QurAlis™

QRL-201-01
Updated ANQUR Interim Analysis

May 2026

TARGET ALS

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-203	STMN2	ALS	FlexASO® backup candidate					
QRL-TBA	FMR1	Fragile X	DC[5] nomination 2026					
QRL-TBA	Undis.	PSP	DC[5] nomination 2026					

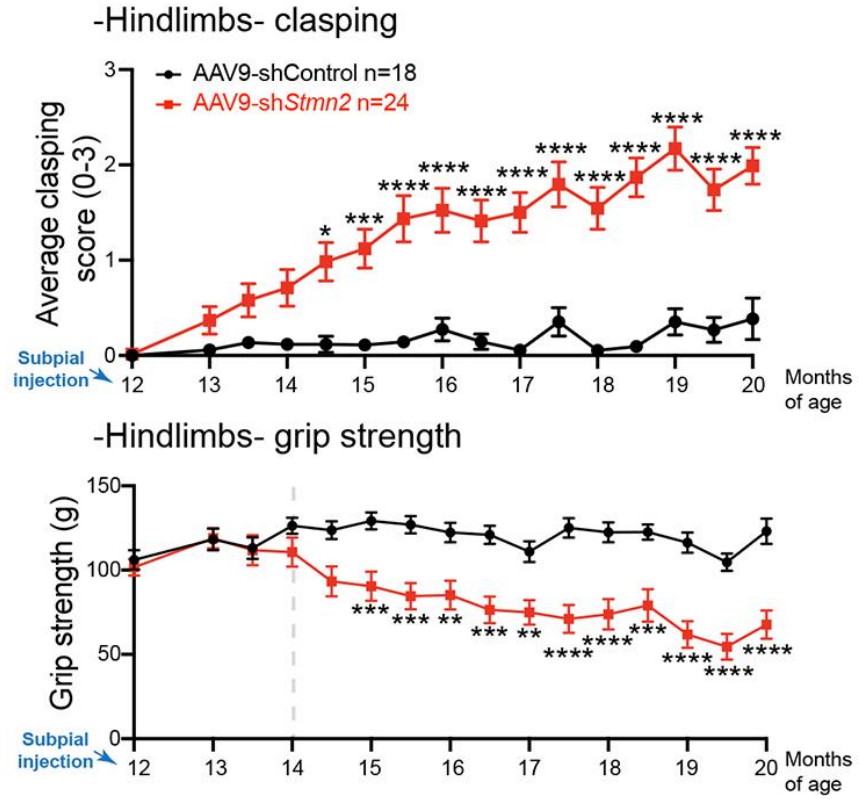
1. PoM = Proof of Mechanism; 2. DEE = Developmental and Epileptic Encephalopathy; 3. PoC = Proof of Concept; 4. Pending Series C funding; 5. DC = development candidate

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

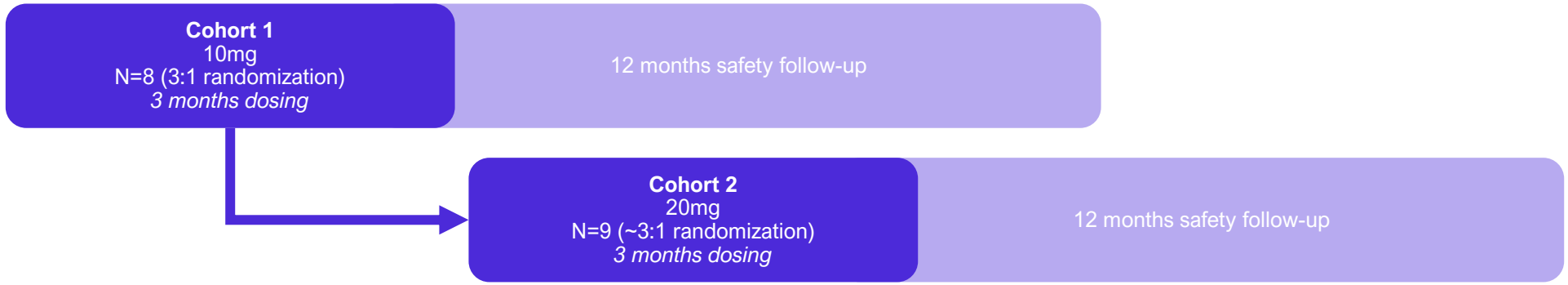


Lopez-Erauskin, Jone, et al. "Stathmin-2 loss leads to neurofilament-dependent axonal collapse driving motor and sensory denervation." *Nature neuroscience* 27.1 (2024): 34-47.

