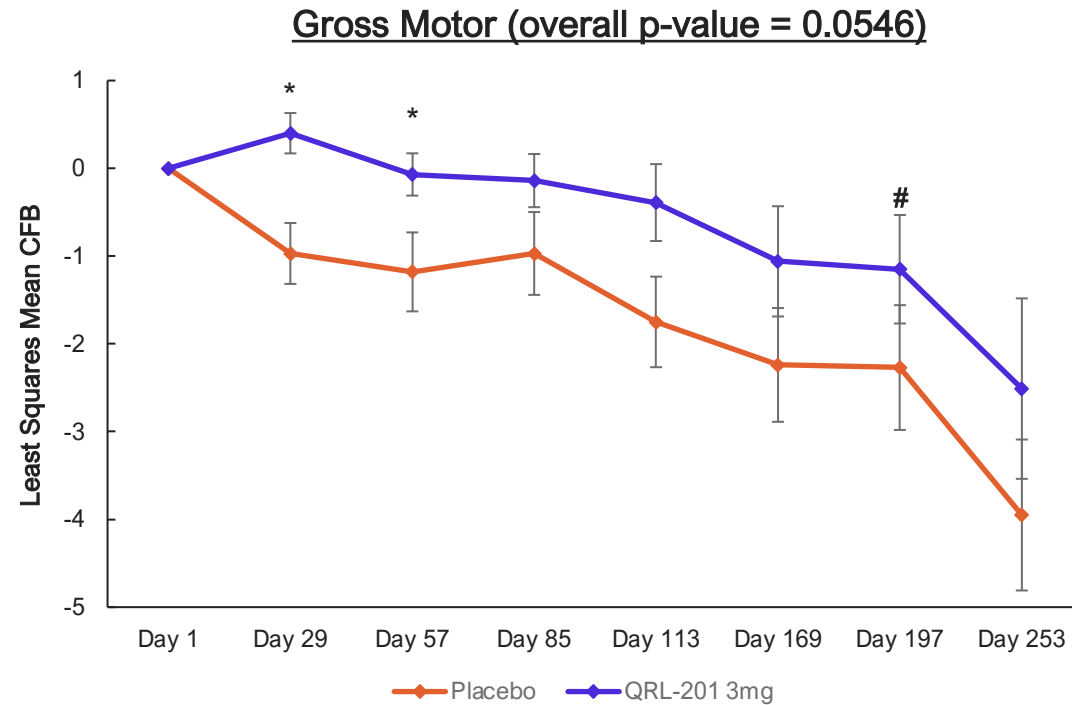
QRL-201 3mg	13	13	13	13	12	12	12	10
Placebo	10	10	10	10	10	8	6	6

	3mg
Discontinuation (death, disease progression, other):	15%
Patients with improved functional score:	15%
Patients with 1 point decrease or less (stable):	15%



ALSFRS-R Subscores sporadic ALS: 3mg dose

Early separation in gross motor score and emerging trend in fine motor score



P<0.05 vs. placebo: *
 P<0.10 vs. placebo: #

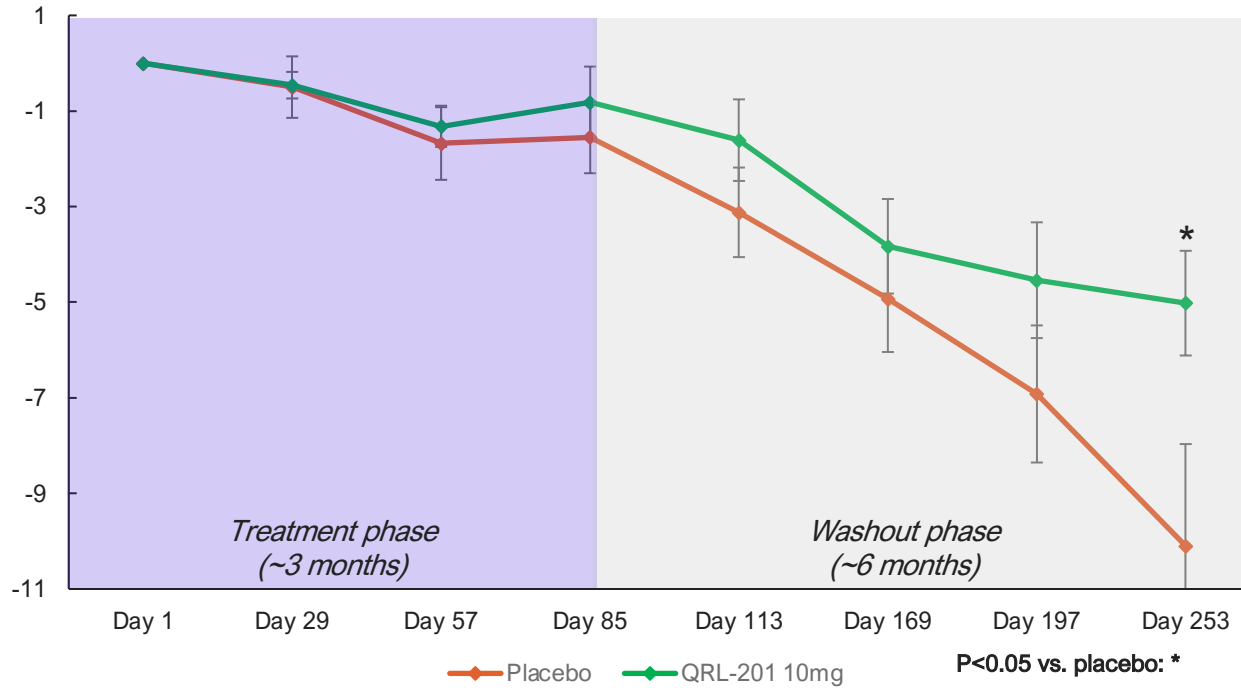
Minimal decline observed on bulbar and respiratory sub-scores in both treatment or placebo groups (≤ 1 point mean change over ~8.5 months) due to inclusion criteria focused on patients with Lower Motor Neuron onset disease

ALSFRS-R Total Score sporadic ALS: 10mg dose

5.08pt (50%) stat. sig. difference with placebo after ~8.5 months

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

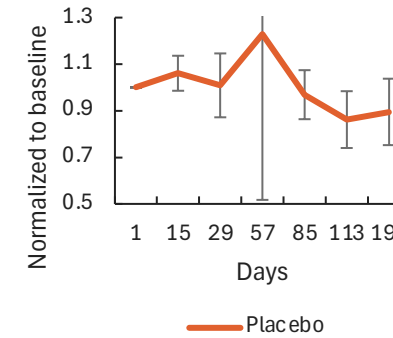
10mg vs. placebo – sporadic DRF group



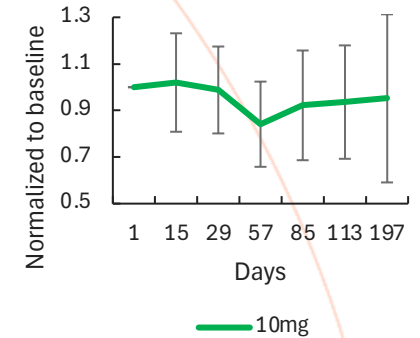
QRL-201 10mg	14	13	14	14	14	14	14	13
Placebo	10	10	10	10	10	8	6	6

