QurAlis™

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

May 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 ANQUR 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	PoC[3] transitioning to OLE, pivotal study initiation expected 2027					
QRL-101	Kv7.2/7.3	DEEs[2]	KCNQ2 PoC[3] initiation H1 2027[4]					
		ALS	PoC[3] planning under way					
		Pain	PoM[1] study initiation H2 2026[4]					
QRL-204	UNC13A	ALS / FTD	In partnership with Lilly					
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
Lilly
LS POLARIS INNOVATION FUND
AMGEN
mission BIOCAPITAL
Dementia Discovery Fund
inkef capital
ALS INVESTMENT FUND
DOLBY FAMILY VENTURES
MP Healthcare Venture Management, Inc.
Mitsubishi Tanabe Pharma Group
MITSUI GLOBAL INVESTMENT
Mass General Brigham Ventures
ALEXANDRIA

Awards

FIERCE Biotech
FIERCE 15
2020 WINNER

NEVY 2020 AWARDS
DELL Technologies
WINNER

THE TERMEER FOUNDATION

Collaborators

Lilly
QRL-101 in-license
QRL-204 out-license

UMass Chan MEDICAL SCHOOL
Fragile X

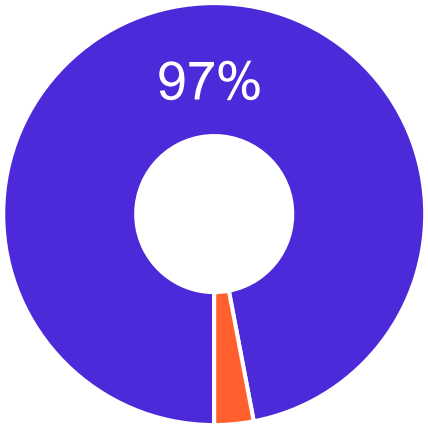
RNA Restoration: STMN-2 Program

QurAlis is pioneering novel genetic treatments for ALS

ALS is a devastating neurodegenerative disease with significant unmet medical need

220,000+
global prevalence (est.)

+25%
Increase in prevalence expected by 2040



2-3 months
Current approved therapies (riluzole, edaravone) only provide modest survival benefit

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

$250,000
Estimated annual out-of-pocket cost for care

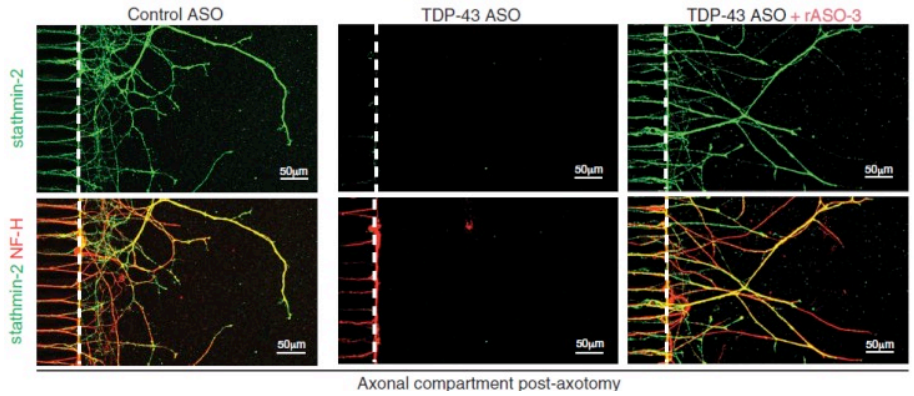
Restoration of STMN2 levels by ASO is a promising therapeutic strategy for the majority of ALS patients

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

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

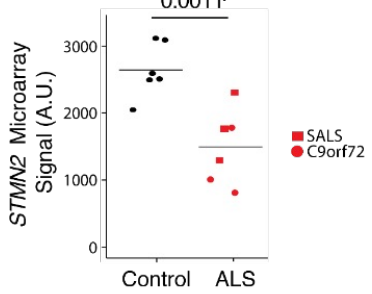
Loss of TDP-43 from the nucleus (ALS hallmark) leads to loss of STMN2

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

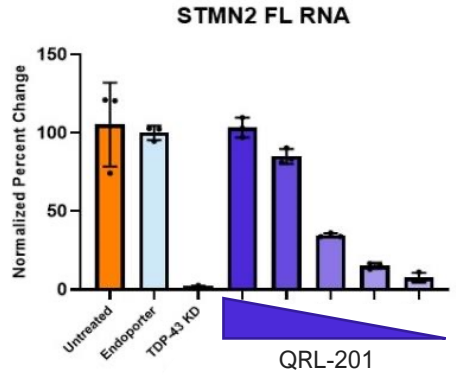


STMN2 is downregulated in ALS patients

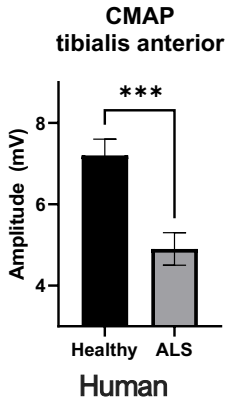
Microarray Laser Capture Motor neuron (Highley et al 2014)



QRL-201 restores STMN2



Loss of STMN2 leads to denervation of muscles



QRL-201 restores neuronal processes

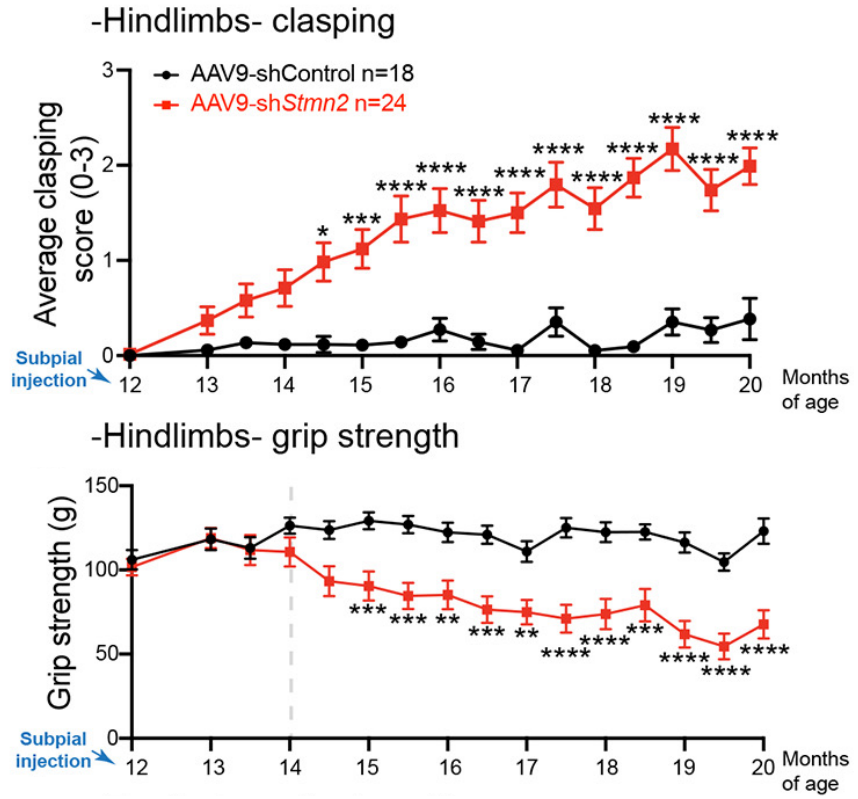
1. Melamed Z, López-Erauskin J, Baughn MW, et al. Premature polyadenylation-mediated loss of stathmin-2 is a hallmark of TDP-43-dependent neurodegeneration. *Nat Neurosci.* 2019;22(2):180-190. doi:10.1038/s41593-018-0293-z
2. Klim, J.R., Williams, L.A., Limone, F. et al. ALS-implicated protein TDP-43 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

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

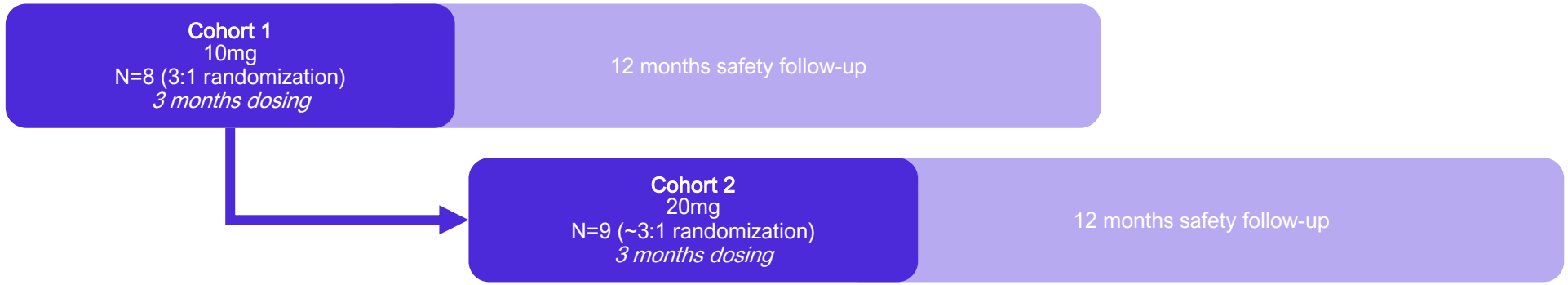
Preliminary data pending QC review

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

AnQur

CSF PK and half-life observed in MAD cohorts supported expansion into DRF[1] 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