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

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

Dose escalation phase



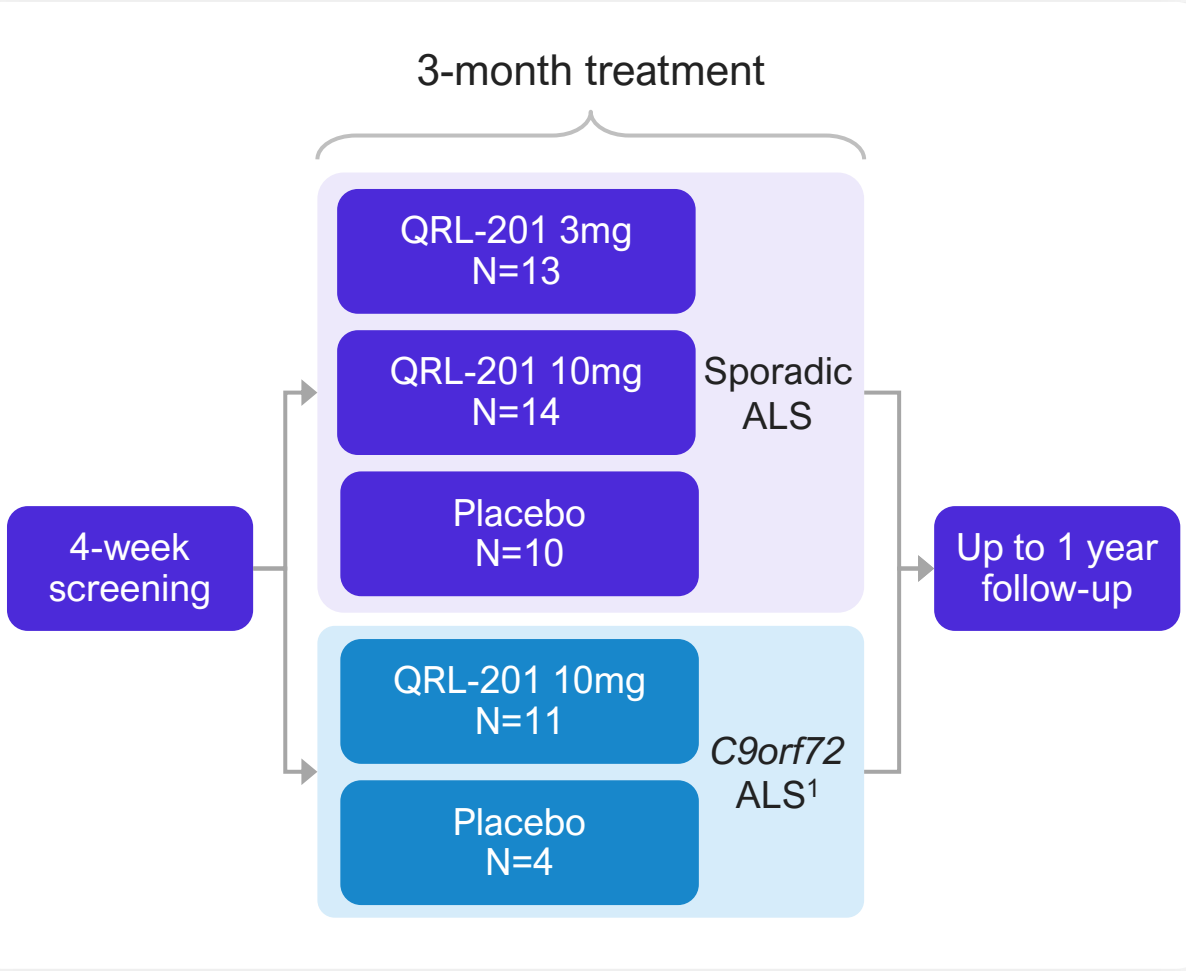
Dose escalation results

- 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

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

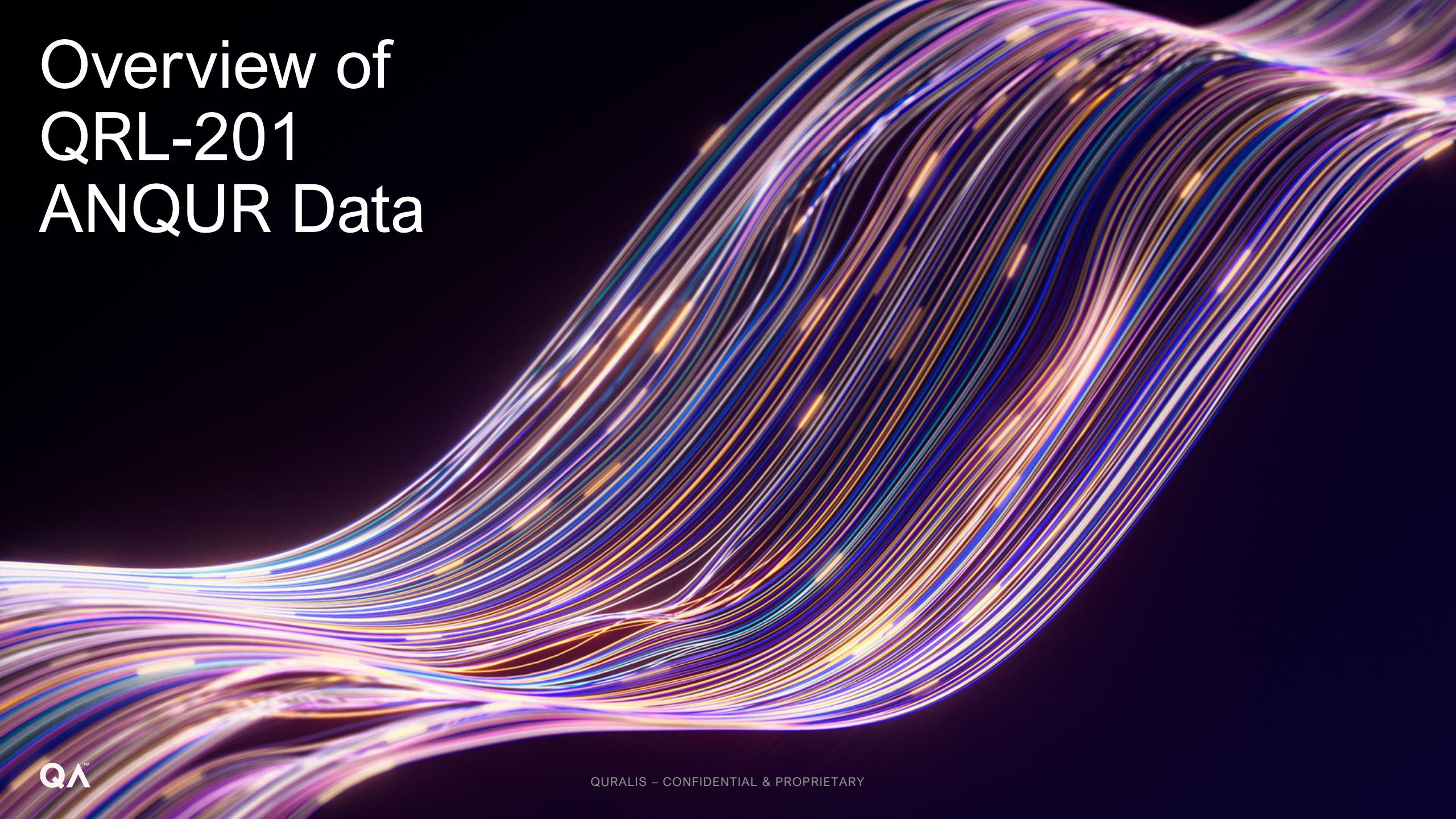
Data to support future development path



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

Overview of QRL-201 ANQUR Data



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 ≥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

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

Baseline characteristics – dose range-finding phase

Balanced ALSFRS-R, neurofilament biomarkers across sporadic groups; C9orf72 groups are unbalanced making data less interpretable

Baseline Characteristic	Sporadic 3mg (N=13)	Sporadic 10mg (N=14)	Sporadic Placebo (N=10)	C9orf72 10mg (N=11)	C9orf72 Placebo (N=4)
Age (Years)	50.5	54.9	46.6	47.6	66.0
Gender (% Male)	77%	64%	60%	64%	100%
Time from Symptom Onset (Months)	14.1	15.3	16.2	12.9	16.8
ALSFRS-R Total Score (mean)	39.1	40.1	39.8	39.6	43.3
Plasma NfL (geomean, pg/mL)	41.9	47.0	47.2	65.3	50.2
CSF NfL (geomean, pg/mL)	3,875	4,086	3,431	5,906	3,670
CSF pNfH (geomean, pg/mL)	7,549	6,766	5,122	7,475	5,443

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[1] *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 all patients, including C9orf72 patients, 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

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*

- **≥2-fold increase of full length STMN2 levels in tissue**, especially robust in brain stem and spinal cord regions. **Statistically significant increase in most regions.**
- The improvement in STMN2/ cryptic STMN2 splicing is **most robust in the lumbar SC**, and was also quite **robustly observed in the brain stem, and cervical SC.**
- 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
Data not QCed

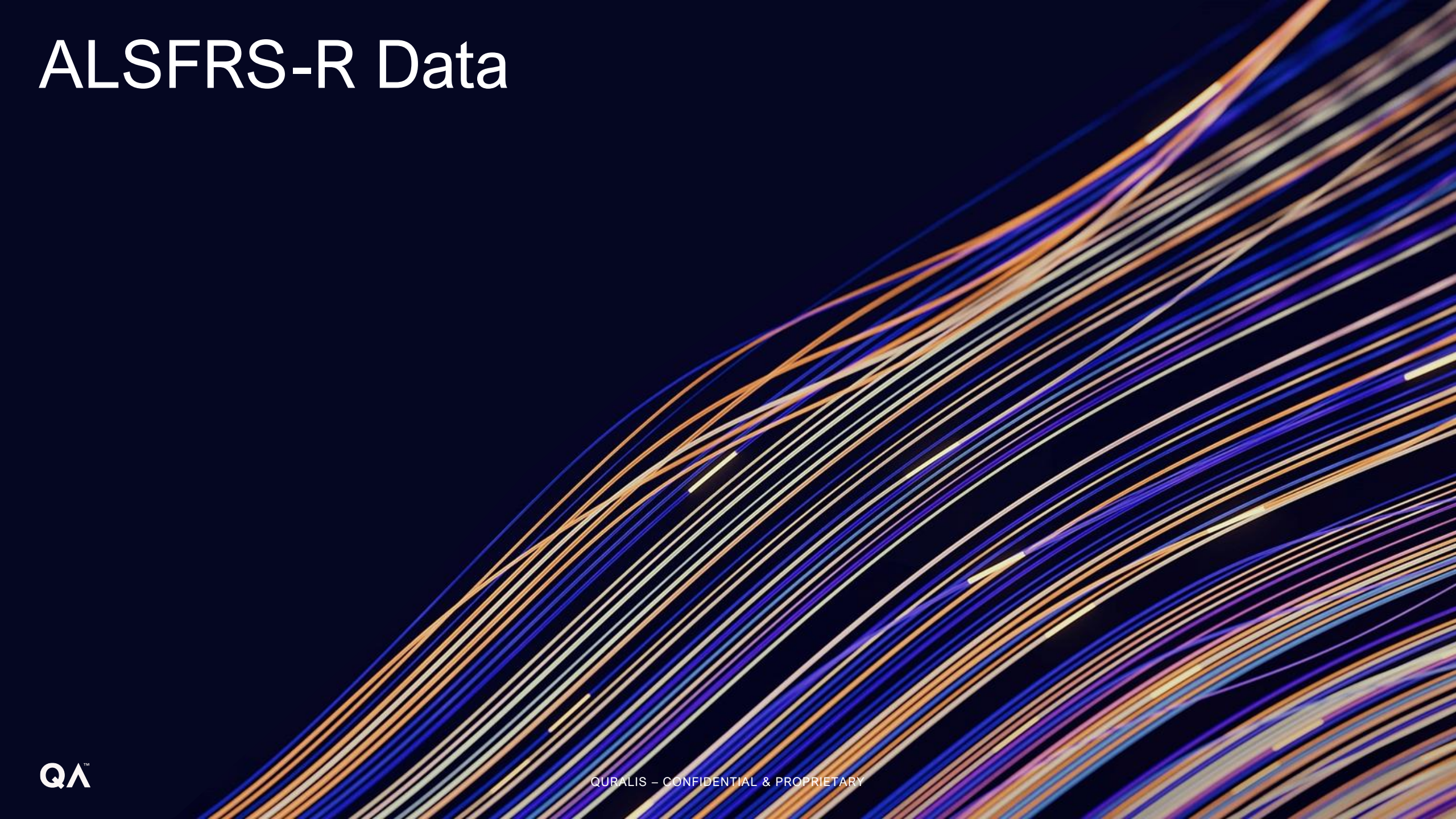
Clinically meaningful effects on both functional endpoints and neurofilament biomarkers

