

Qura^{li}s™

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

September 2025

Driving scientific breakthroughs into powerful precision medicines

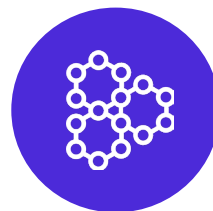


Groundbreaking science

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

Targeting **RNA restoration** in validated genetic disease resulting from **mis-splicing targets** in neurodegeneration and beyond

Proprietary FlexASO® platform can potential expand to additional RNA restoration therapies



First & best-in-class programs

Multiple programs in the clinic with near-term data readouts

Three first-in-class programs for sporadic ALS **on novel genetic targets**

Utilizing **biomarkers** for patient selection, target engagement, and efficacy



World-class team to execute

Experienced executive team

UNC13A partnership with Lilly underscores value of FlexASO® platform

\$143.5M equity raised, in addition to Lilly partnership upfront

QurAlis' expertise and technologies enable two distinct franchises

Pursuing treatment for CNS disorders with innovative biology and proven modalities

Ion Channel Recovery

(small molecule)

- Neurological disorders often result from ion channel dysfunction
- Kv7.2/7.3 potassium channel is a drug target for >10 high unmet need indications, multiple indications with clinical validation, including:
 - Epilepsy
 - Pain
 - >50% of ALS
 - Mood disorders
- QRL-101, a highly selective Kv7.2/7.3 opener, is well positioned as potential best-in-class therapeutic:
 - High selectivity, lack of off-target engagement controls AE rates
 - Formulations optimized for different indications

RNA Restoration

(antisense oligonucleotide, "ASO")

- Potential to develop first-in-class and best-in-class medicines through FlexASO® platform
 - One active ASO candidate currently in clinical trials (QRL-201) and one in IND-enabling studies (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 reproducible path to IND and Proof of Concept (PoC)

Advancing precision neuroscience pipeline across multiple clinical and preclinical programs

Program	MOA	Indication	Upcoming Milestone(s)	Discovery	IND-Enabling	Ph1 Safety / PoM ²	Proof of Concept	Registration Studies	Partner
QRL-201	STMN2	ALS	ANQUR readout H1 2026						
QRL-101	Kv7.2/3	Rare Epilepsy / DEE	Proof of Concept initiation H1 2026 ¹						
		Pain	PainCart® study topline H1 2026						
		ALS	Patient PoM ² study topline Q4 2025						
QRL-204	UNC13A	ALS / FTD	IND-enabling studies ongoing ³						
QRL-TBA	FMR1	Fragile X	DC ⁴ nomination 2026						
QRL-TBA	Undis.	PSP	DC ⁴ nomination 2026						

Lilly

1. Pending Series C funding 2. PoM = Proof of Mechanism; 3. In partnership with Lilly; 4. DC = development candidate

Pioneers with unrelenting commitment to patients



Kasper Roet,
PhD
CEO
Co-founder



Emma Bowden,
PhD
Head of
Development



Jason Brown,
MBA
CFO & COO



Hagen Cramer,
PhD
CTO



Dan Elbaum,
PhD
CSO



Vikas Sharma,
PhD
CBO



Robin Wojcieszek,
RPh
Head of
Regulatory Affairs
& Drug Safety



Supported and recognized by investors, pharma, and industry



Investors



EQT
Life Sciences

sanofi ventures



DROIA ventures



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 15
2020 WINNER



THE
TERMEER
FOUNDATION



Collaborators



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



UMass Chan
MEDICAL SCHOOL

Fragile X

RNA Restoration: STMN-2 Program

QRL-201: STMN2-targeting ASO leads RNA restoration franchise

STMN2 is the most consistently downregulated gene in sporadic ALS patients

- Restoration of STMN2 pre-mRNA mis-splicing through ASO treatment restores neuronal processes, Golgi outposts, and protects neuronal activity in human motor neurons with TDP-43 pathology
- Genetic target in sporadic ALS (90% of patients) and FTD (50% of patients) as well as Alzheimer's disease (~33% of patients)
- Two approved ASO therapies for motor neuron diseases (Spinraza® for SMA and Qalsody® for ALS) demonstrate that an ASO therapy strategy to restore STMN2 in ALS patients is technologically feasible