	10mg
Discontinuation (death, disease progression, other):	7%
Patients with improved functional score:	14%
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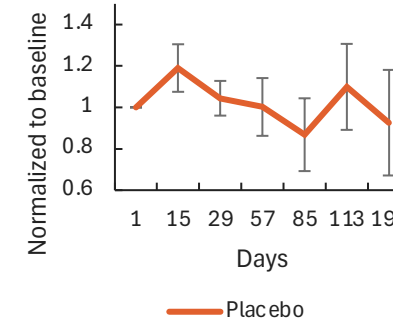
pNfH CSF Placebo



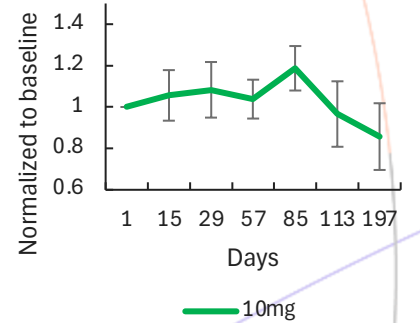
pNfH CSF 10mg



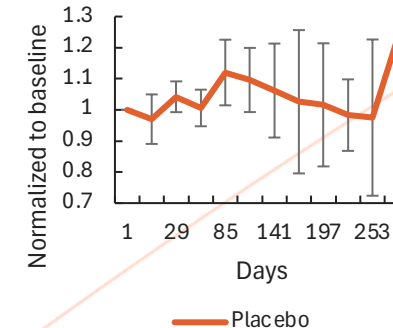
NfL CSF Placebo



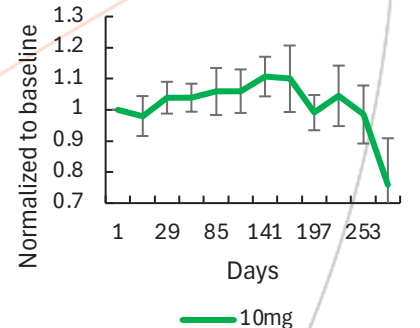
NfL CSF 10mg



NfL Plasma Placebo

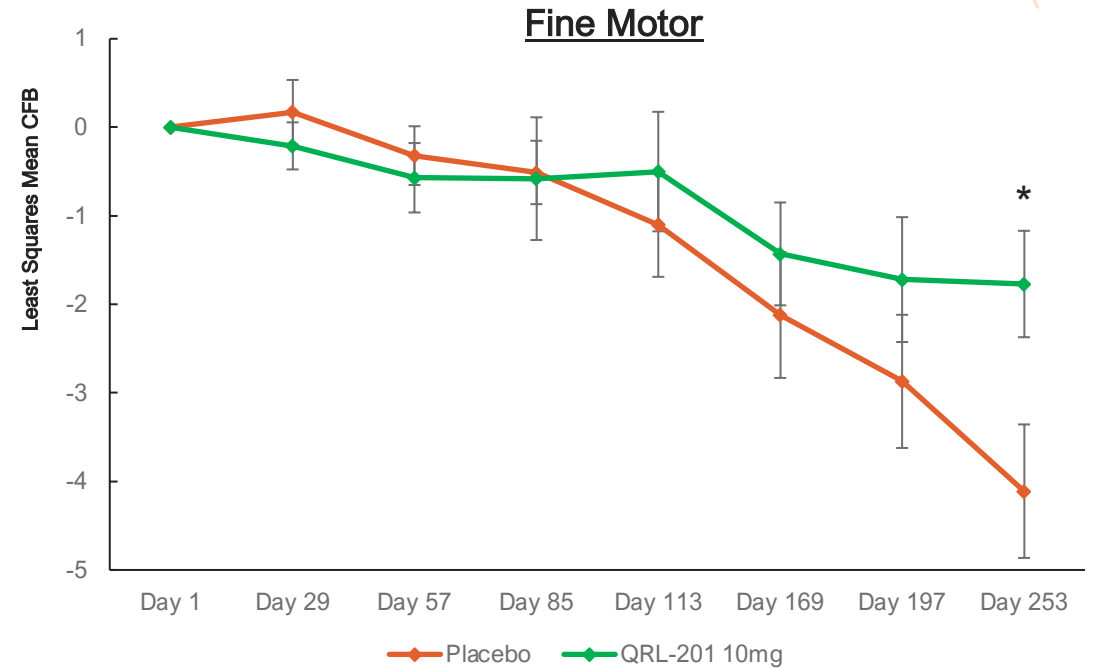
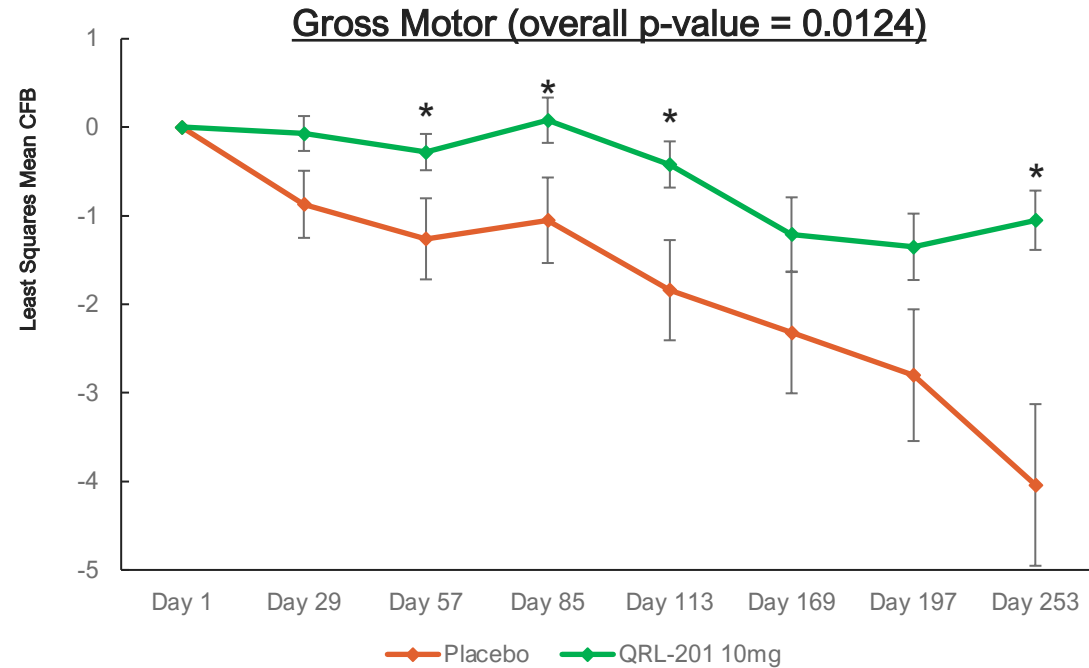