	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

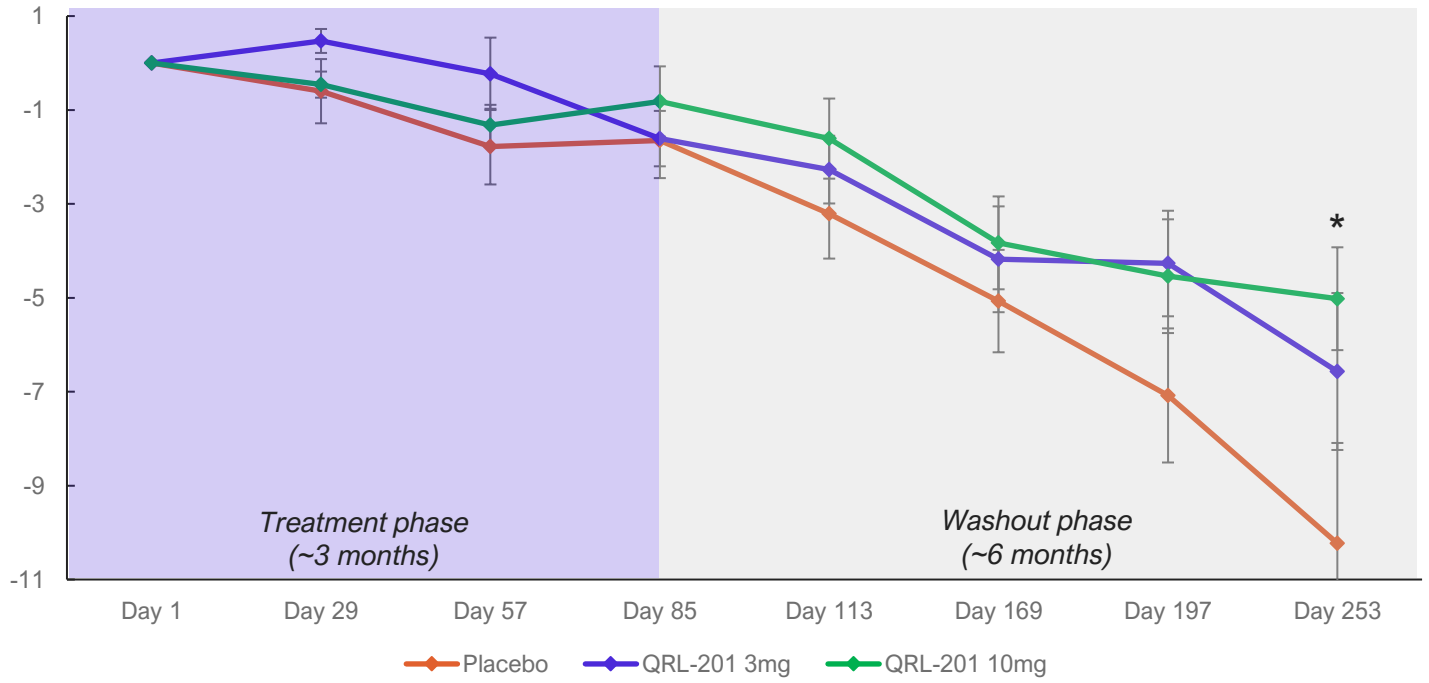
ALSFRS-R Data



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

3mg and 10mg vs. placebo – sporadic DRF group



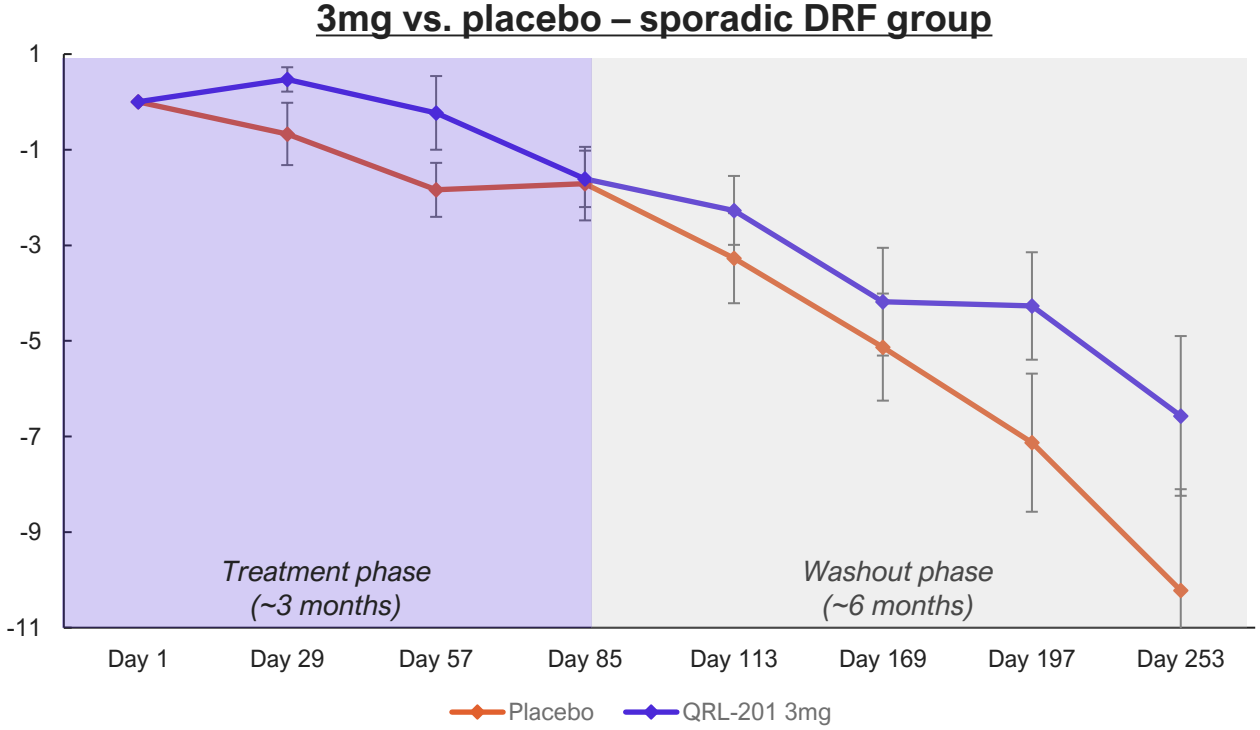
QRL-201 3mg	13	13	13	13	12	12	12	10
QRL-201 10mg	14	13	14	14	14	14	14	13
Placebo	10	10	10	10	10	8	6	6