- QurAlis is developing QRL-201, a highly potent splice-switching ASO targeting STMN2
- ANQUR study expanded to dose range-finding portion (at two dose levels) which is fully-enrolled with favorable safety and tolerability profile to date
 - Multiple biomarkers being assessment to support future development strategy
- QurAlis retains full global rights; CoM patent through 2039 plus potential PTE, pending issuance

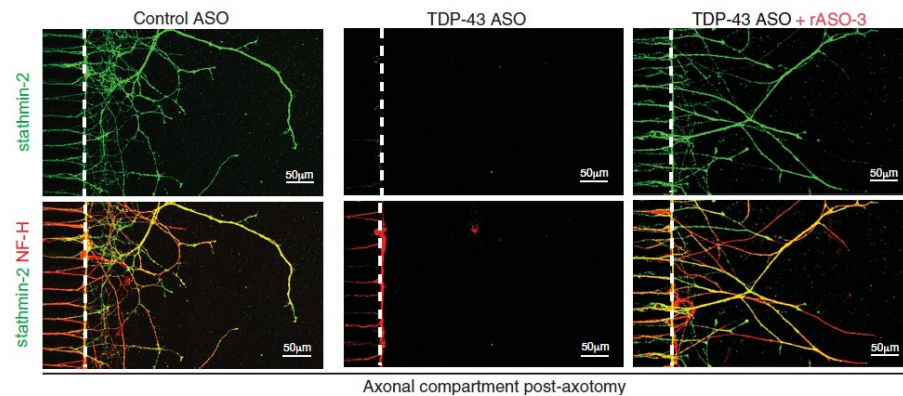
Restoration of STMN2 levels by ASO is a promising therapeutic strategy for the majority of ALS patients

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

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

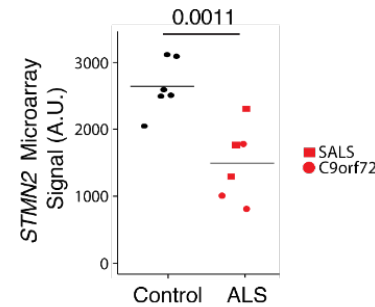
Loss of TDP-43 from the nucleus (ALS hallmark) leads to loss of STMN2

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

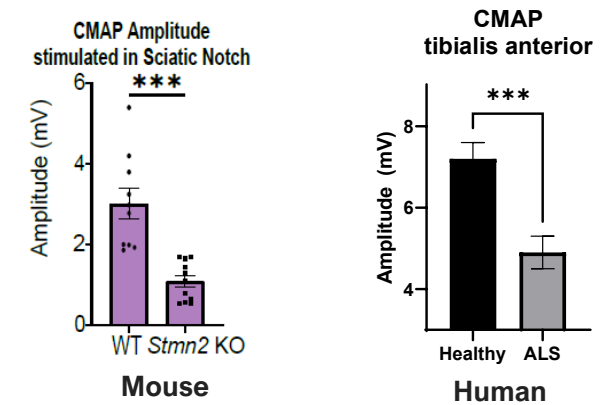


STMN2 is downregulated in ALS patients

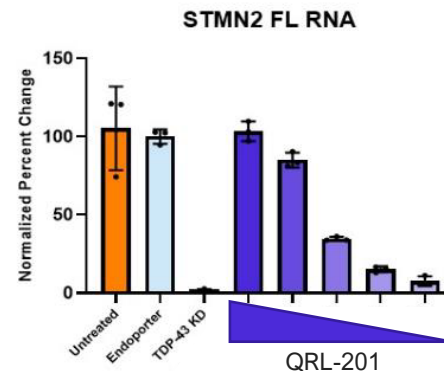
Highley et al 2014 Microarray Laser Capture Motor neuron