NfL Plasma 10mg



ALSFRS-R Subscores sporadic ALS: 10mg dose

Significant and sustained stabilization of gross motor and fine motor subscores consistent with STMN2 mechanism of action



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Minimal decline observed on bulbar and respiratory sub-scores in both treatment or placebo groups (≤ 1 point mean change over ~8.5 months) due to inclusion criteria focused on patients with Lower Motor Neuron onset disease

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

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- PK profile supports durable exposure with less frequent dosing
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C Clear evidence of target engagement

- Statistically significant $\geq 2x$ 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

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

ANQUR open-label extension on-going
Pivotal planning is under way with study expected to initiate in 2027

QRL-101 Epilepsy Program



Ion channel dysfunction is implicated across wide range of CNS disorders

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



- GSK's ezogabine was marketed for partial-onset seizures
- Flupirtine was also approved in Europe for 6 different pain indications
- Kv7.2/3 in epilepsy has been demonstrated 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

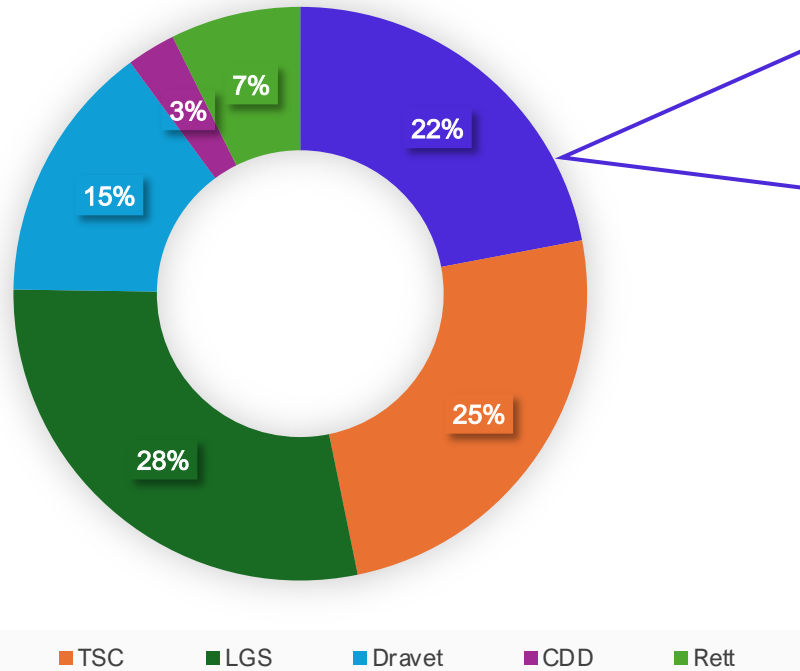


- QurAlis' QRL-101 is a highly selective Kv7.2/3 channel opener:
 - High affinity to Kv7.2/3
 - Lack of affinity for GABA-A receptors and other Kv7 subtypes
 - Human target engagement observed in Phase 1 studies relevant for epilepsy, pain and ALS

Approved therapies constitutes 5 DEE type - number of “other” DEEs is a significant market opportunity

Improved genetic diagnosis, high refractory rates, polypharmacy further expand the commercial opportunity

7MM Distribution of Developmental & Epileptic Encephalopathies (DEEs)



NO APPROVED THERAPIES FOR “Other” DEEs

- DUP15q Syndrome
- SCN2A-DEE
- SCN8A-DEE
- **KCNQ2-DEE**
- **KCNQ3-DEE**
- Angelman Syndrome
- Landau-Kleffner Syndrome
- Early Myoclonic Encephalopathy
- KCNT1-DEE
- SynGAP1-DEE
- Ohtahara Syndrome
- PCDH19
- EE w/ Continuous Spike-Wave
- Myoclonic Atonic Epilepsy
- Ring14
- Ring20
- Others

~4,000 US patients¹

1. U.S. registry & genetic testing data (Mullen SA et al., Neurology 2018; Millichap JJ et al., Epilepsia 2020; Invitae cohort 2023)
 2. Estimated diagnosed prevalent DEE patients in the 7MM (US, EU4/UK, Japan). Directional estimates synthesized from published epidemiology and industry analyses. “Other DEEs” represent heterogeneous genetic/structural DEEs without FDA-approved, subtype-labeled therapies.
 3. DelveInsight / Research & Markets reports
 4. Other DEE % calculated based on currently available information, however the % is higher than reported as reported by other companies
 5. Definitions: LGS = Lennox-Gastaut Syndrome, CDD = CDKL5 Deficiency Disorder, TSC = Tuberous Sclerosis Complex; DEE = Developmental and Epileptic Encephalopathy

Robust Phase 1 data package supports future development

QRL-101 has been dosed in 163 subjects to date¹

Phase 1 clinical package

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)