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

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

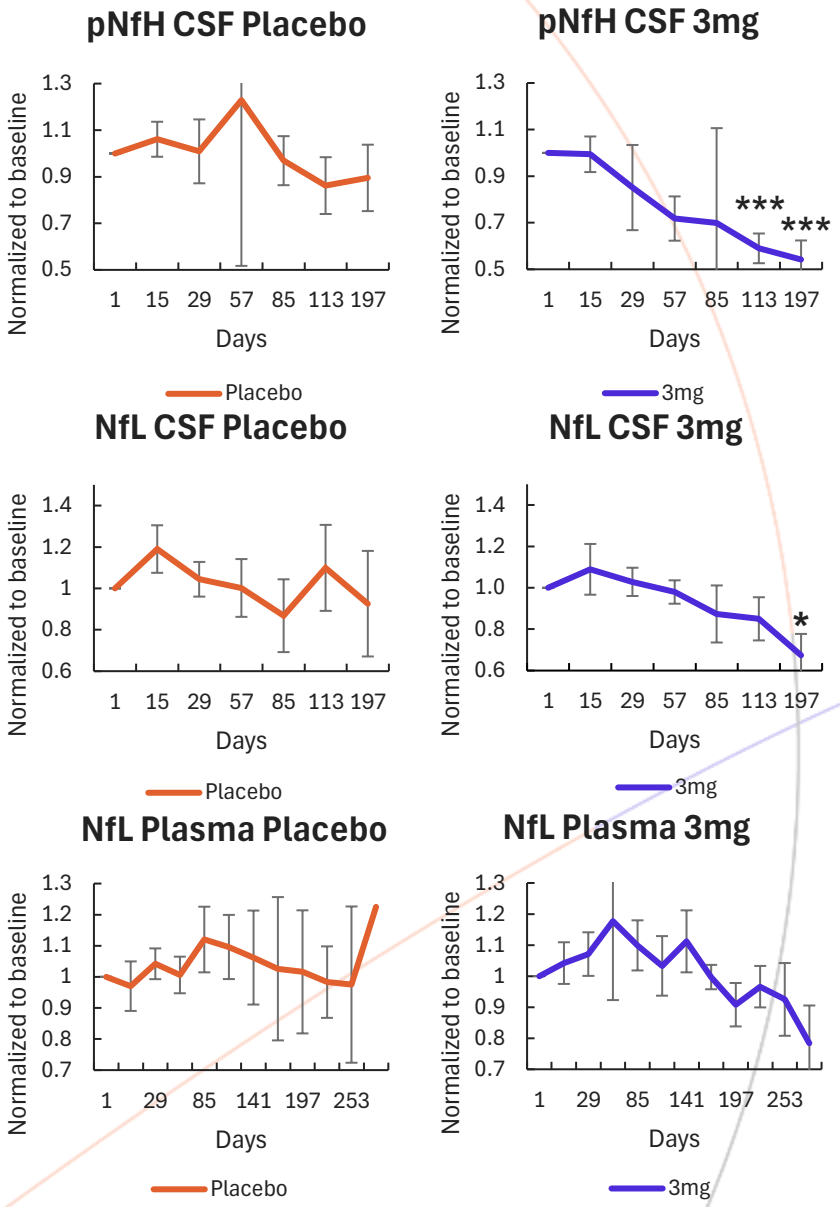
ALSFRS-R Total Score sporadic ALS: 3mg dose

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%**

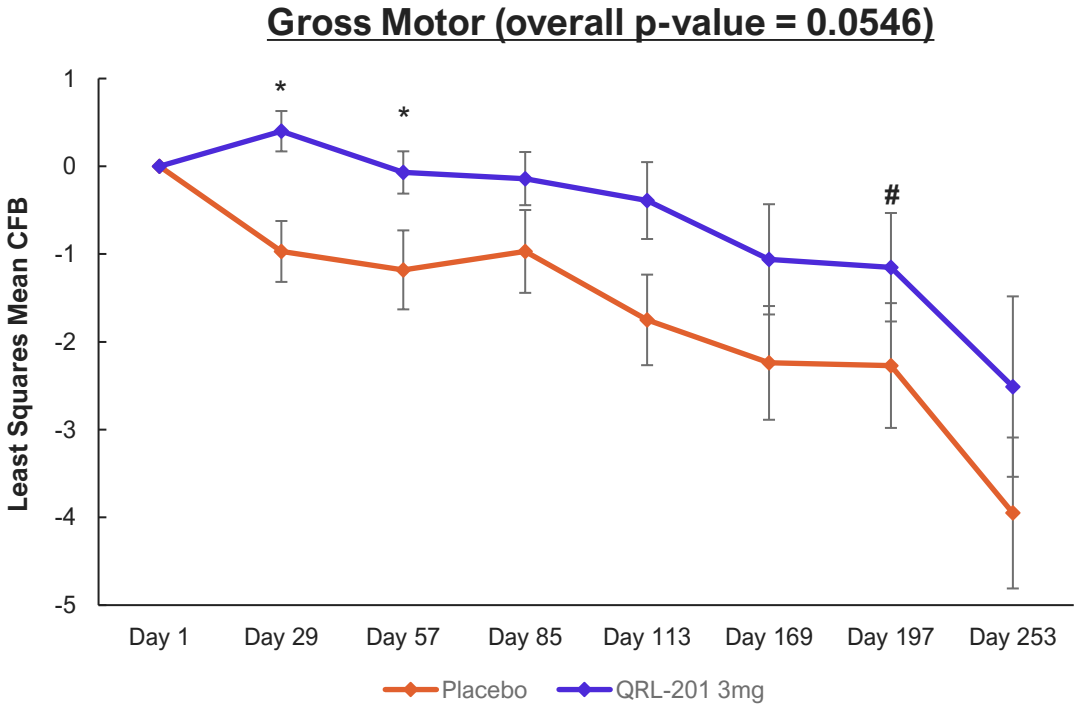


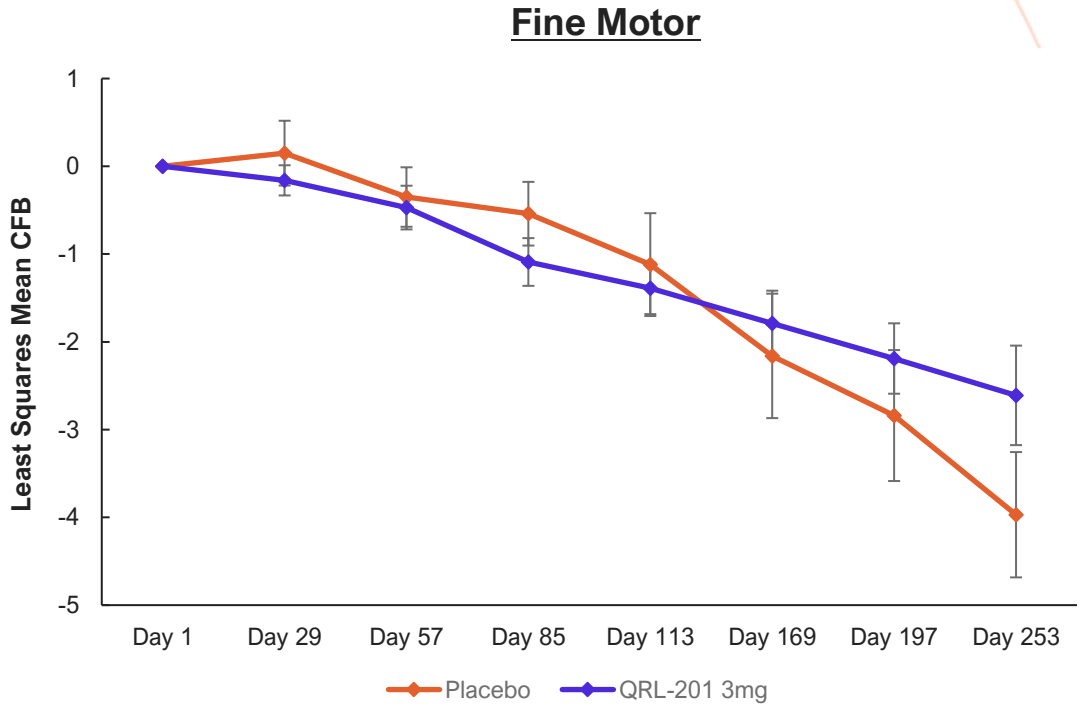
Note: Patients with 1 point decrease or less (stable) includes patients with improved functional score