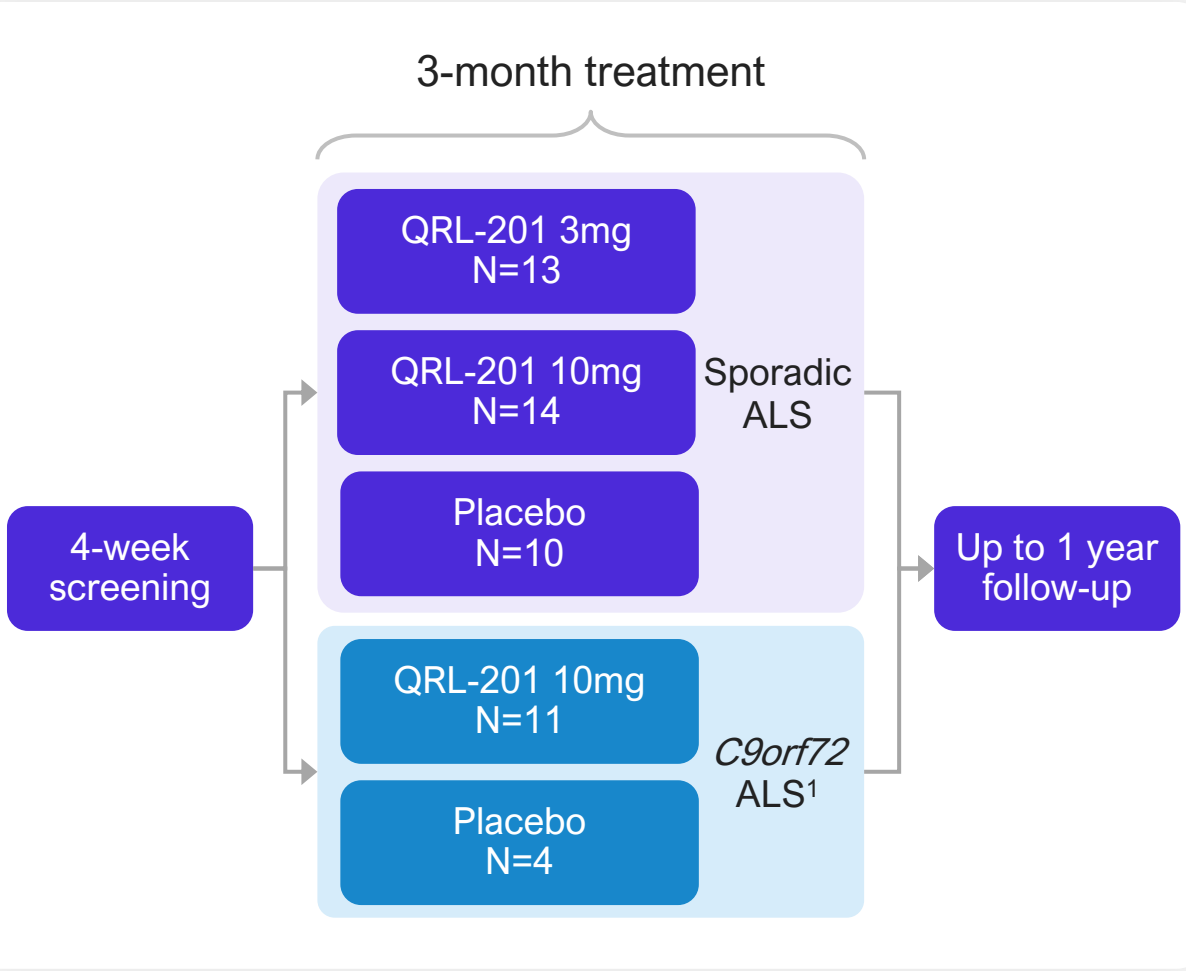
[1]DRF = Dose Range Finding

QA™

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

AnQur

Data to support future development path



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

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

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 *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: (4) Pleocytosis and (1) Dysaethesia

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

B

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

C

Target Engagement

- Autopsy samples were obtained from the MAD phase of the study[2]
- 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

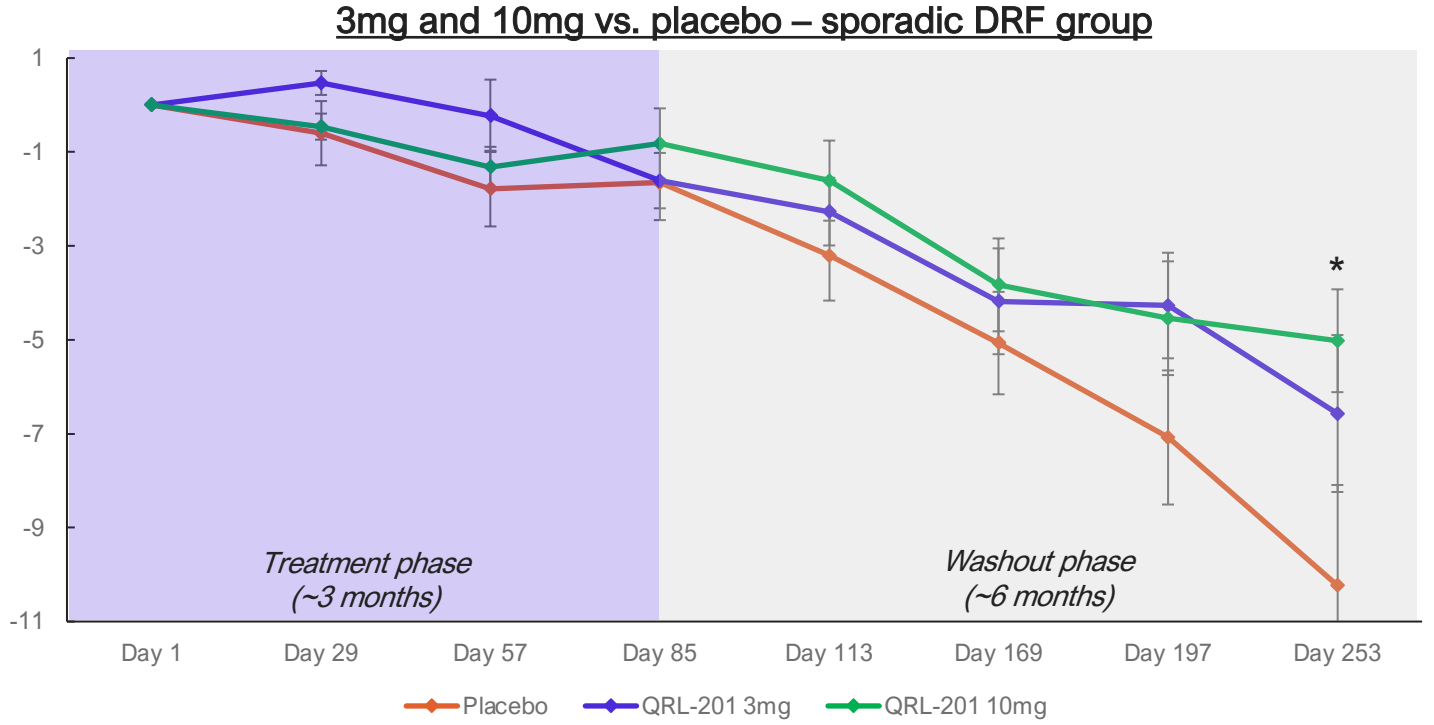
	Endpoint	Significance	QRL-201 Impact: 3mg Dose	QRL-201 Impact: 10mg Dose
D	ALSFRS-R	Captures whether the biologic effect translates to slowed disease progression and is the registrational endpoint in ALS	36% Effect vs Placebo at 8.5mo	50% (p<0.05) Effect vs Placebo at 8.5mo
E	pNfH (CSF)	Reflects motor neuron axonal degeneration and is highly correlated to disease progression in sporadic ALS, directly regulated by STMN2 expression	~46% (p<0.0001) Decrease from Baseline at 6.5mo	~5% Decrease from Baseline at 6.5mo
E	NfL (CSF)	Serves as a quantitative marker of disease activity in some ALS subgroups (i.e. SOD1), measuring rate of progression	~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)	Provides a peripheral, longitudinally accessible readout of neuroaxonal injury, tracks directionally with CSF NfL but with a temporal lag	~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

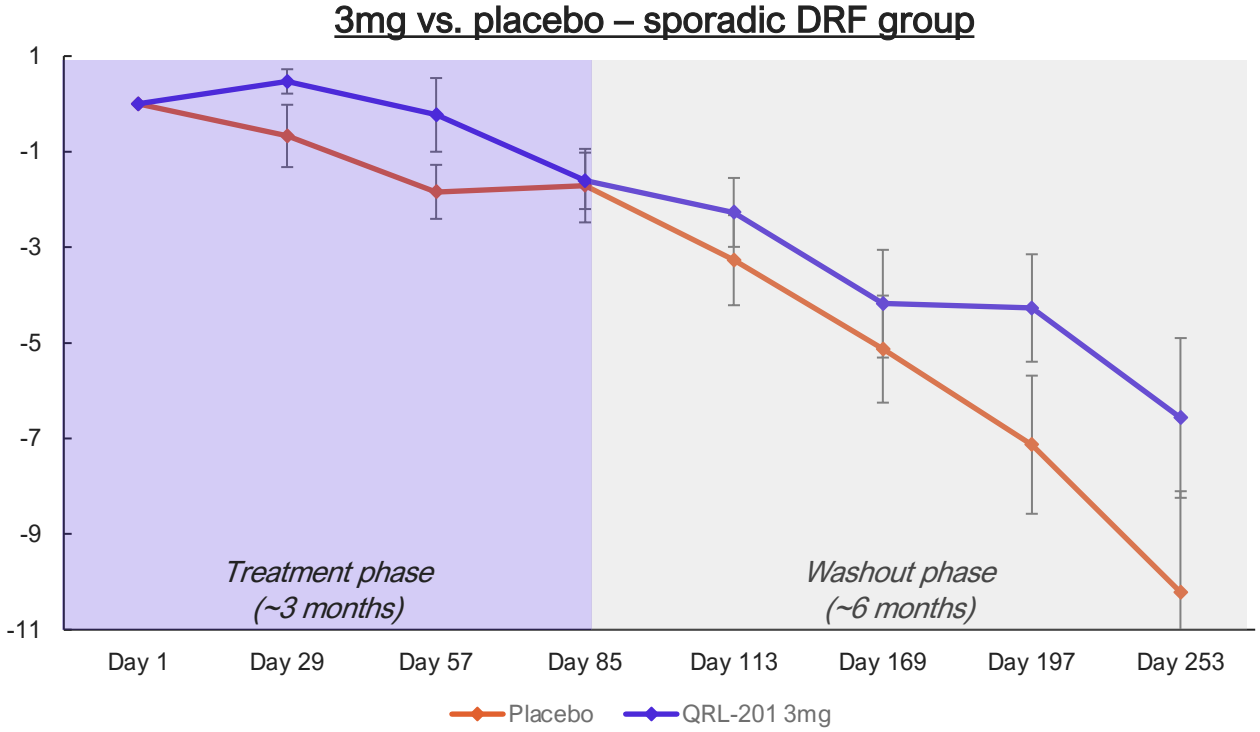
	3mg	10mg	Placebo
Discontinuation (death, disease progression, other):	15%	7%	40%