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

¹As of December 31, 2025

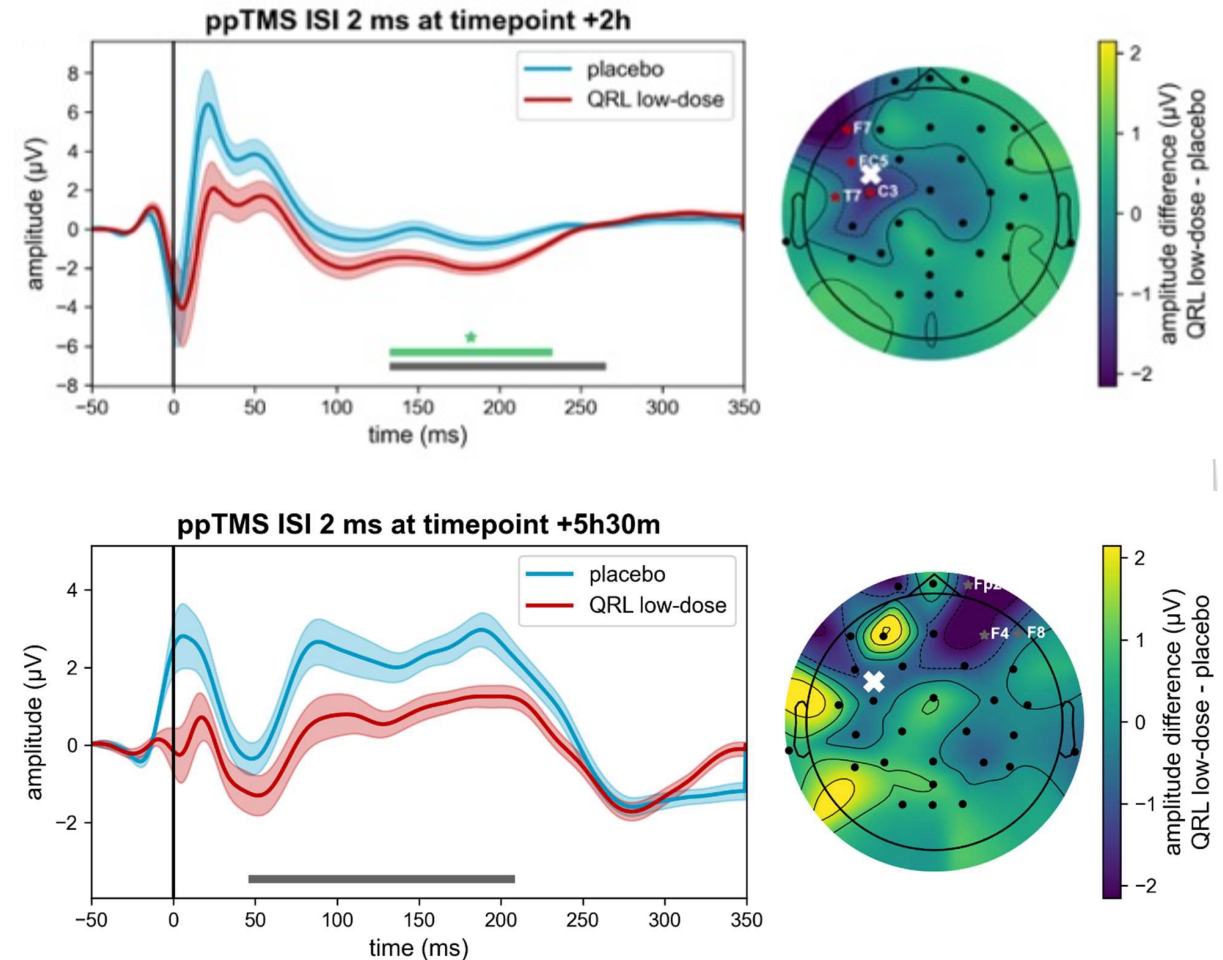
HVs: Healthy Volunteers; SAD: Single Ascending Dose; MAD: Multiple Ascending Dose; PoM: Proof of Mechanism; PK: Pharmacokinetics

QRL-101 shows inhibition in TEP measurements even at the low dose of the PoM study

QRL-101-05 study evaluated multiple biomarkers relevant for CNS target engagement in 27 healthy volunteers in a three-way crossover study:

- ☑ **TMS-Evoked Potential** (pictured right) low dose demonstrated statistically significant reductions vs. placebo at both timepoints
- ☑ **Passive EEG** demonstrated statistically significant effects on high-frequency beta & gamma bands associated with anti-seizure activity, while not having impact on low-frequency delta & theta bands associated with sedation
- ☑ **TMS-EMG** showed statistically significant changes in intracortical facilitation (ICF), measuring the effect on inhibition / excitability ratio

TMS Evoked Potential Results



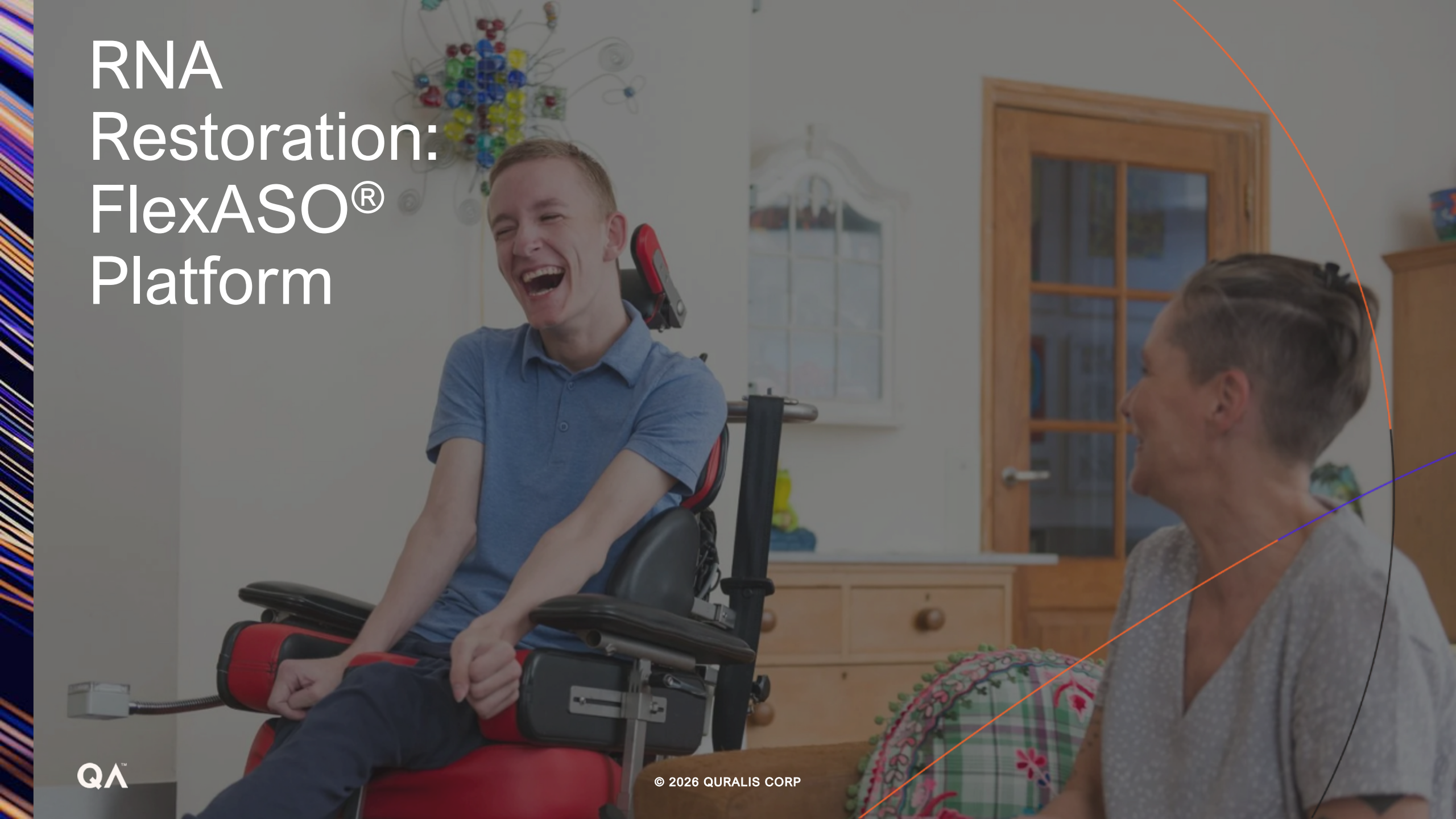
Aktiva7e KCNQ2 epilepsy trial design

Initiation expected H1 2027



DESIGN	Randomized, double-blind, placebo-controlled trial
POPULATION	Subjects 12-65 years of age with Ultra Rare Epilepsy (KCNQ2) Loss of Function (LoF)
SAMPLE SIZE	n=9, randomized 2:1 (QRL-101:PBO)
KEY ENTRY CRITERIA	Age 12-65 and diagnosed with KCNQ2 having >2 seizures/month
ENDPOINTS	Primary: Safety, tolerability Secondary: PK & seizure endpoints Exploratory: non-seizure efficacy endpoints