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 sub-scores sporadic ALS: 3mg dose

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



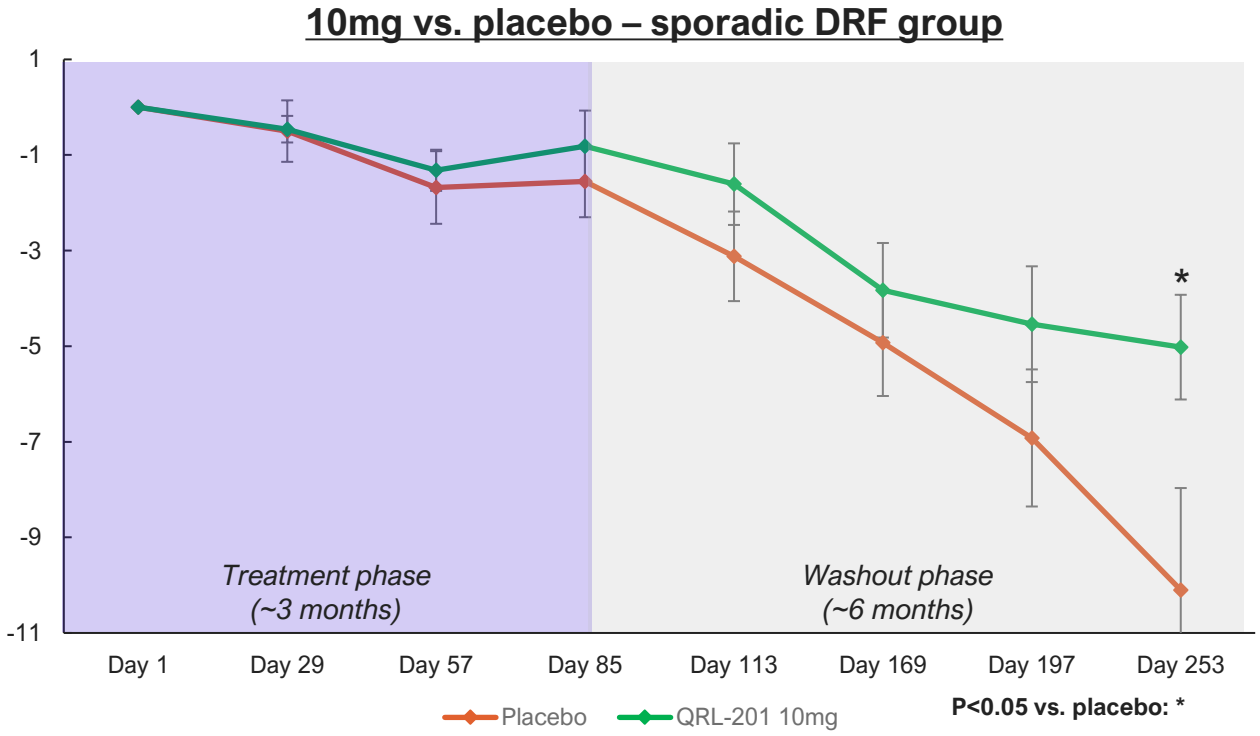


P<0.05 vs. placebo: *
P<0.10 vs. placebo: #

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

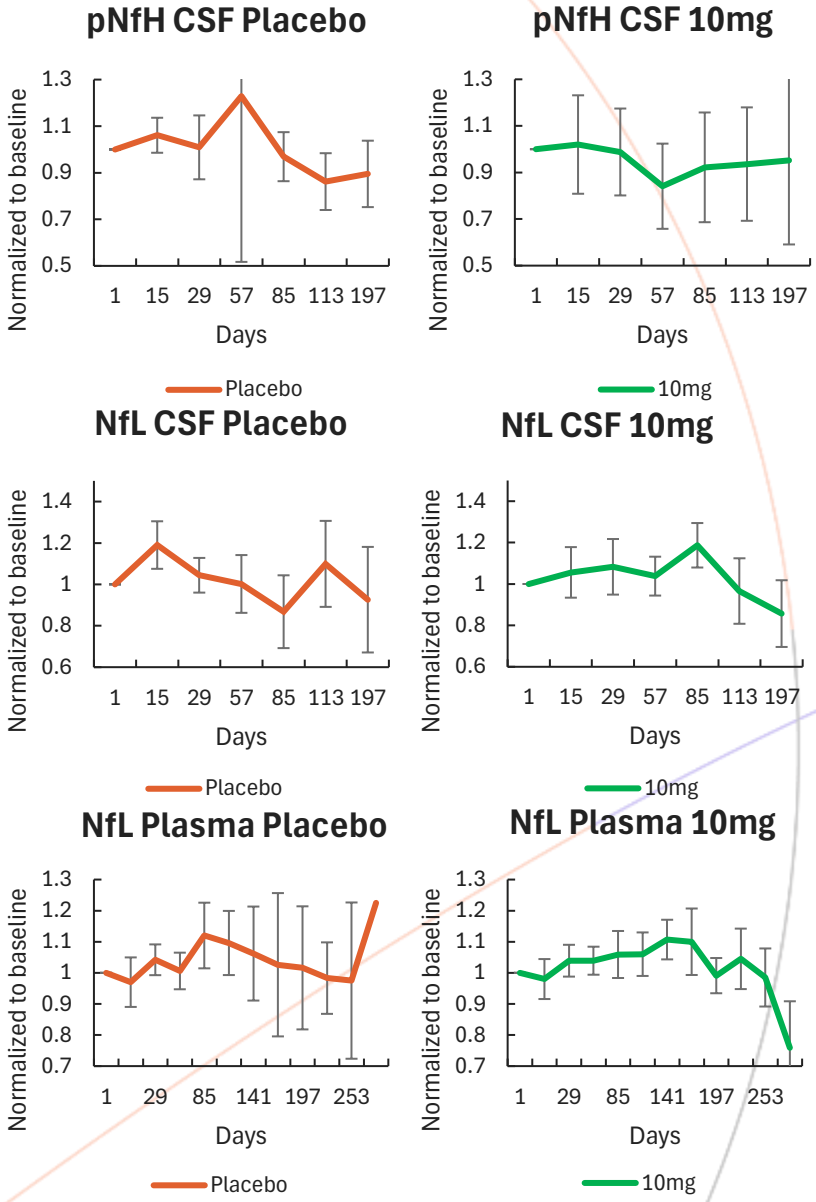
ALSFRS-R Total Score sporadic ALS: 10mg dose