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

ALSFRS-R Total Score sporadic ALS: 3mg dose

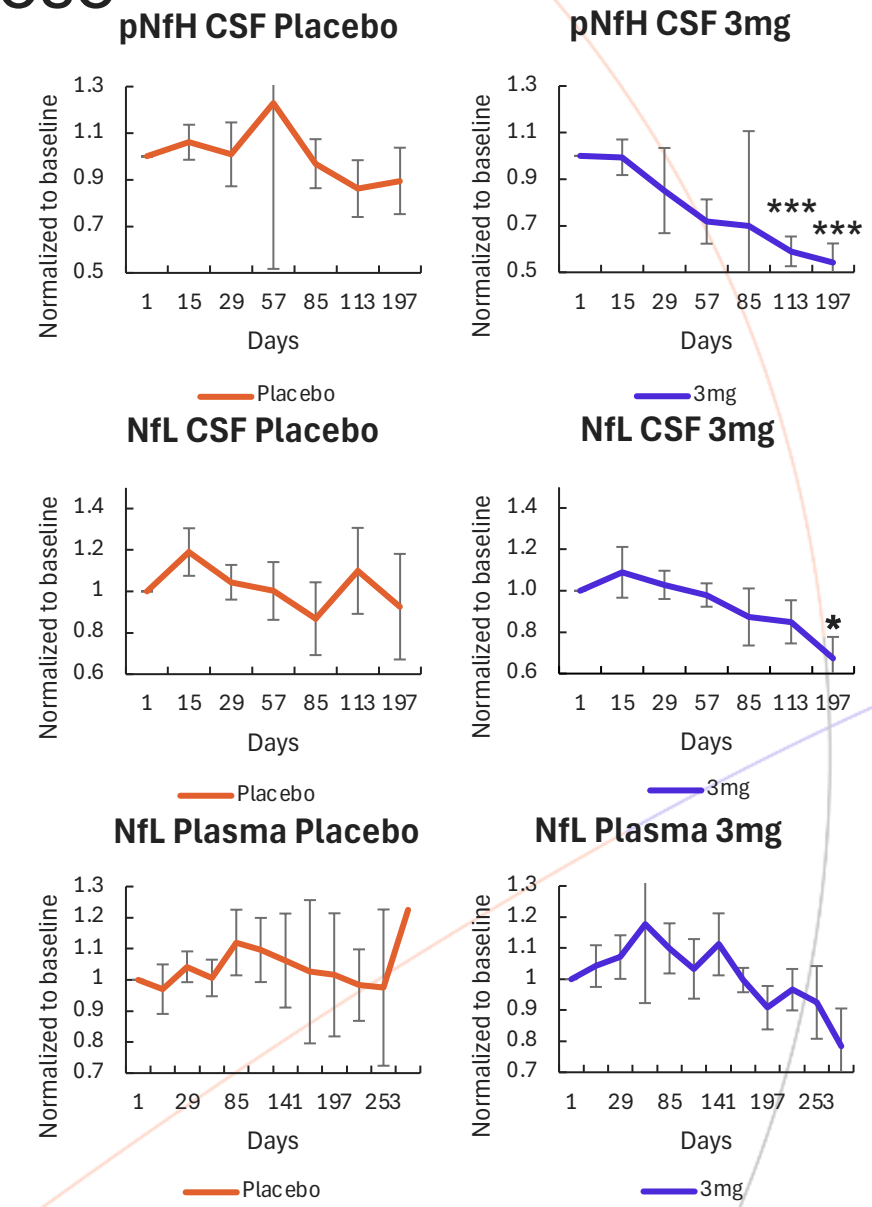
3.66pt (36%) difference with placebo after ~8.5 months

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%

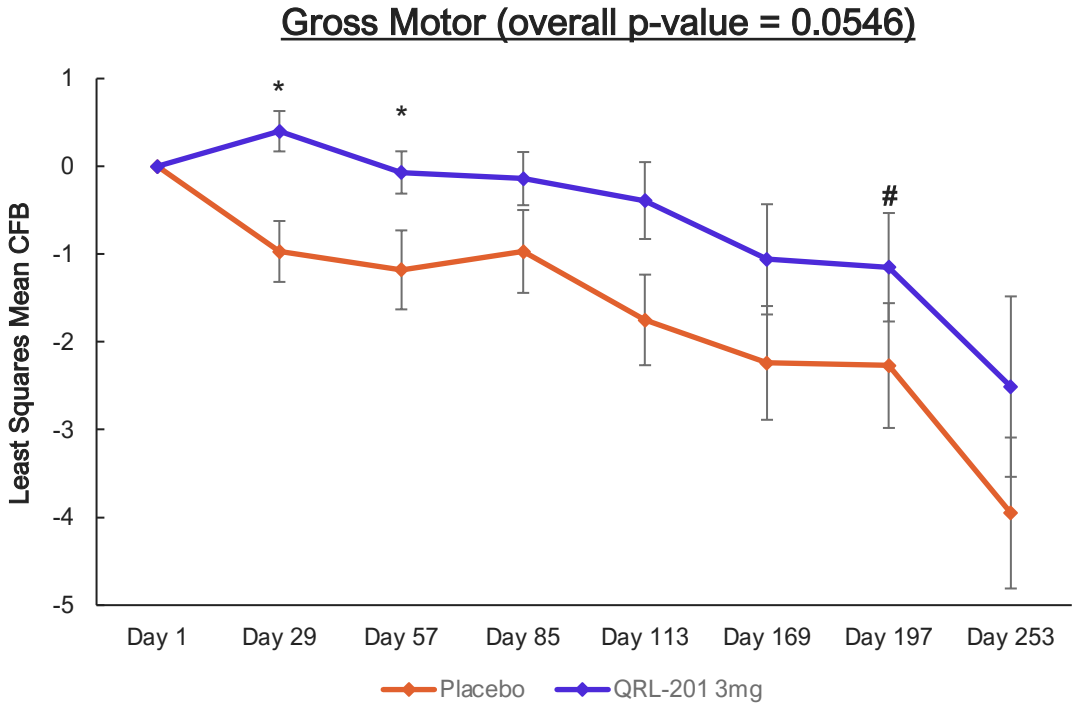


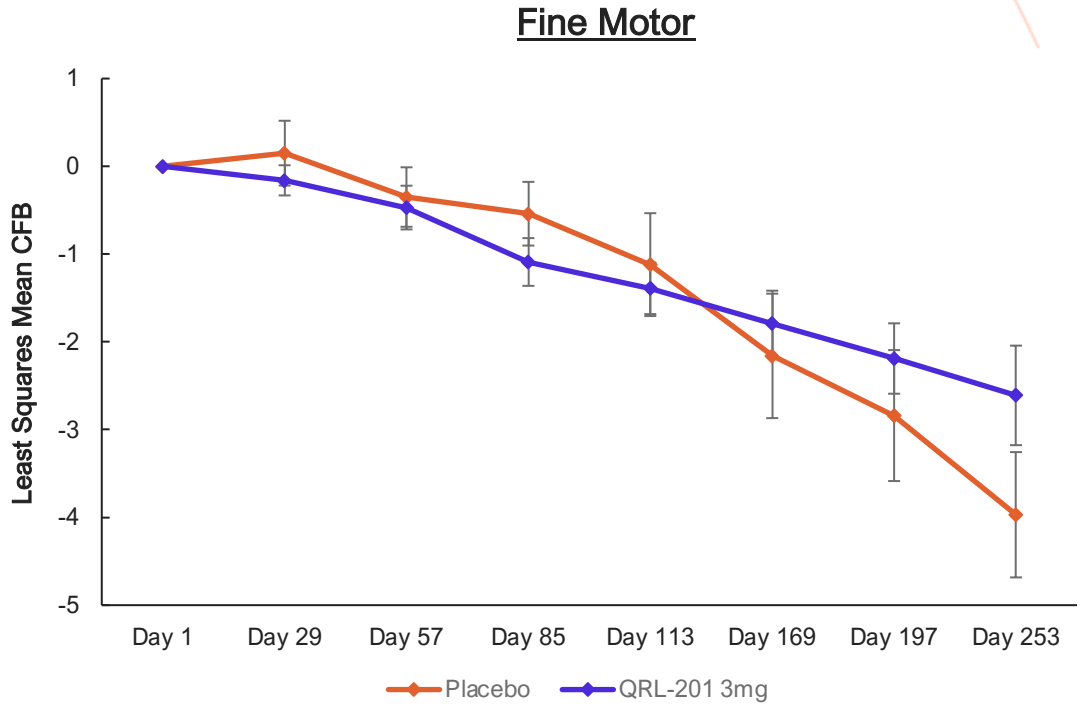
Note: Patients with 1 point decrease or less (stable) includes patients with improved functional score