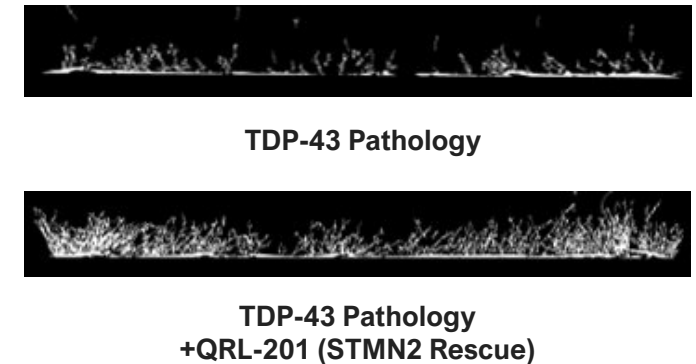
Loss of STMN2 leads to denervation of muscles as measured by CMAP Amplitude



QRL-201 restores STMN2



QRL-201 restores neuronal processes



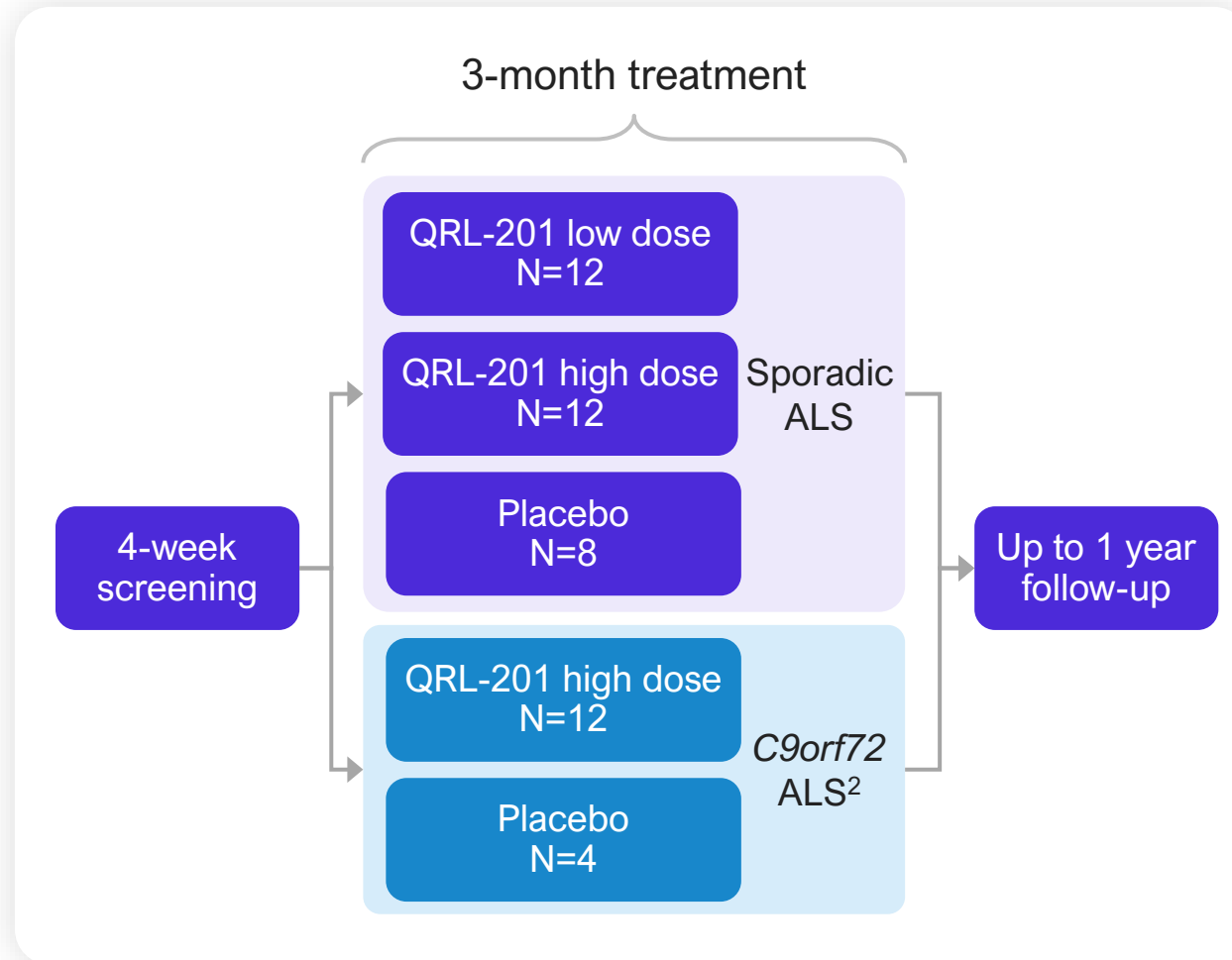
1. Melamed Z, López-Erauskin J, Baughn MW, et al. Premature polyadenylation-mediated loss of stathmin-2 is a hallmark of TDP-43-dependent neurodegeneration. *Nat Neurosci*. 2019;22(2):180-190. doi:10.1038/s41593-018-0293-z
2. Klim, J.R., Williams, L.A., Limone, F. et al. ALS-implicated protein TDP-43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