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

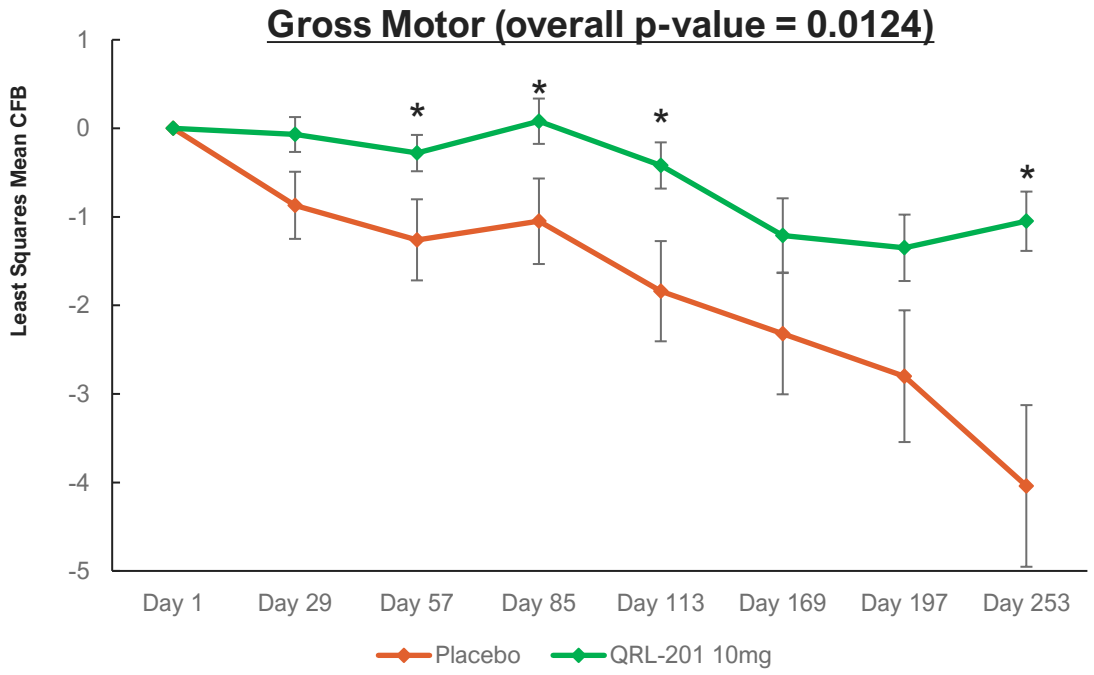
	10mg
Discontinuation (death, disease progression, other):	**7%**
Patients with improved functional score:	**14%**
Patients with 1 point decrease or less (stable):	**36%**

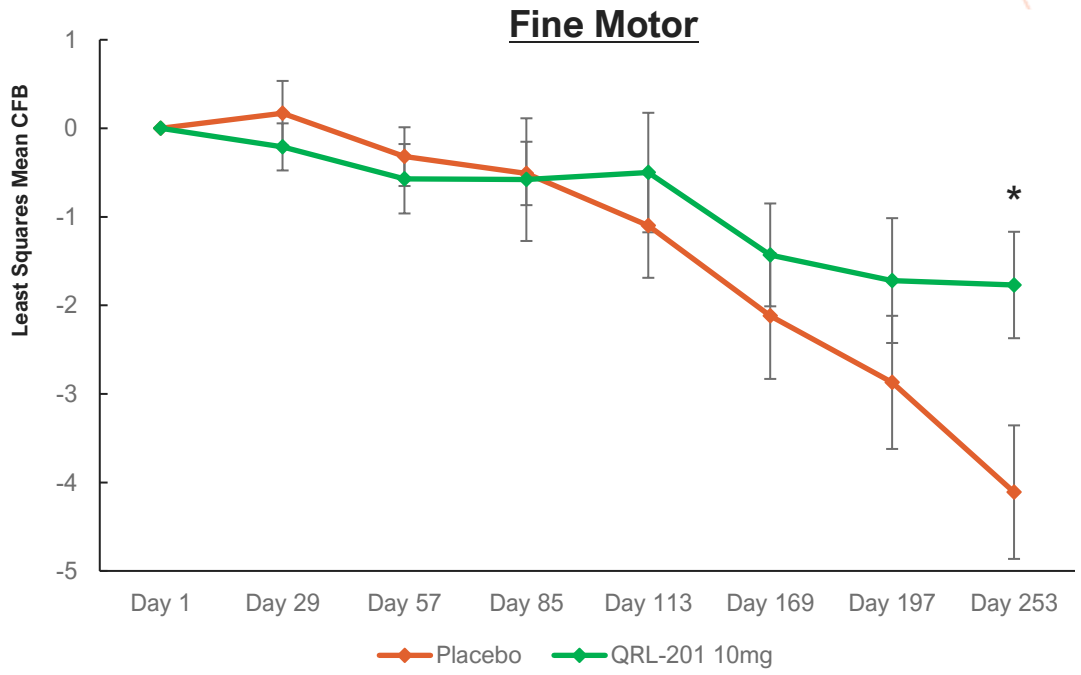


Note: Patients with 1 point decrease or less (stable) includes patients with improved functional score

ALSFRS-R Subscores sporadic ALS: 10mg dose

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





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

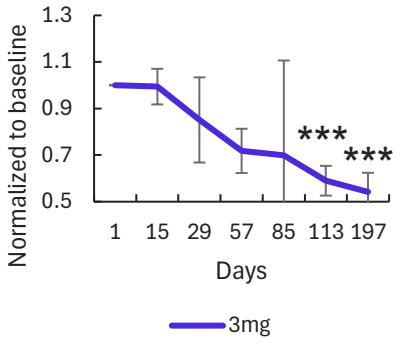
Minimal decline observed on bulbar and respiratory sub-scores in both treatment or placebo groups (≤1 point mean change over ~8.5 months) due to inclusion criteria focused on patients with Lower Motor Neuron onset disease

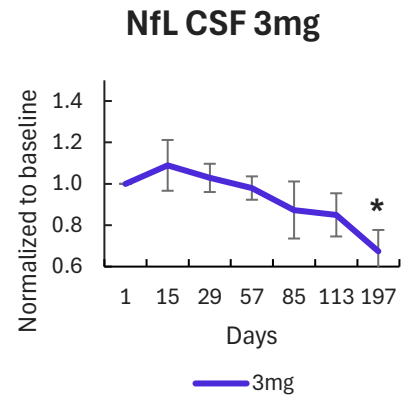
Neurofilaments Dynamics in Relationship to Dosing Frequency/ PK

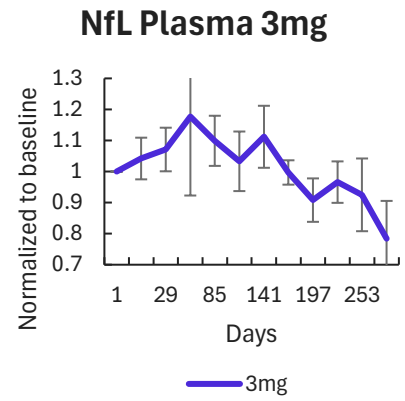
Neurofilament analysis shows significant decrease with 3mg dose

Decrease of 46% in pNFH (p<0.0001) and 33% NfL CSF (p<0.05) over 6 months with 3mg dose

Meaningful trend of 22% decrease in plasma NfL with 3mg dose after 11.5 months



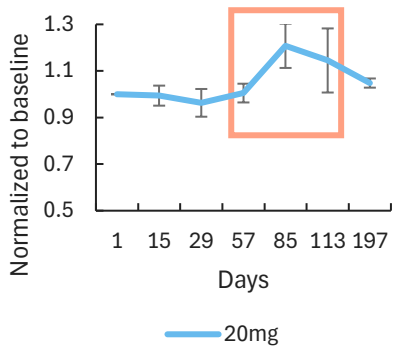


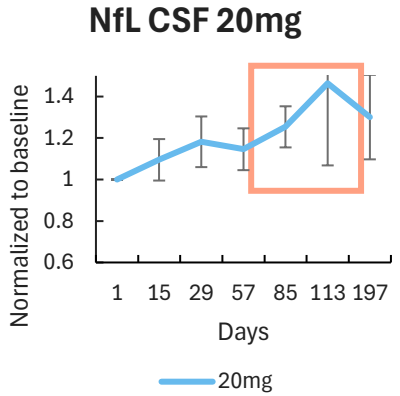


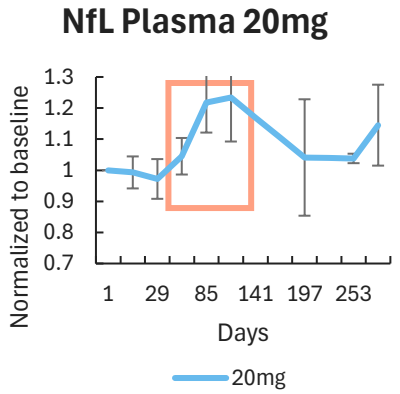
P<0.0001 vs. baseline: *
P<0.05 vs. baseline: *
All groups are Sporadic ALS, excluding MAD Cohort 1 (due to inclusion criteria differences)
NfL CSF 3mg: patient with injury excluded; p-value based on non-QCed post-hoc analysis (t-test)