**Administered as a BID extended-release granules (SDD)*



RNA Restoration: FlexASO[®] Platform

FlexASO[®] delivers powerful combination of therapeutic benefits

FlexASO[®] Architecture

- ✓ **Novel backbone design:** Sugar-backbone modification unlocks structural flexibility
- ✓ **Optimized architecture:** ASO length and location of Flex modifications tuned for target
- ✓ **Controlled hybridization:** These modifications additionally reduce off-target hybridization

Therapeutic Advantages



Greater Therapeutic Potency

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



Enhanced Precision & Safety

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



Prolonged Therapeutic Effects & Less Frequent Dosing

Optimizes CNS biodistribution, reaching deep-layer degenerative neurons for sustained therapeutic impact.

Genetic understanding of diseases and tech breakthroughs generate opportunity to develop RNA restoration therapies

Technological breakthroughs



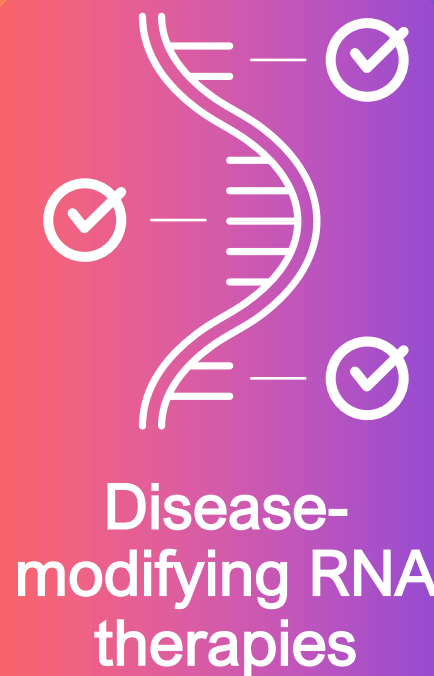
Patient-derived human disease models increase probability of success



Technology to potentially support 2x / year dosing has been developed (e.g., FlexASO[®] tech.)



Technology to cross blood-brain-barrier has matured (e.g., transferrin receptor)



RNA restoration oligonucleotides targets

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



Diseases caused by haploinsufficiency (e.g., Dravet)



Previously undruggable targets for large indications





QuralisTM

Thank you

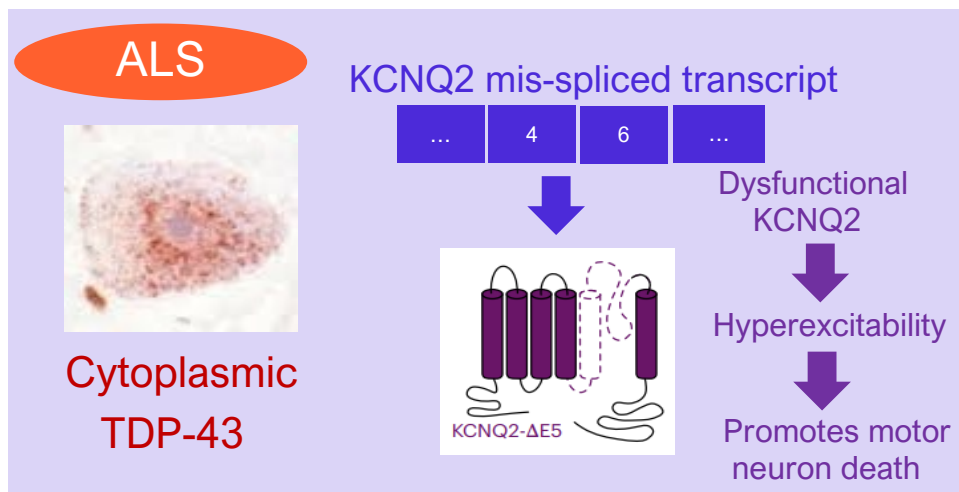
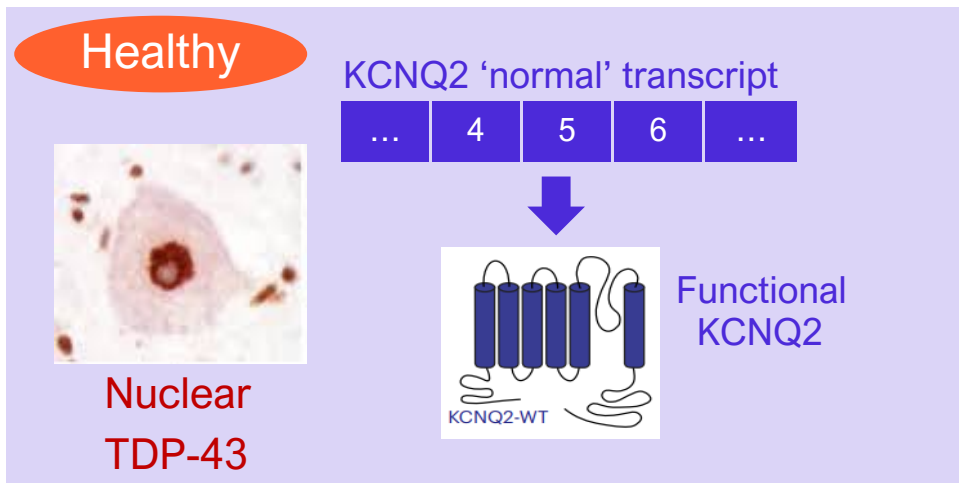
For more information contact:
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jason.brown@quralis.com