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

Enrollment complete, interim data¹ expected H1 2026

QRL-201

AnQur



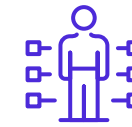
Design

Randomized, double-blind, placebo-controlled



Population

32 sporadic ALS patients
16 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

1°: Safety & tolerability
2°: Efficacy & biomarker panel

¹ Exact interim data cut to be finalized

² C9orf72 patients are a homogenous population with consistently decreased STMN2 levels

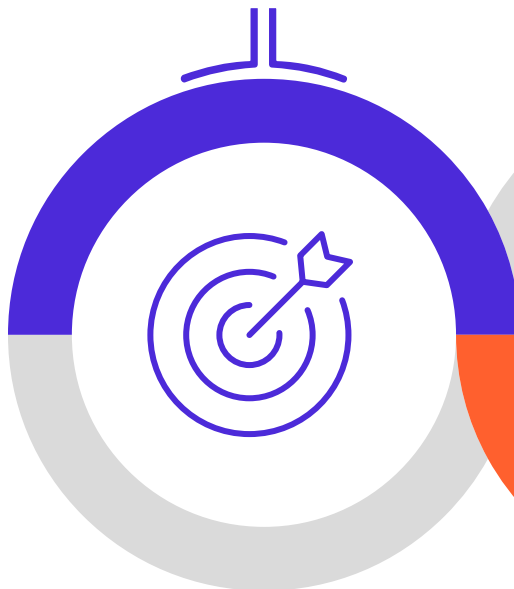
Combination of clinical readouts and extensive biomarker analysis to inform optimal registrational studies

QRL-201

AnQur

Target engagement

- STMN2 levels



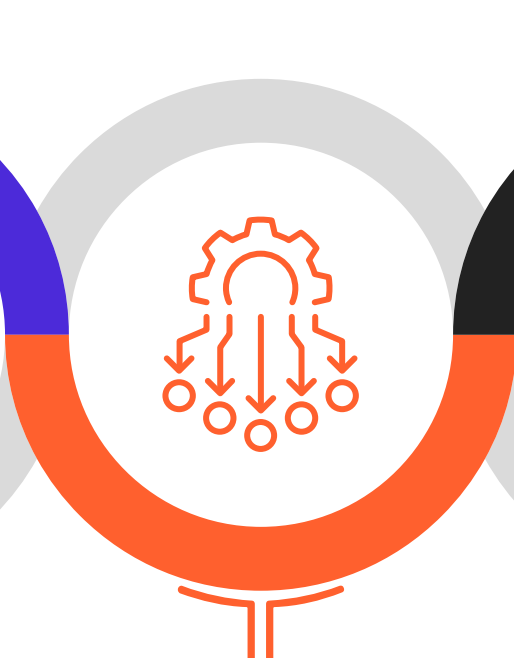
Biomarkers of neuronal loss

- NfL and other exploratory biomarkers



Mechanism of action (MOA)