Neurofilament analysis of 20mg dose suggests dosing frequency is too high

Increase of NfL and pNfH after 2-3 doses in 20mg dose group (between Day 57 and Day 113) suggest dosing frequency of 5 loading doses in 3 months is too high





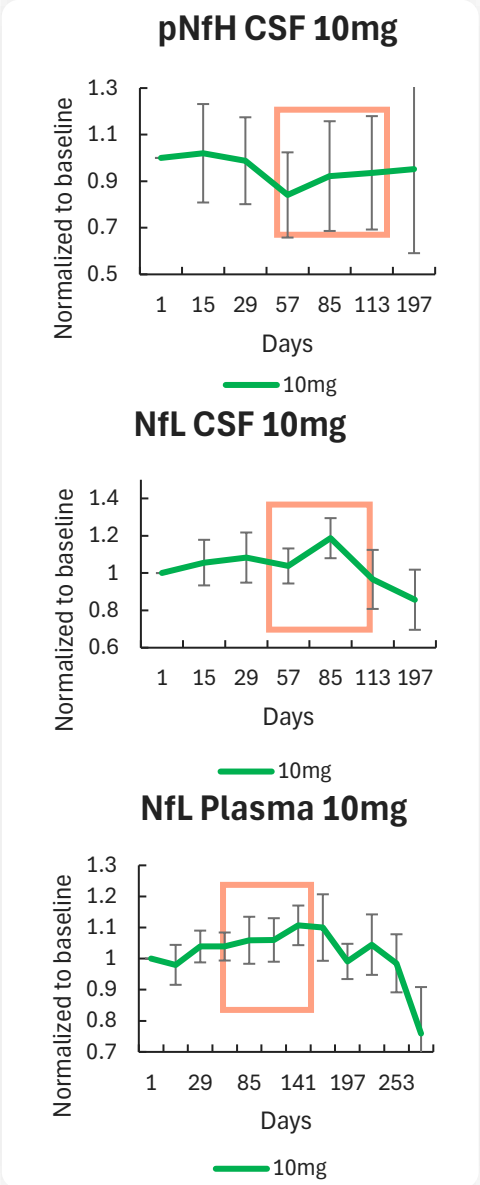


All groups are Sporadic ALS, excluding MAD Cohort 1 (due to inclusion criteria differences)

Neurofilament analysis of 10mg dose suggests initial dosing frequency may be too high, NfL decreases after dosing

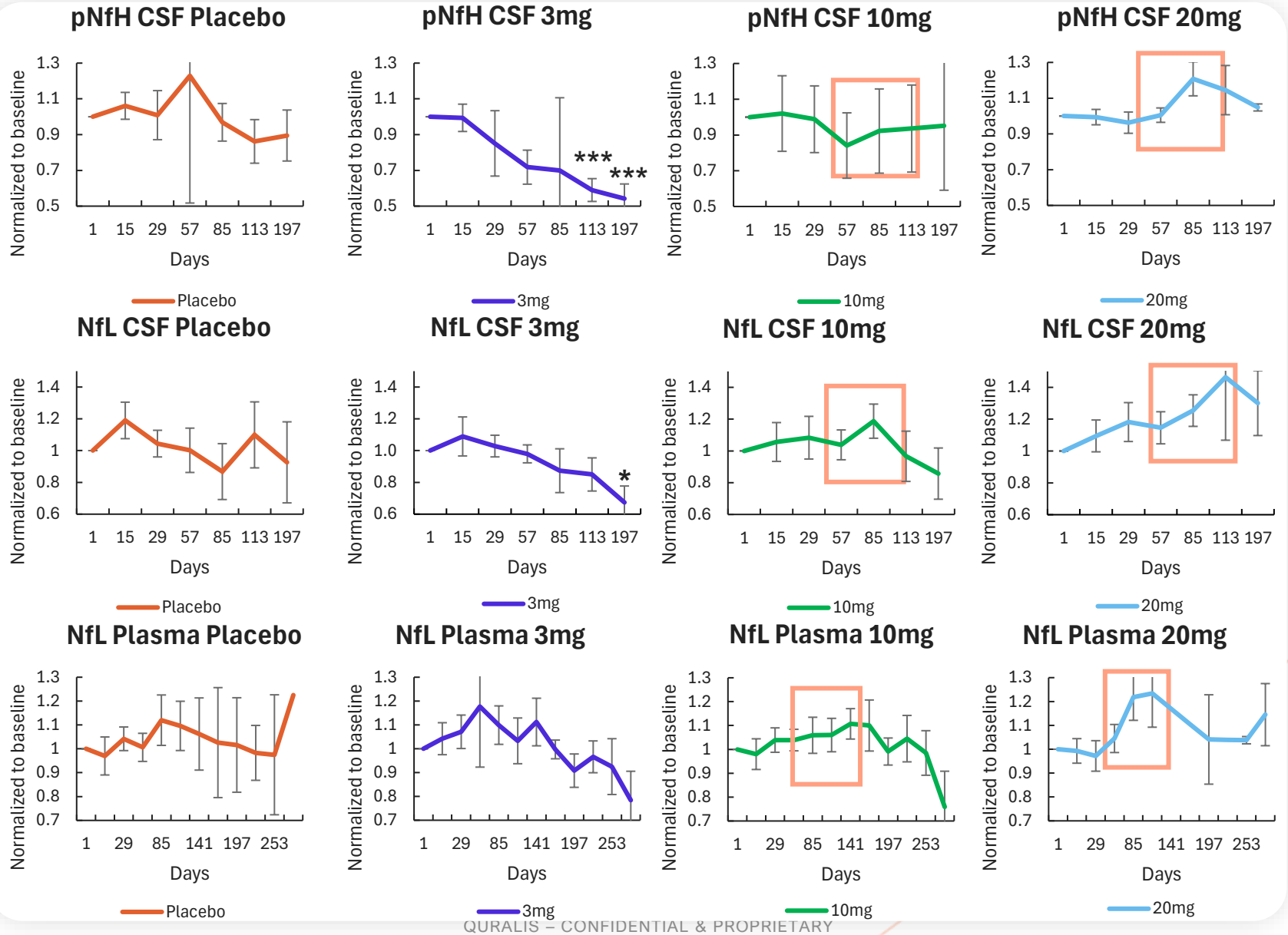
Stabilization of NfL and pNfH after 2-3 doses in 10mg dose groups (between Day 57 and Day 113) suggest dosing frequency of 5 doses in 3 months is too high

Trend of NfL decrease after dosing loading phase



All groups are Sporadic ALS, excluding MAD Cohort 1 (due to inclusion criteria differences)

The neurofilament data suggests that the optimal loading frequency is different for the 3mg, 10mg and 20mg groups



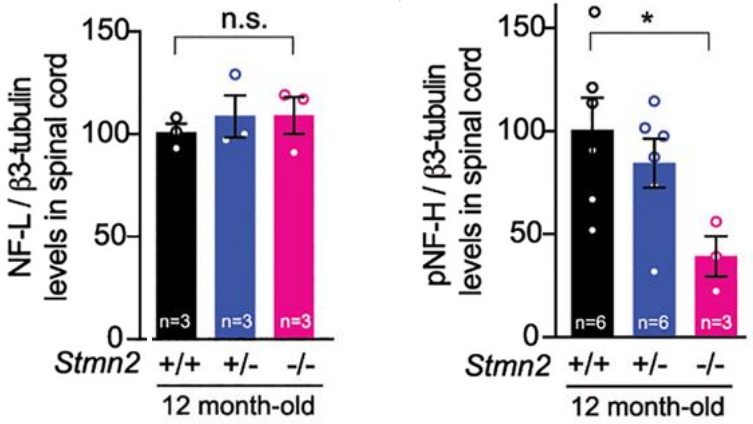
P<0.0001 vs. baseline: *
P<0.05 vs. baseline: *