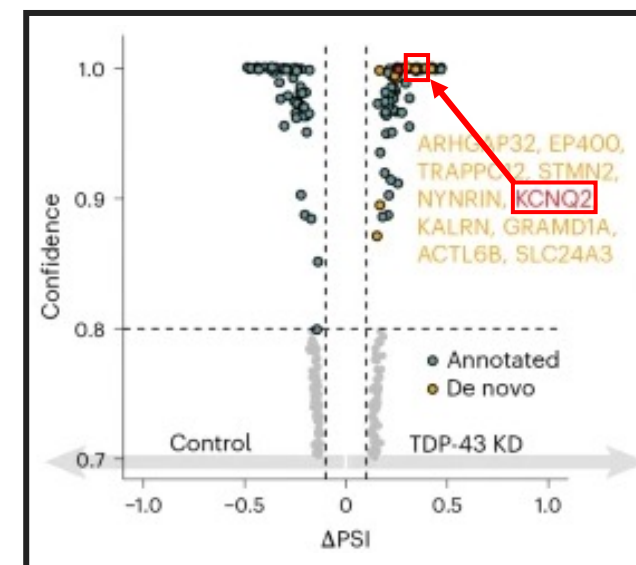
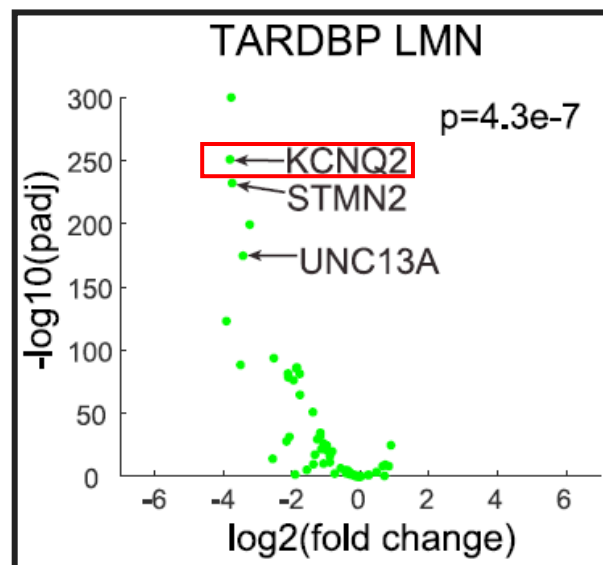
Appendix: QRL-101 Expansion Opportunities

KCNQ2 mis-splicing in ALS with TDP-43 pathology

RNA mis-splicing of the voltage gated potassium channel KCNQ2 is a key hallmark of ALS related TDP-43 proteinopathy




KCNQ2 is one of the top mis-spliced RNAs in TDP-43 depleted motor neurons in ALS postmortem tissue
(Held et al 2021, Joseph et al 2025)



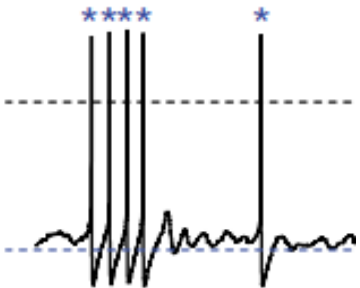
KCNQ2 mis-splicing accelerates motor neuron disease

Promotes hyperexcitability, motor neuron death and accelerates ALS disease progression

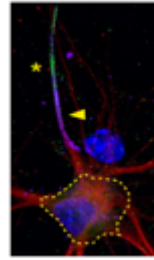
Healthy



Nuclear TDP-43
Normal KCNQ2 function




Normal neuronal activity

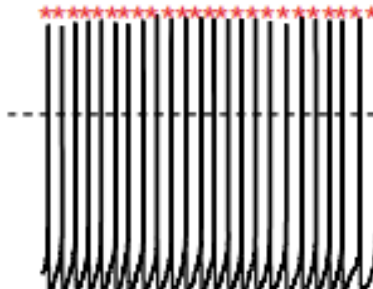


Functional KCNQ2

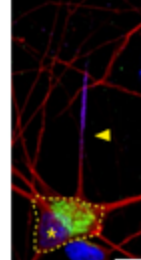
ALS



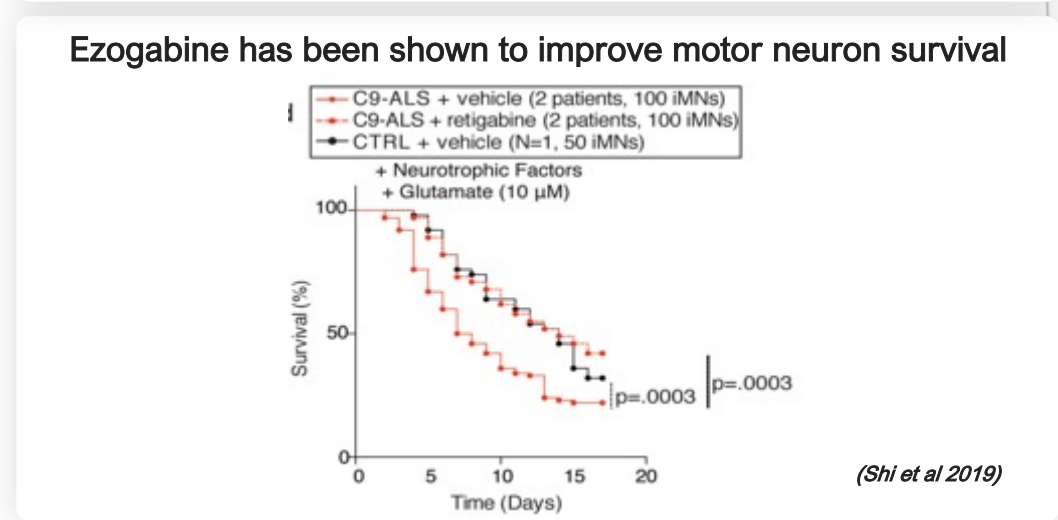
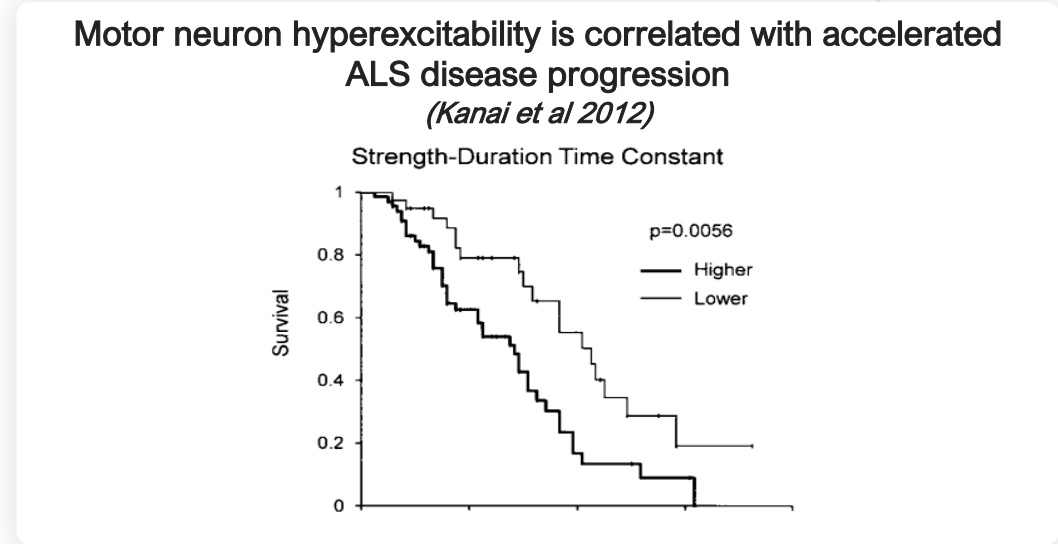
TDP-43 loss of function
KCNQ2 RNA mis-splicing