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



Clinical measurements

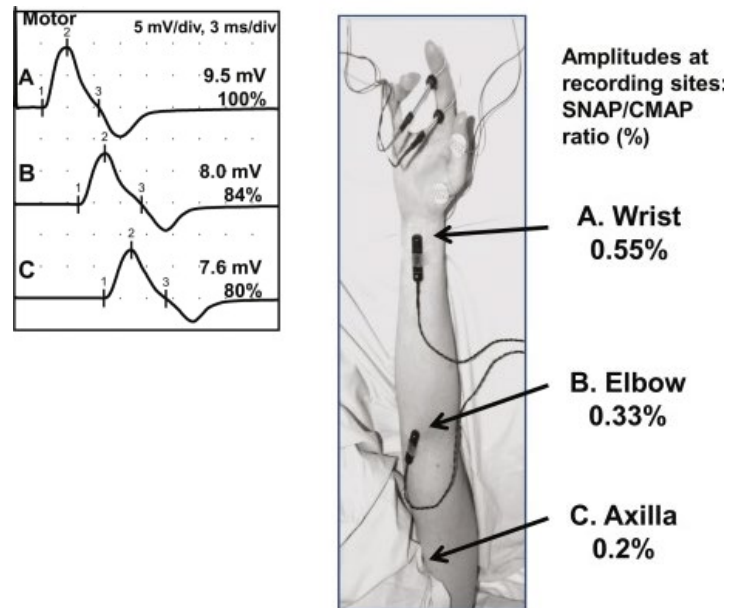
- ALSFRS-R, ROADS, SVC, HHD
- Ventilation assistance-free survival
- Time-to-event measures



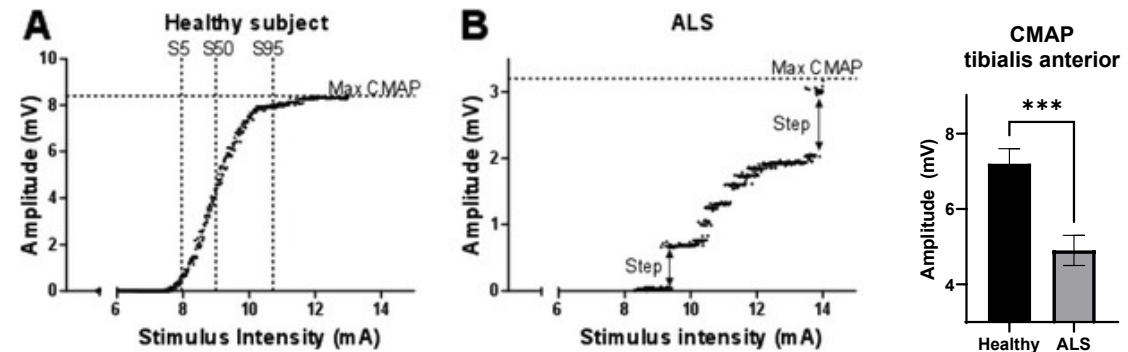
CMAP is a powerful disease progression and efficacy biomarker that measures muscle innervation in ALS

QRL-201

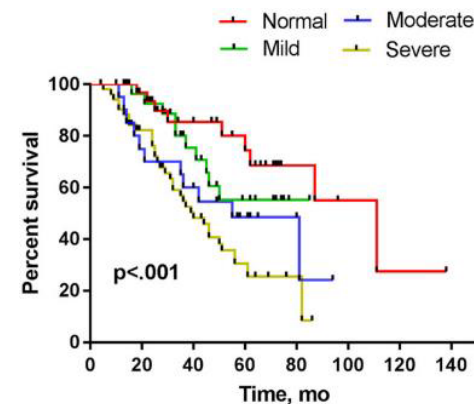
CMAP amplitude measures signal strength from nerve to muscle: number of innervating fibers



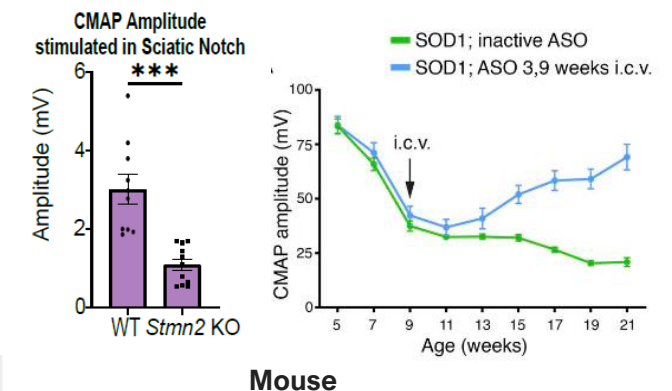
CMAP is used to monitor disease progression in ALS patients