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)

ALSFRS-R Subscores sporadic ALS: 3mg dose

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



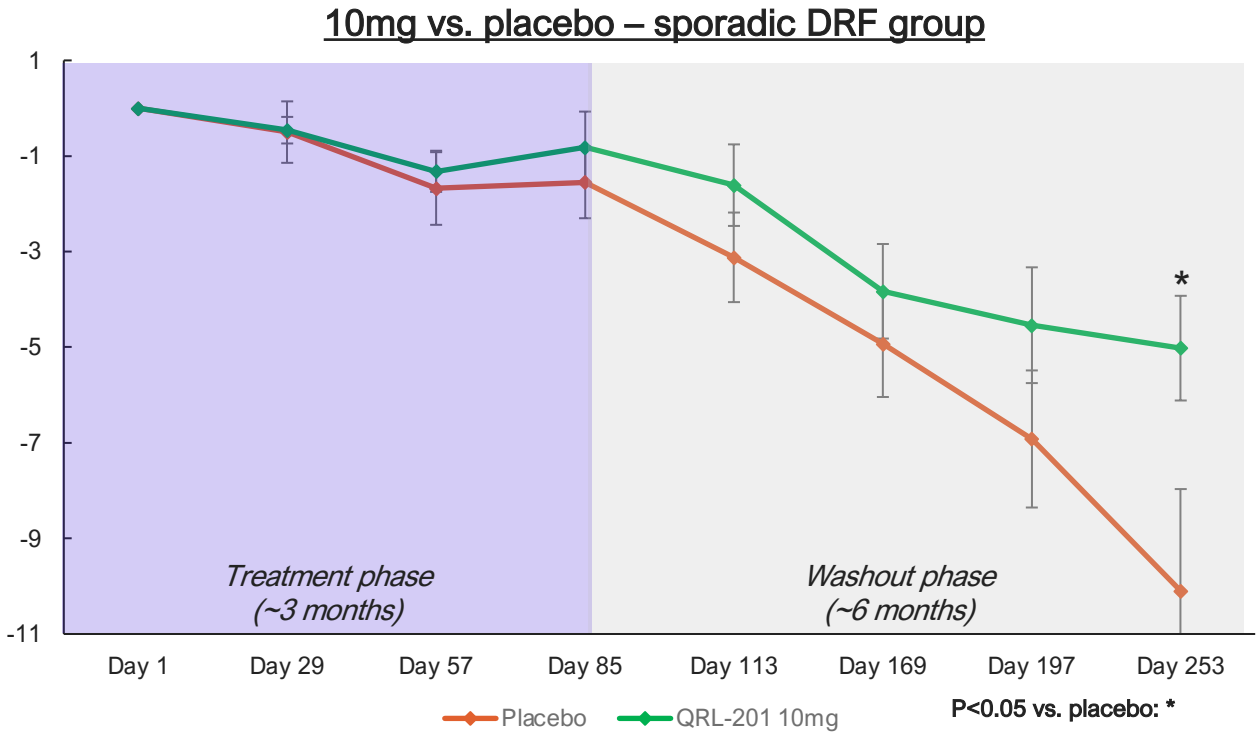


P<0.05 vs. placebo: *
P<0.10 vs. placebo: #

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

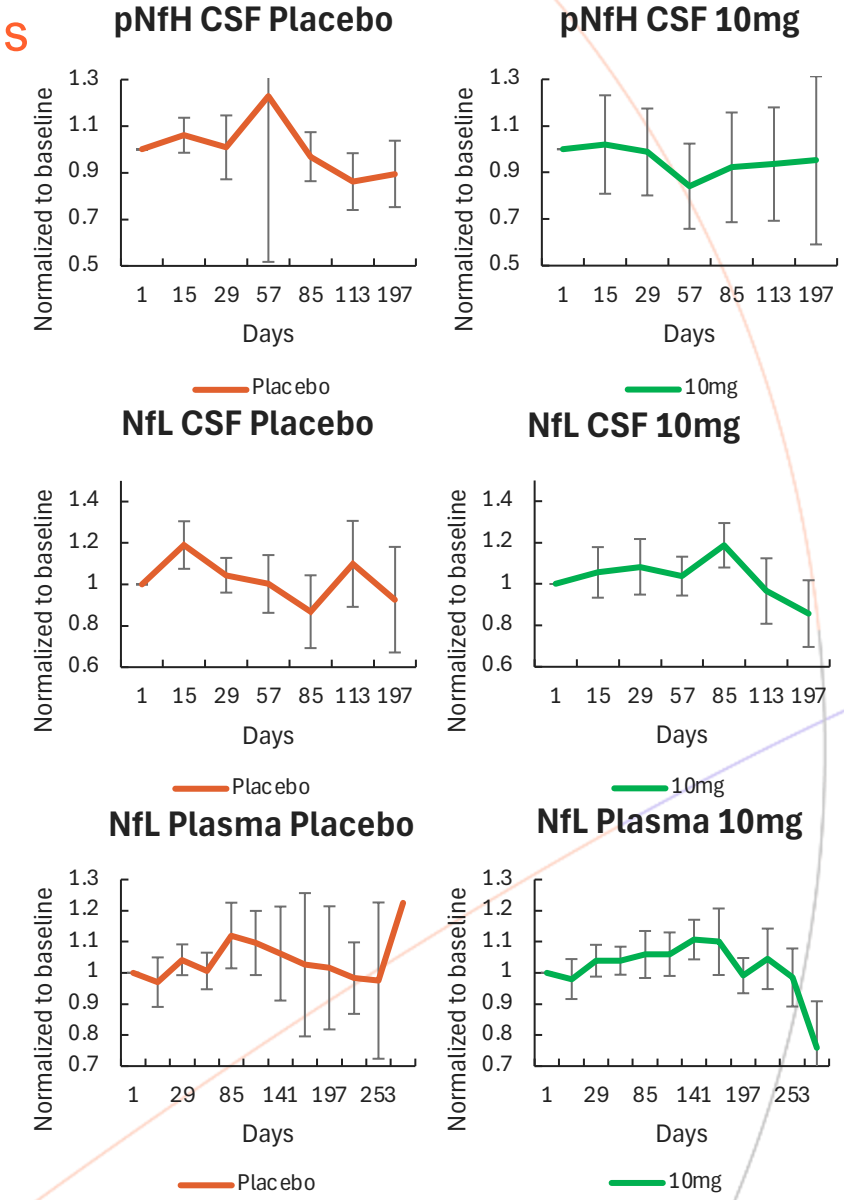
ALSFRS-R Total Score sporadic ALS: 10mg dose

5.08pt (50%) stat. sig. difference with placebo after ~8.5 months
Trend of decrease in NfL CSF and plasma after ~6 months



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%
Patients with 1 point decrease or less (stable):	36%



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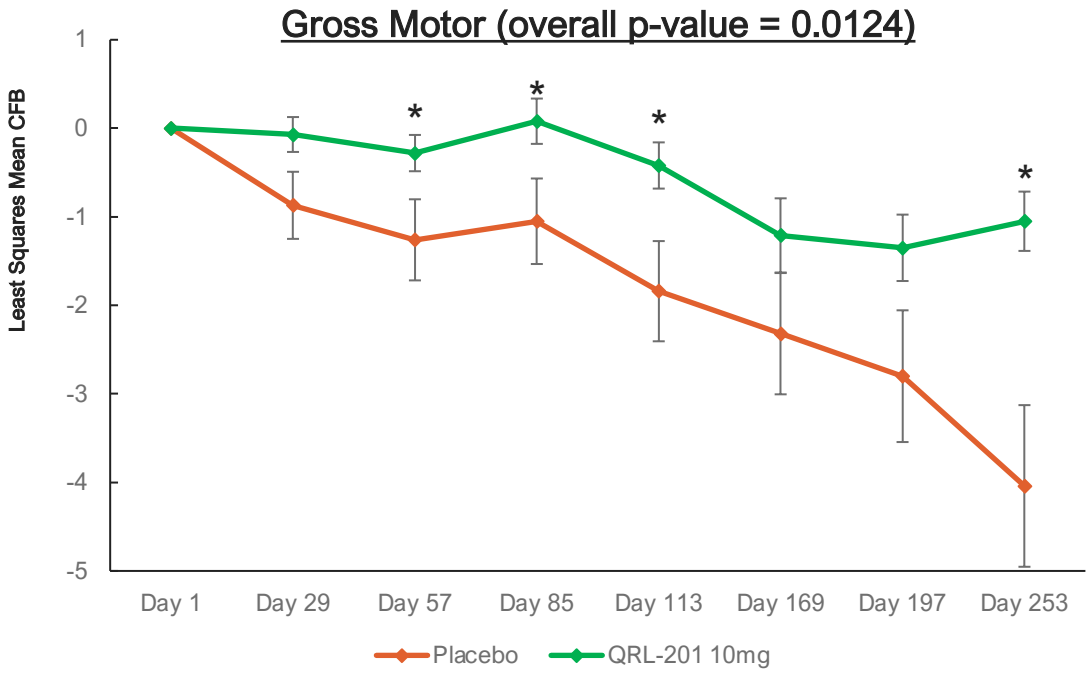
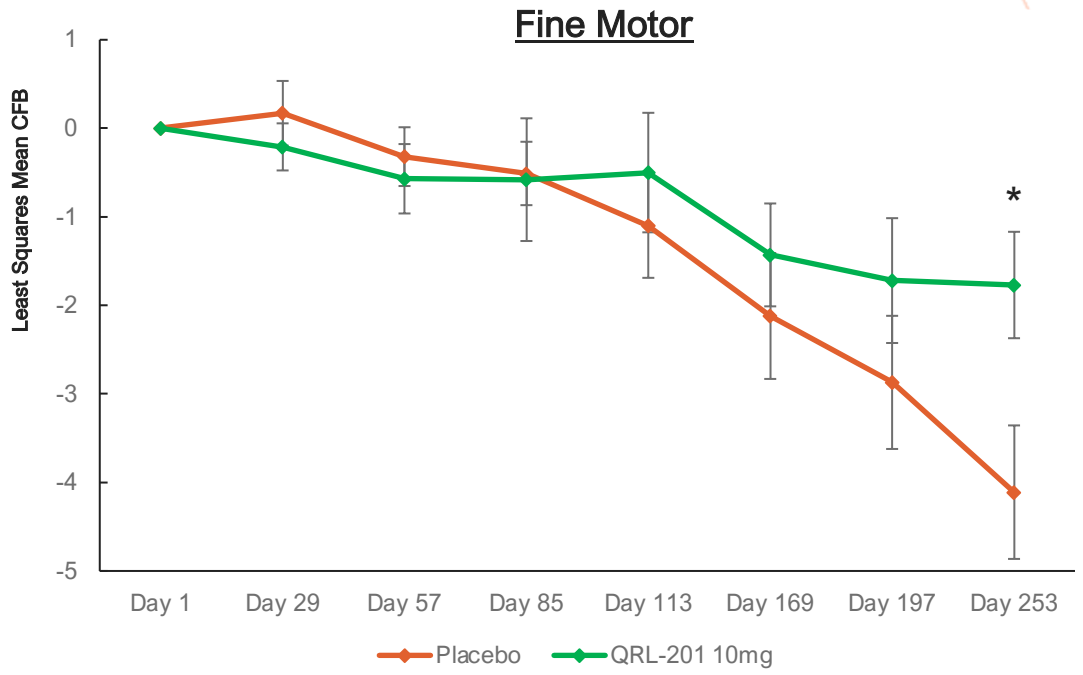
ALSFRS-R Subscores sporadic ALS: 10mg dose