Hyperexcitability



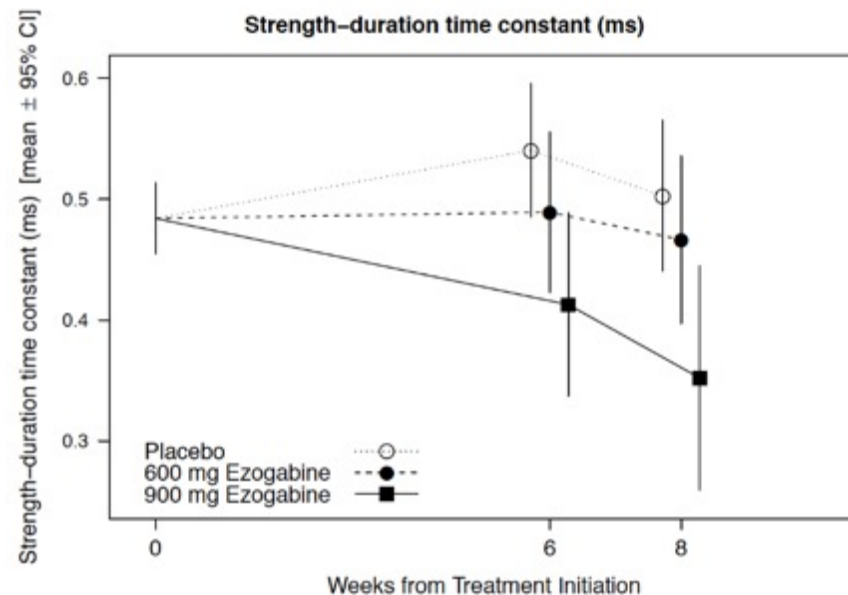
Mislocalized, Dysfunctional KCNQ2



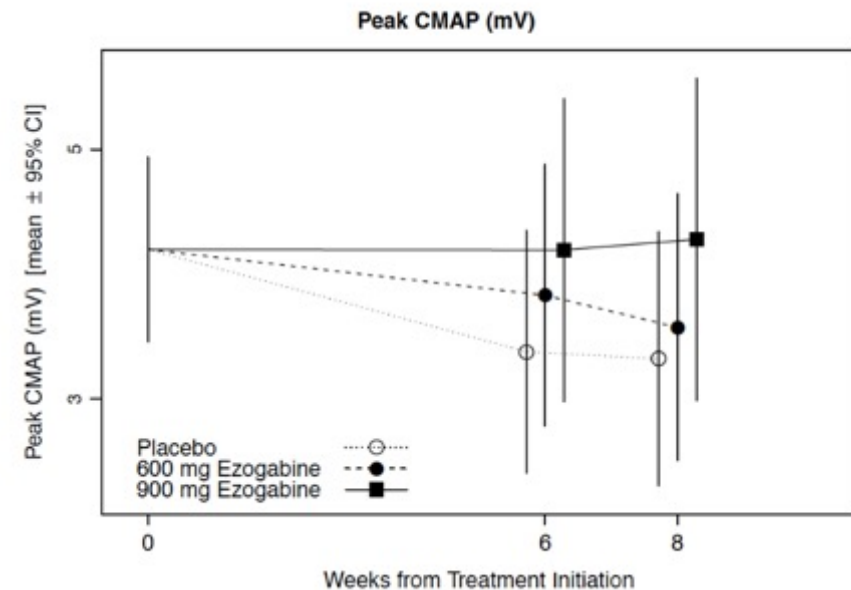
Clinical impact of Kv7 on hyperexcitability in ALS was first demonstrated by the first-generation Kv7 ezogabine¹

Small investigator-led study demonstrated meaningful impact on disease progression biomarkers

Statistically significant² dose-dependent effects on biomarkers that predict patient survival



Statistically significant² impact on critical disease progression & efficacy biomarker (CMAP)



Nearly all (97%) participants in the trial reported at least one adverse event
Most frequent adverse events among participants in the ezogabine arms were fatigue and dizziness

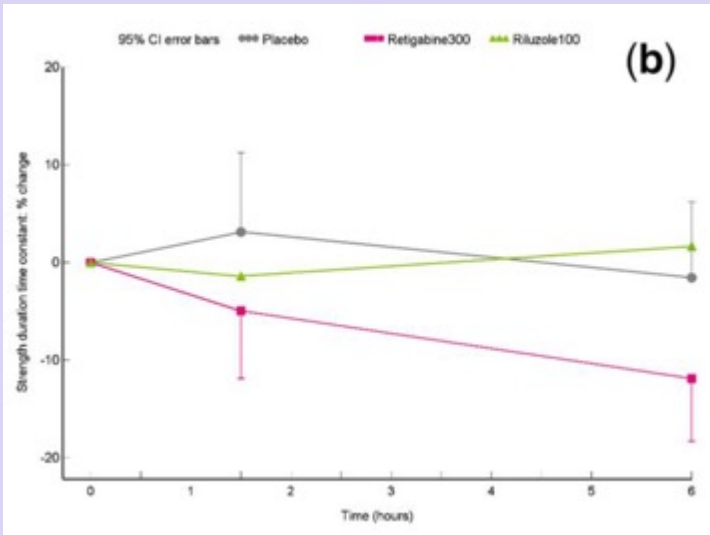
¹Wainger BJ, Macklin EA, Vucic S, et al. *JAMA Neurol.* 2021;78(2):186–196. doi:10.1001/jamaneurol.2020.4300

²Error bars (directly from JAMA) represent standard deviations, results are statistically significant

Compelling QRL-101 results on hyperexcitability biomarkers in both ALS patients and healthy volunteers