CMAP amplitude predicts survival in ALS



CMAP amplitude can show therapeutic effect of ASO

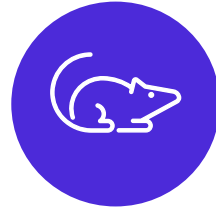


1. Clarissa Crone, Christian Krarup, in *Handbook of Clinical Neurology*, 2013
2. Maathuis et al., 2013 *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, 2013; 14: 217–223
3. Yu et al., 2021 *Front Neurol*. 2021 Feb 11;12:574919. doi: 10.3389/fneur.2021.574919
4. McCampbell et al., 2018 *J Clin Invest*. 2018;128(8):3558–3567. <https://doi.org/10.1172/JCI99081>.
5. Krus et al., 2022 *Cell Rep* Jun 28;39(13):111001. doi: 10.1016/j.celrep.2022.111001

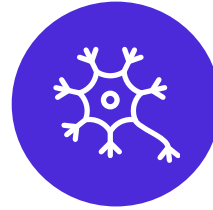
QRL-201 key take-aways



STMN2 is the most consistently observed mis-spliced protein in sporadic ALS leading to loss of function



Downregulation and loss of STMN2 alone in mice leads to loss of muscle innervation, motor neuron axonopathy and muscle atrophy, all hallmarks of ALS



QRL-201 restores STMN2 levels in human ALS motor neurons



Preliminary cohorts in the ANQR study demonstrate that QRL-201 can be well tolerated in ALS patients at exposures far above the predicted minimally efficacious exposure



A dose range-finding study for QRL-201 is currently active in six countries with biomarkers that can measure efficacy in ALS patients

ANQR study is fully enrolled with interim efficacy marker & safety data expected H1 2026
Next Ph2 / Ph3 study is a potential registrational study

Ion Channel Recovery

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 studied in multiple indications including pain, seizure, and mood disorders and marketed for partial-onset seizures before being withdrawn (2017) for undesirable side effect profile, limiting commercial potential
- Further validation of Kv7.2/3 in epilepsy has been demonstrated by XEN1101 and other clinical programs
- Kv7.2/7.3 compound flupirtine was also approved in Europe for 6 different pain indications



- QurAlis is developing QRL-101, 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 ALS, epilepsy, and pain

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

Proof of mechanism in healthy volunteers (QRL-101-05)

Evidence of both central & peripheral target engagement

- **mNETT (Threshold Tracking) (ALS / Pain)**

- Several measures were significantly altered by QRL-101 demonstrating inhibitory effects on peripheral nerve excitability
- SDTC, Rheobase, and several other measures appeared to have a dose dependent response

- **Passive EEG (Epilepsy)**

- Clear central activation/brain penetration with several EEG measures impacted
- Little to no activation of the slow wave frequency (delta and theta) associated with sedation and GABA-A activation

- **TMS-EMG & TMS-EEG (ALS / Epilepsy)**

- ICF TMS-EMG had statistically significant change with QRL-101 treatment
- Statistically significant changes to TMS Evoked Potential (TEP)

- **Safety & tolerability**

- Adverse event (AE) profile consistent with prior studies of QRL-101, no serious AEs or discontinuations due to AEs
- No clinically meaningful signal of somnolence or persistent dizziness has been observed in any study of QRL-101 to date
- Formulation work has resulted in lower cMax, while maintaining AUC, to alleviate GI AEs seen with liquid formulation