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





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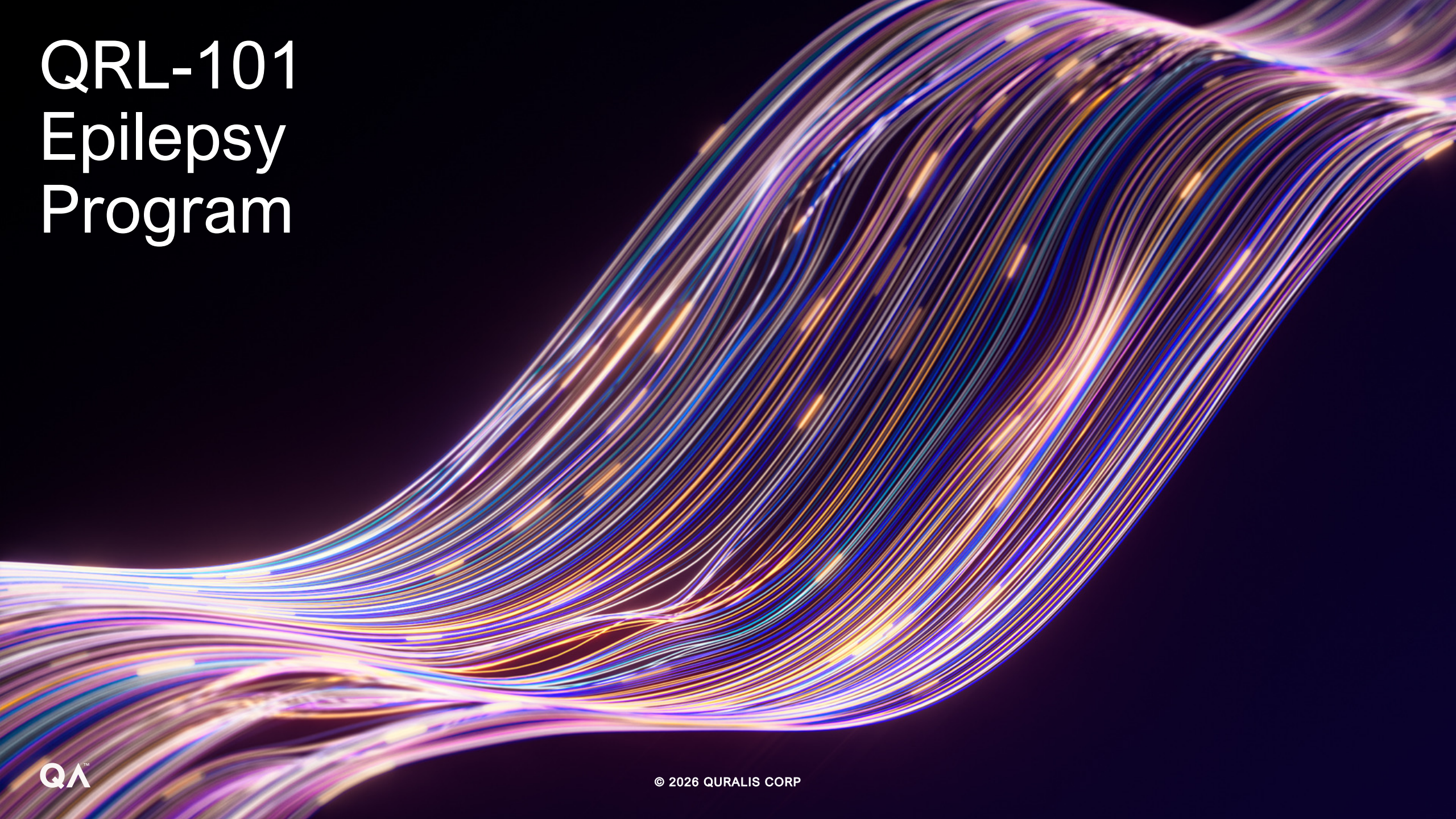
ANQUR open-label extension approved in all countries
Pivotal planning is under way with study expected to initiate in 2027

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

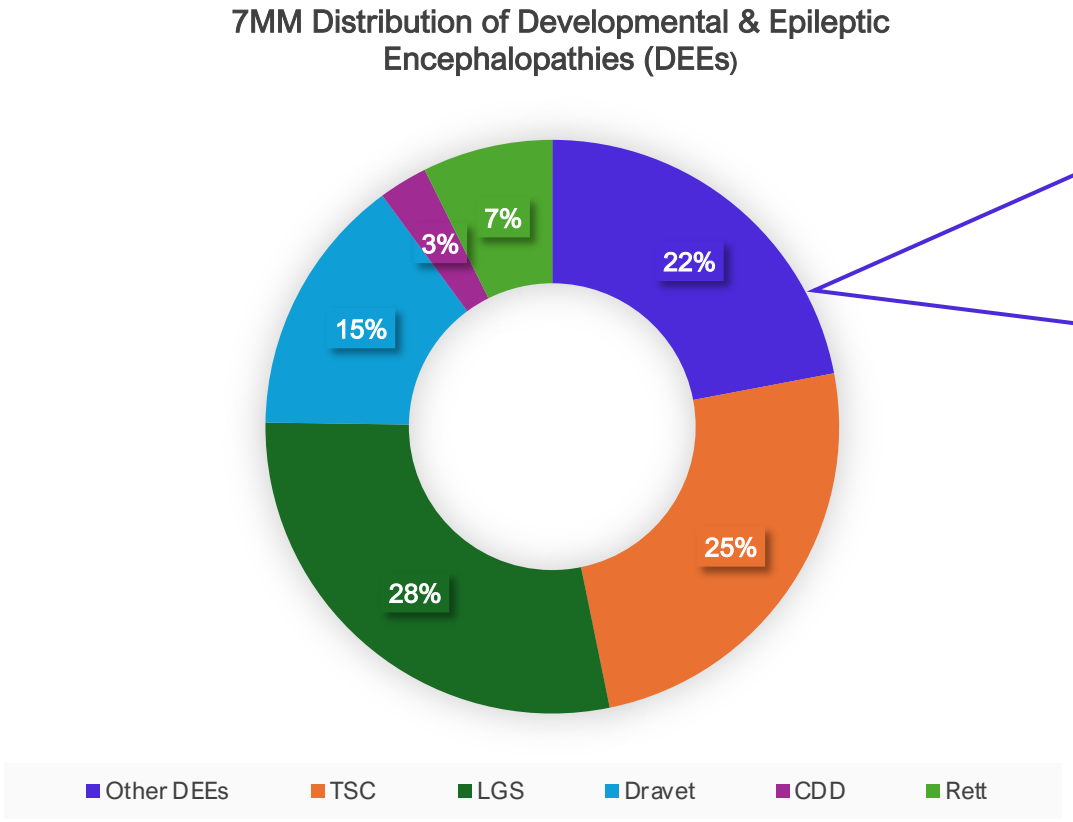
Older generation Kv7 ion channel openers exhibited safety & adverse event liabilities due to:

- 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



NO APPROVED THERAPIES FOR “Other” DEEs

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

~4,000 US patients[1]

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 date[1]