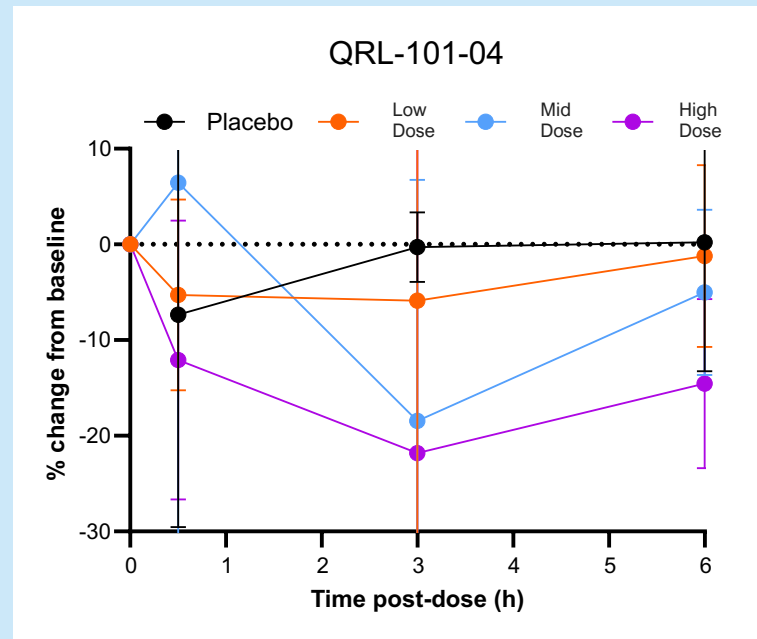
Evaluating next steps of development

Retigabine statistically significantly¹ reduced SDTC, a biomarker predictive of patient survival

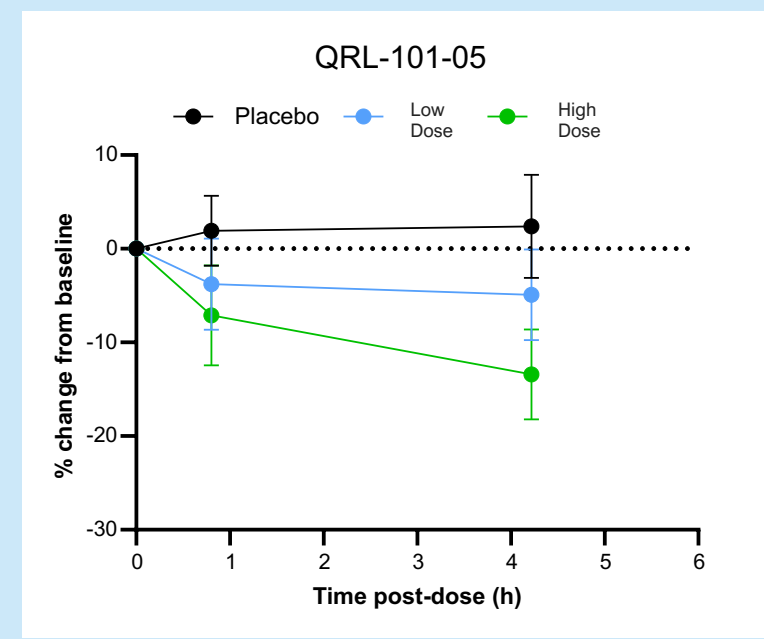


- N=18 ALS patients
- Single dose cross-over study at Utrecht, each compared to self on placebo
- Treatment v. placebo effect p=0.001

QRL-101 reduces SDTC in a dose dependent manner in healthy and ALS patients. The window of effect is larger in ALS



- N=3/group ALS patients
- Single dose study at Utrecht, placebo group is unique individuals



- N=26 / group healthy volunteers
- Single dose cross-over study at CHDR, each compared to self on placebo
- Treatment v. placebo effect p=<0.0001

Kv7 channel activation to treat pain: A proven therapeutic strategy

Chronic pain affects tens of millions—and existing options fall short

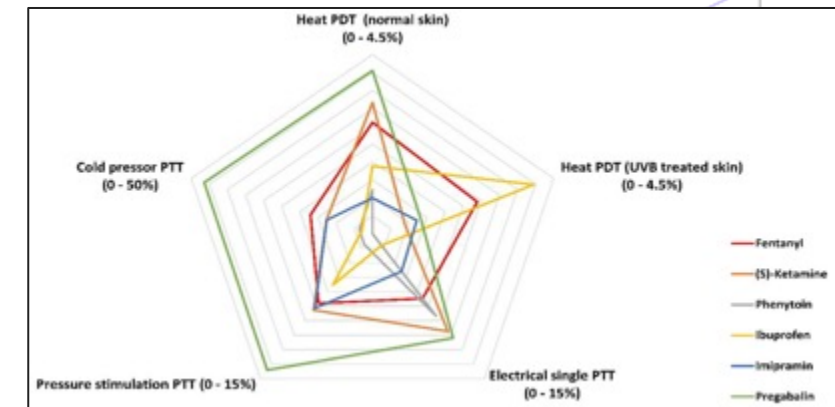
- **More than 20% of U.S. adults** reported experiencing chronic pain (pain lasting three months or more) in the past 3 months¹
 - **8.5% of adults reported high-impact chronic pain** — pain that frequently limits life or work activities¹
- Neuronal hyperexcitability is a central driver of pain
 - **Kv7 channels tightly regulate sensory neuron firing**, controlling pain signal initiation
 - Function as a **voltage clamp**, preventing small depolarizations from triggering aberrant pain signals
- Clinical validation of the mechanism
 - **Flupirtine, a Kv7 opener, demonstrated broad analgesic efficacy** (neuropathic, post-operative, back pain, headache, dysmenorrhea and others)
 - Used for **>20 years in Europe**, withdrawn due to hepatic toxicity with chronic use—*not lack of efficacy*
- Potential to deliver **effective pain relief without the limitations of current standards of care**

¹ Centers for Disease Control & Prevention (CDC)

Exploratory Phase 1 induced-pain study planned to investigate analgesic effects of QRL-101

PainCart® proof-of-mechanism study expected to initiate in H2 2026

- Kv7 opener flupiritine was prescribed for 6+ indications in multiple European countries, before being withdrawn from the market due to hepatic toxicity in chronic use
- PainCart® is designed for indication selection through testing multiple different modalities, physiology, and leveraging quantitative and qualitative outcome measures
 - Models: cold pressor, electrical stimulation, pneumatic pressure, conditional pain modulation, thermal stimulation, UV-B model, capsaicin model
 - Three-way cross-over design with placebo, low and high dose, utilizing SDD formulation to further characterize PK / PD profile
- Provides unique profile which can be compared to existing treatments:



QRL-101 key take-aways



Multiple Kv7 ion channel openers have shown signals of efficacy in epilepsy, pain, ALS



Off-target liabilities associated with past generation Kv7 agonists resulted in commercial limitations and market withdrawals



QRL-101 is an ultra-selective Kv7.2/3 channel opener that exhibits superior selectivity profile
163 subjects dosed till date



Human target engagement observed in Phase 1 studies relevant for epilepsy, pain and ALS
QurAlis preparing to initiate PoC study in KCNQ2-DEE

Potential for positive outcomes in DEEs, pain and ALS differentiating QRL-101 from competitors and presents a global commercial opportunity