All groups are Sporadic ALS, excluding MAD Cohort 1 (due to inclusion criteria differences)
NfL CSF 3mg: patient with injury excluded; p-value based on non-QCed post-hoc analysis (t-test)

In mice STMN2 loss decreases pNfH but not NfL levels QRL-201 restores pNfH neurites

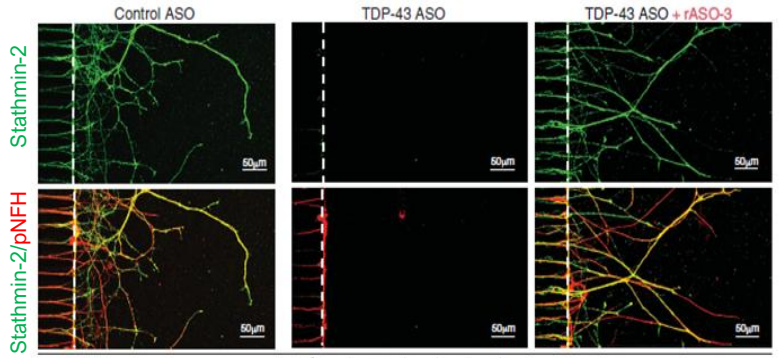
Increases in *intracellular* pNfH corresponds to decrease in *extracellular* pNfH (what was measured in ANQUR); while NfL levels were not impacted

STMN2 loss in mice leads to decreased intra-neuronal pNfH



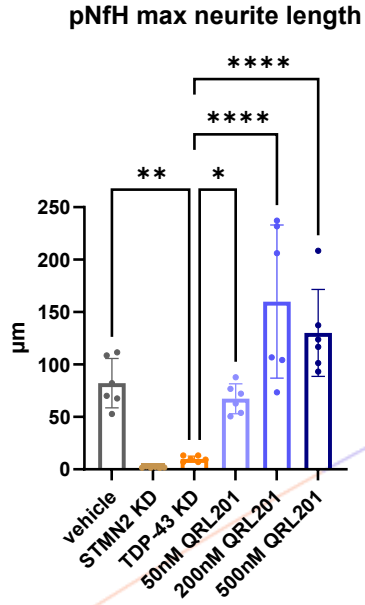
- pNfH, but not NfL, is regulated by STMN2 expression

pNfH axons require STMN2 for regeneration



- Correction of STMN2 splicing restores pNfH quantity through regeneration*
- Figure above conducted with tool ASO by Cleveland et al

QRL-201 restores pNfH neurite outgrowth in human motor neurons



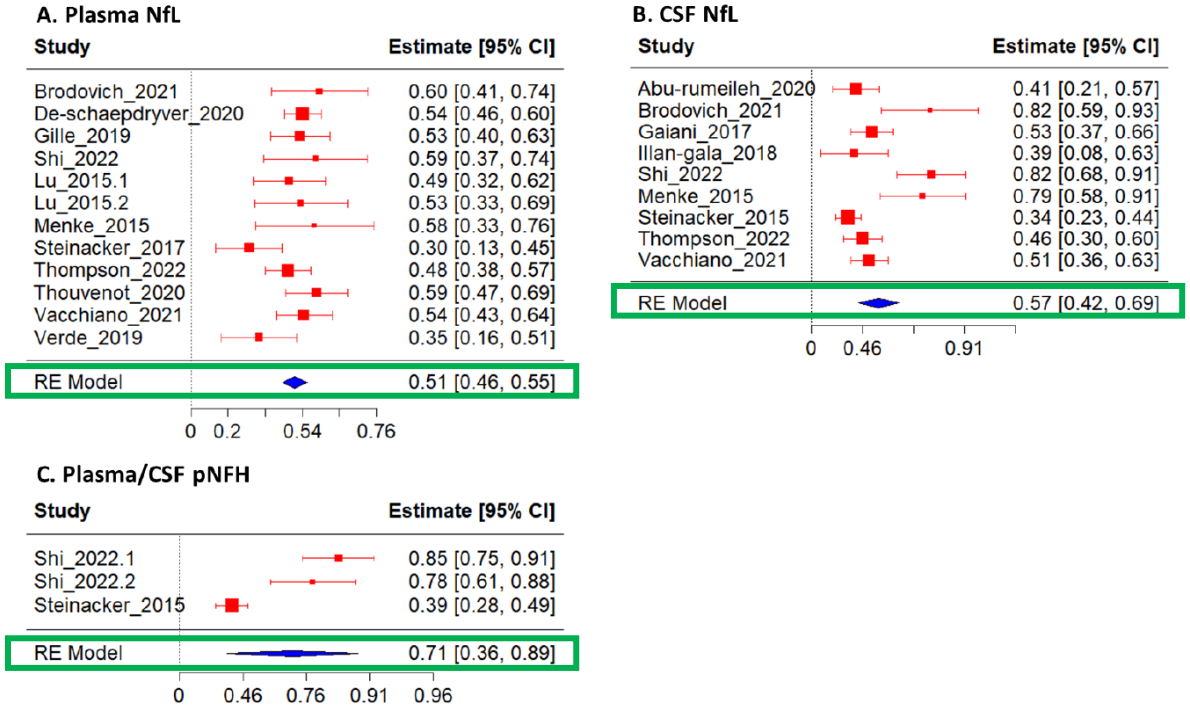
- QRL-201 increases pNfH neurite length

Lopez-Erauskin et al., 2023; Baughn et al., 2023; QurAlis internal data

Predictive value of neurofilaments in ALS disease progression

pNfH predictive value in FDA meta-analysis suggests strong correlation to ALS disease progression slope, however this effect was observed less robustly in SOD1 ALS (Qalsody/Tofersen VALOR study)

Correlation Coefficients for the Relationship Between ALS Disease Progression Slope and Neurofilaments



Source: Reviewer's analysis
Abbreviations: CI, confidence interval; CSF, cerebrospinal fluid; RE, random effect; NfL, neurofilament light chain; pNfH, phosphorylated neurofilament heavy chain

Correlation Between SOD-1 ALS Disease Progression Slope and Neurofilaments in VALOR Results (SOD-1 ALS)

Baseline Characteristic	Pearson Correlation Coefficients
Baseline NfL (pg/mL)	-0.65
NfL change (pg/mL)	-0.30
NfL change (%)	-0.10
NfL ratio to baseline	-0.10
NfL-time slope	-0.22
Log NfL (pg/mL)	-0.57
Log daily area under NfL-time curve (pg/mL)	-0.60
Log linear-model-estimated area under NfL-time curve until Week 28 (pg.day/mL)	-0.60
Baseline NfH (pg/mL)	-0.36
NfH change (pg/mL)	-0.18
NfH change (%)	0.03
NfH ratio to baseline	0.03
NfH-time slope	-0.17

Baseline Characteristic	Pearson Correlation Coefficients
Log NfH (pg/mL)	-0.36
Log daily area under NfH-time curve (pg/mL)	-0.42
Log linear-model-estimated area under NfH-time curve until Week 28 (pg.day/mL)	-0.40

Management Commentary

- Based on meta-analysis of ALS publications, pNfH is predictive of ALS disease progression slope, potentially with higher correlation than NfL
- Results of Qalsody/tofersen VALOR study suggests NfL effect observed is consistent with literature but pNfH may be a less important predictor of disease progression in SOD-1 ALS

Source: Qalsody (tofersen) FDA NDA review

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 ≥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

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

Thank you

For more information contact:
Kasper Roet (CEO & Cofounder)
kasper.roet@quralis.com

TARGET ALS