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

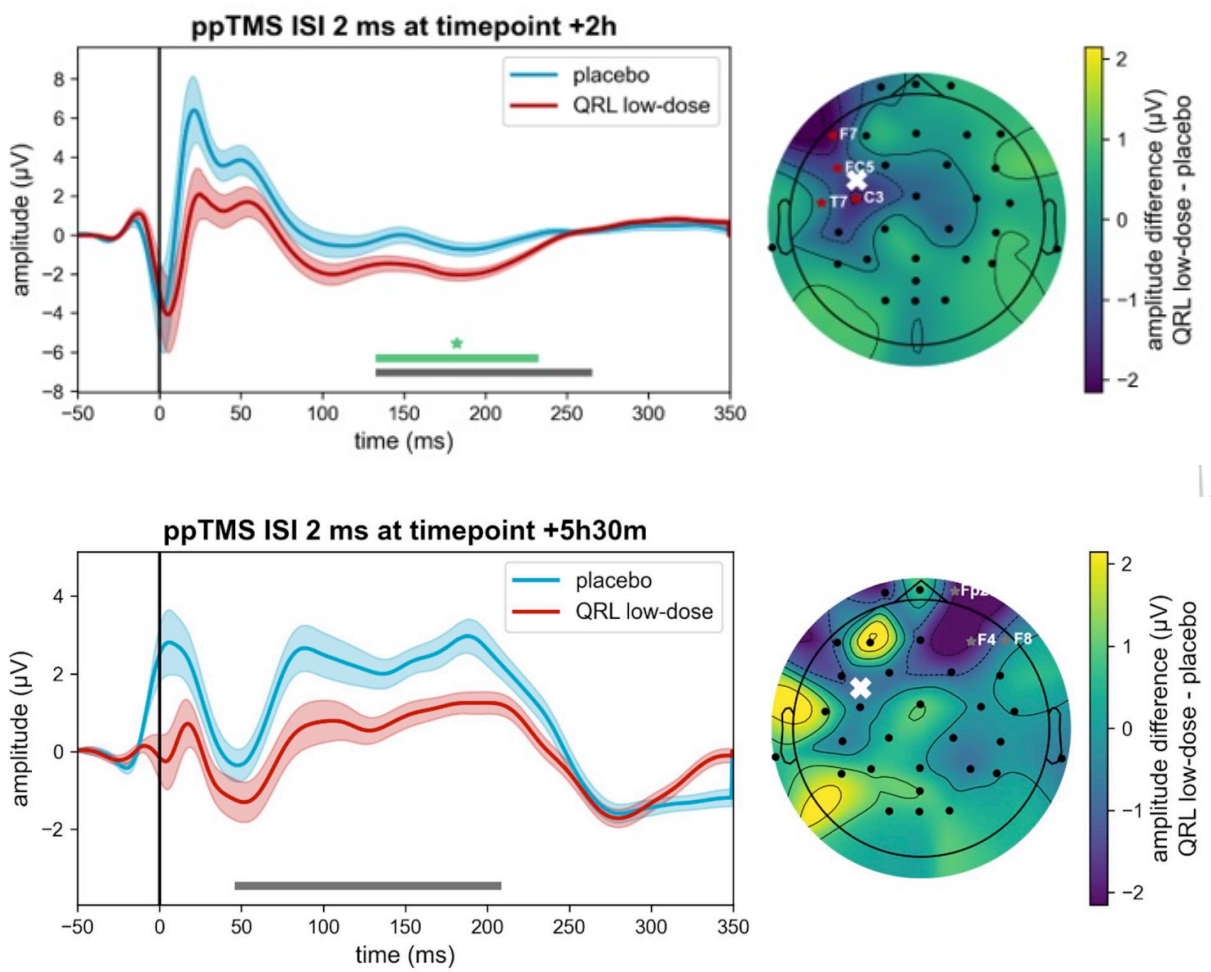
[1]As of December 31, 2025
HVs: Healthy Volunteers; SAD: Single Ascending Dose; MAD: Multiple Ascending Dose; PoM: Proof of Mechanism; PK: Pharmacokinetics

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:

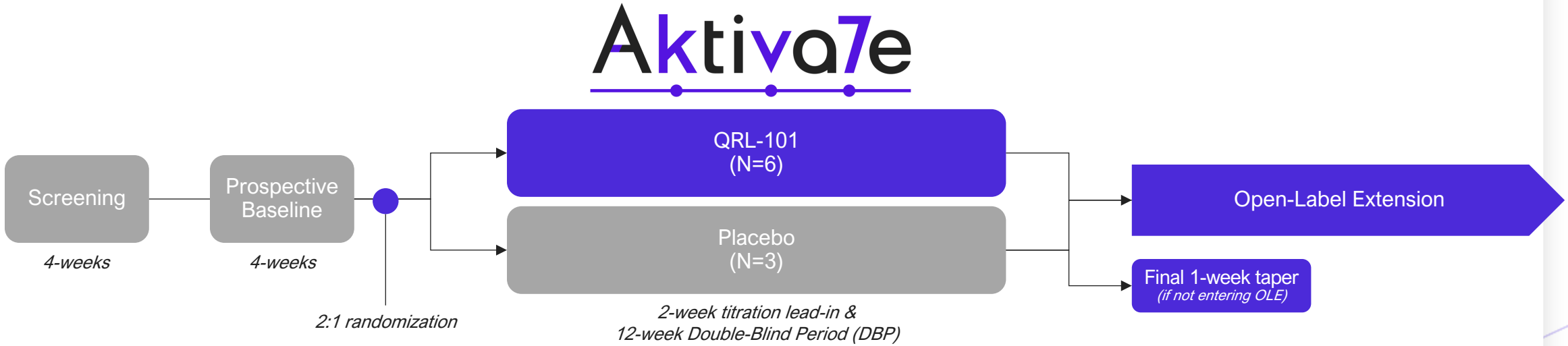
- ☑ **TMS-Evoked Potential** (pictured right) low dose demonstrated statistically significant reductions vs. placebo at both timepoints
- ☑ **Passive EEG** demonstrated statistically significant effects on high-frequency beta & gamma bands associated with anti-seizure activity, while not having impact 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

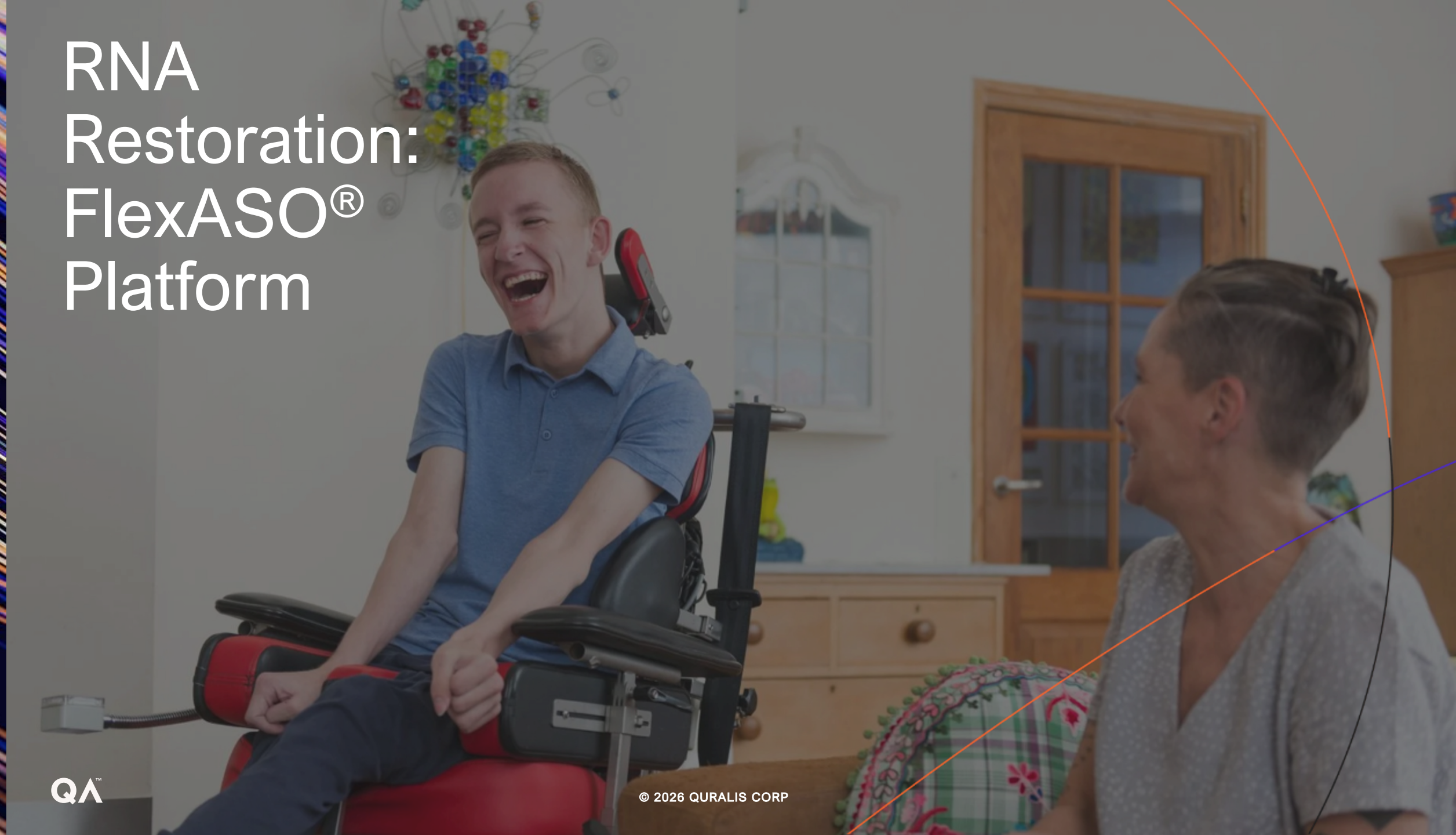
Initiation expected H1 2027



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.

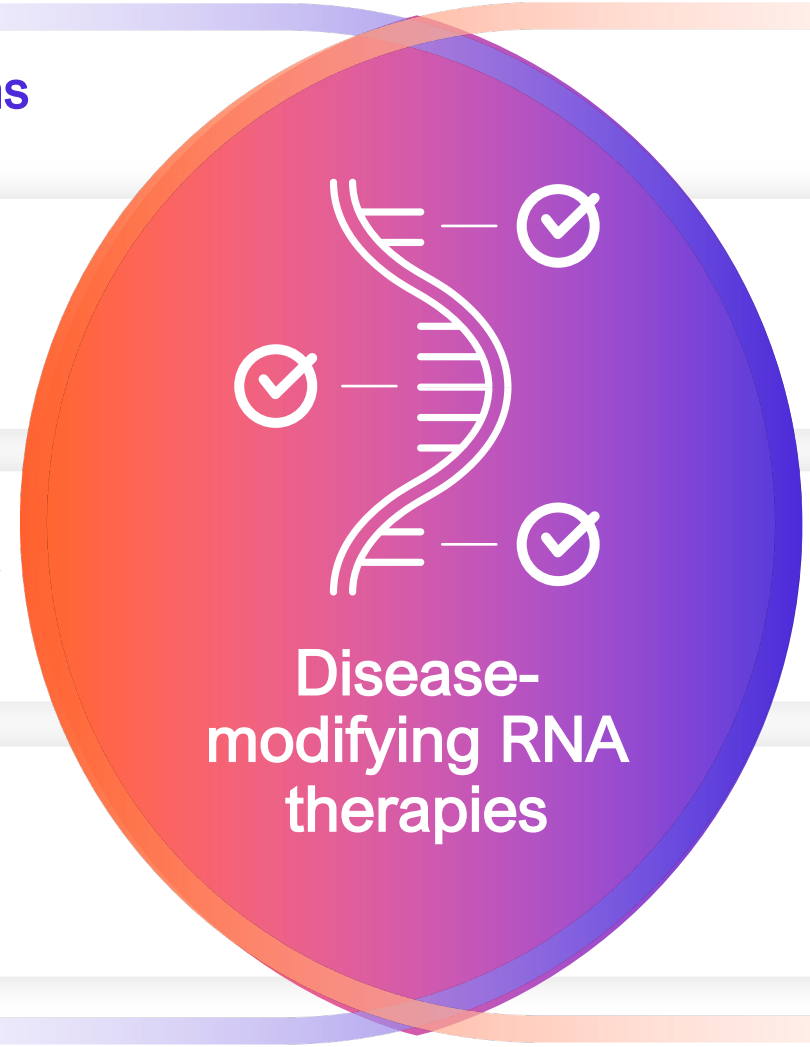
Prolonged Therapeutic Effects & Less Frequent Dosing

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

Thank you

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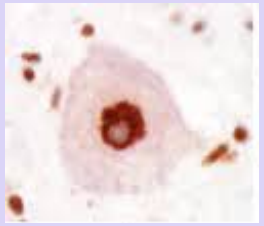
jason.brown@quralis.com

Appendix: QRL-101 Expansion Opportunities

KCNQ2 mis-splicing in ALS with TDP-43 pathology

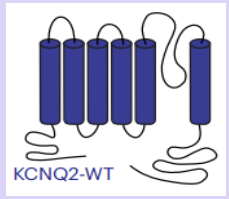
RNA mis-splicing of the voltage gated potassium channel KCNQ2 is a key hallmark of ALS related TDP-43 proteinopathy

Healthy



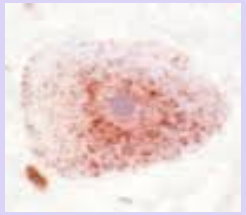
Nuclear TDP-43

KCNQ2 'normal' transcript



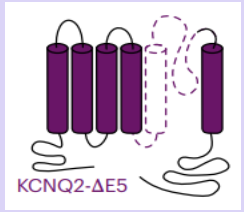
Functional KCNQ2

ALS



Cytoplasmic TDP-43

KCNQ2 mis-spliced transcript



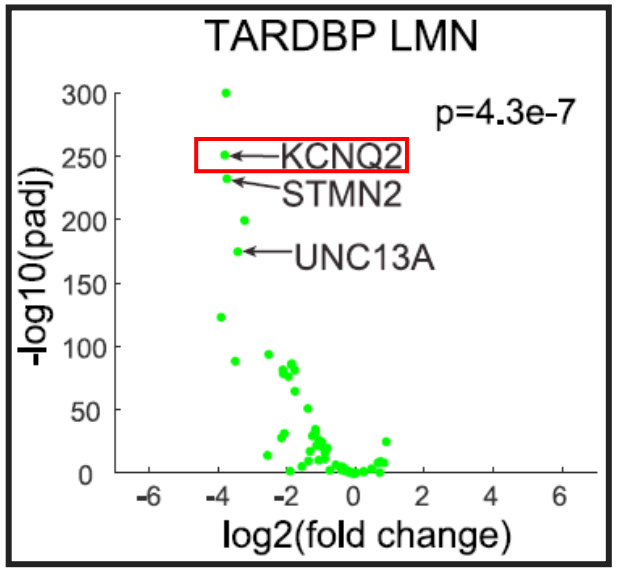
Dysfunctional KCNQ2

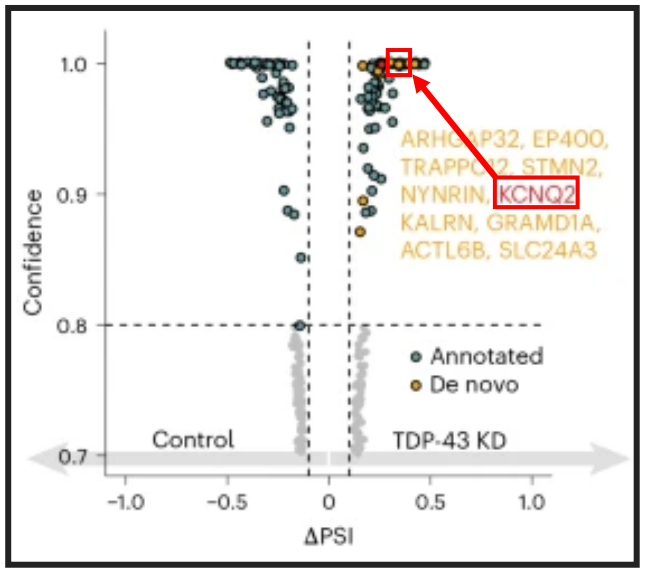
Hyperexcitability

Promotes motor neuron death

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)



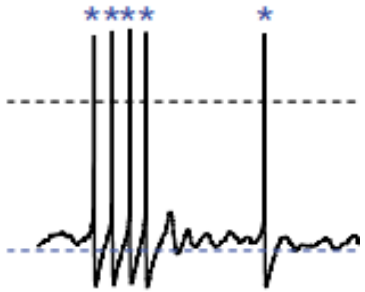


KCNQ2 mis-splicing accelerates motor neuron disease

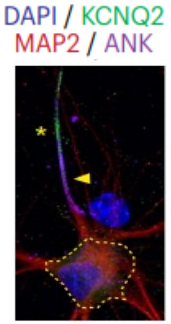
Promotes hyperexcitability, motor neuron death and accelerates ALS disease progression

Healthy

Nuclear TDP-43
Normal KCNQ2 function



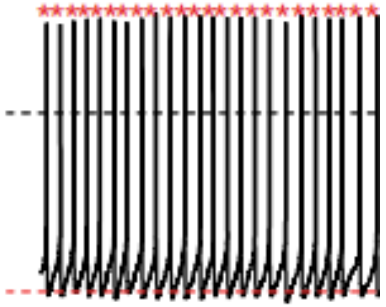
Normal neuronal activity



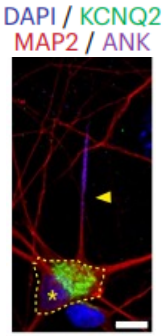
Functional KCNQ2

ALS

TDP-43 loss of function
KCNQ2 RNA mis-splicing



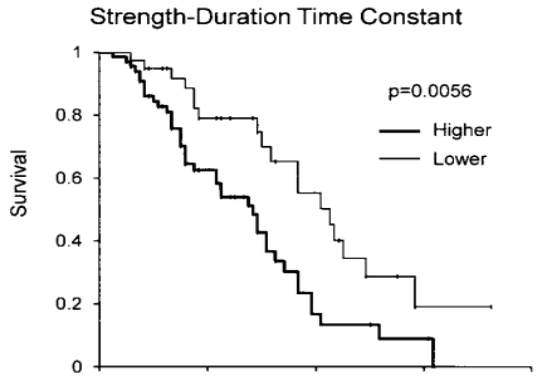
Hyperexcitability



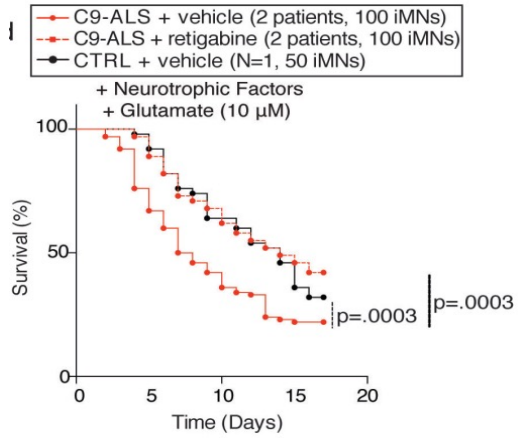
Mislocalized, Dysfunctional KCNQ2

Motor neuron hyperexcitability is correlated with accelerated ALS disease progression

(Kanai et al 2012)



Ezogabine has been shown to improve motor neuron survival

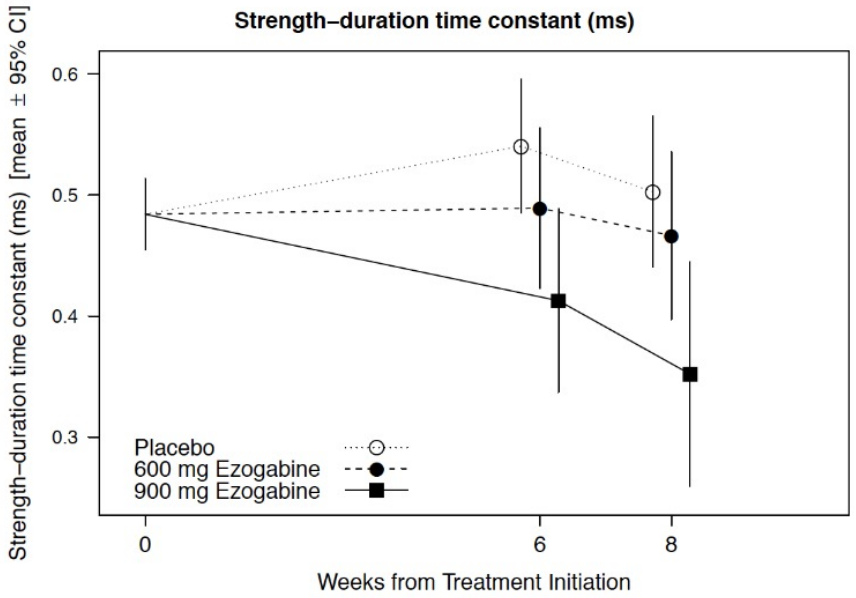


(Shi et al 2019)

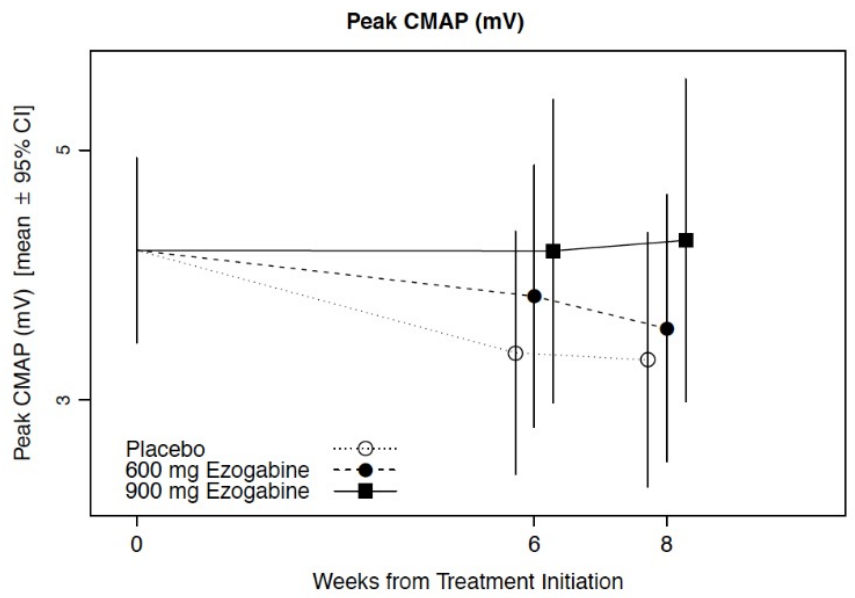
Clinical impact of Kv7 on hyperexcitability in ALS was first demonstrated by the first-generation Kv7 ezogabine[1]

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

Statistically significant[2] dose-dependent effects on biomarkers that predict patient survival



Statistically significant[2] impact on critical disease progression & efficacy biomarker (CMAP)



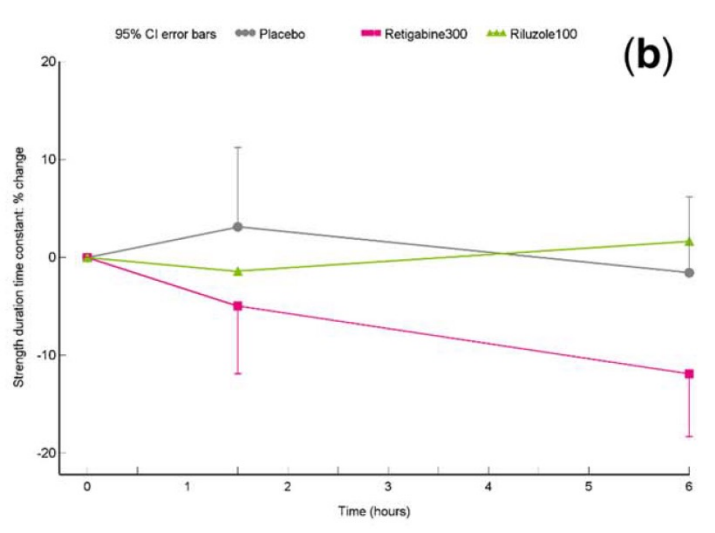
Nearly all (97%) participants in the trial reported at least one adverse event
Most frequent adverse events among participants in the ezogabine arms were fatigue and dizziness

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

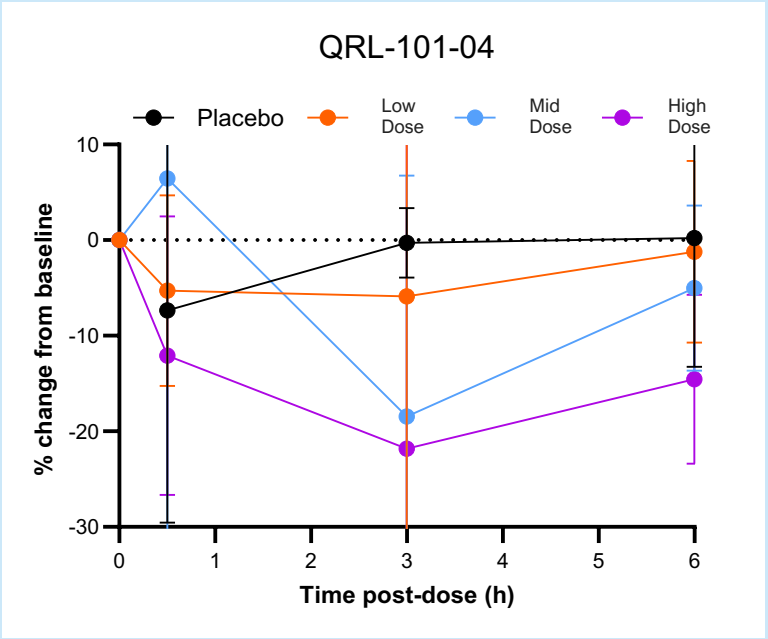
Evaluating next steps of development

Retigabine statistically significantly[1] reduced SDTC, a biomarker predictive of patient survival

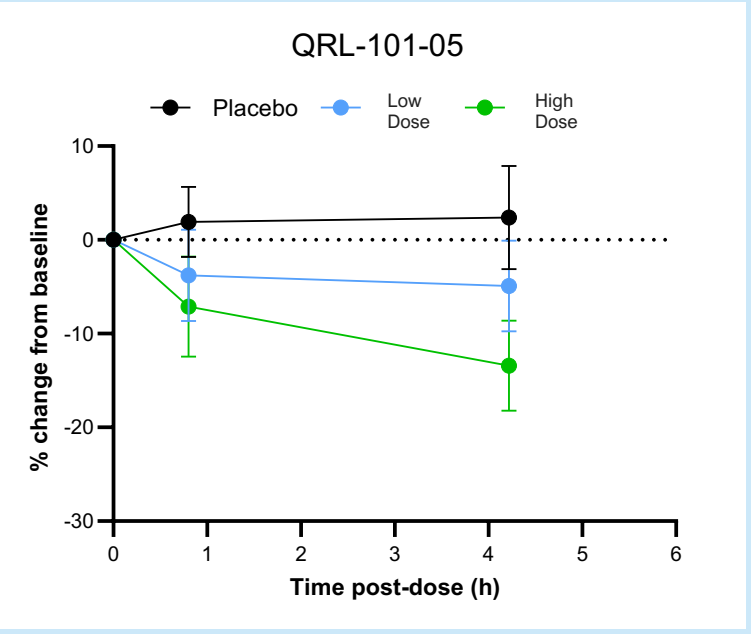


- N=18 ALS patients
- Single dose cross-over study at Utrecht, each compared to self on placebo
- Treatment v. placebo effect p=0.001

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

All graphs; symbols=mean; error bars=95% CI

[1]Kovalchuk MO, et al. Clin Pharmacol Ther. 2018 Dec;104(6):1136-1145. doi: 10.1002/cpt.1096. Epub 2018 Jun 19. PMID: 29672831.

Kv7 channel activation to treat pain: A proven therapeutic strategy

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

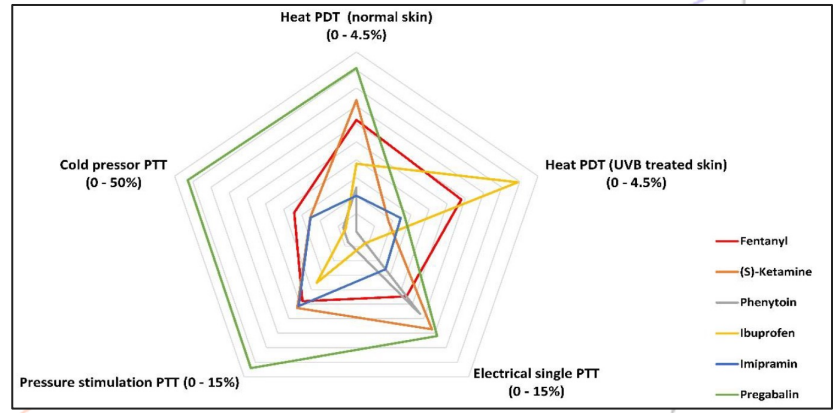
- **More than 20% of U.S. adults** reported experiencing chronic pain (pain lasting three months or more) in the past 3 months[1]
  - **8.5% of adults reported high-impact chronic pain** — pain that frequently limits life or work activities[1]
- Neuronal hyperexcitability is a central driver of pain
  - **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