CONTEXT

Inhibition of nerve excitability

Target engagement & brain penetration

No sedative effects

Effect inhibition/ excitability ratio

Target engagement & brain penetration

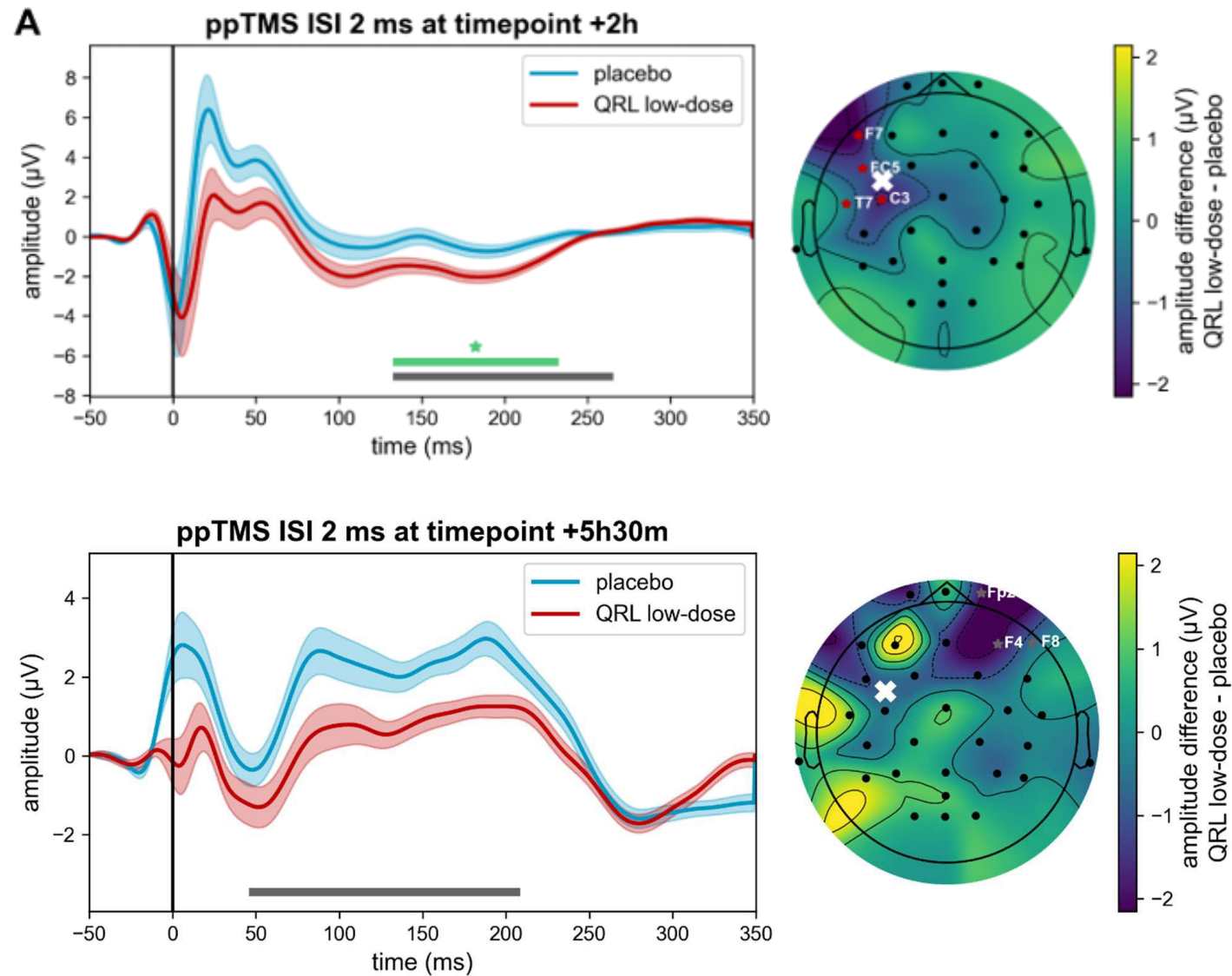
Summary of analysis results – strong biomarker readouts for epilepsy, pain, and ALS

Indication	PD measure	p-value treatment v. placebo	
		Low Dose	High Dose
Pain/ALS	Refractoriness at 2.5 ms (%)	<0.0001	<0.0001
Pain/ALS	Refractory period (ms)	0.0002	<0.0001
Pain/ALS	Superexcitability (%)	0.001	<0.0001
Pain/ALS	Superexcitability at 7 msec (%)	0.0016	<0.0001
Pain/ALS	Superexcitability at 5 msec (%)	0.0024	<0.0001
Pain/ALS	Strength-Duration Time Constant (ms) SDTC	0.0039	<0.0001
Pain/ALS	Hyperpolarizing I/V-slope	0.0057	<0.0001
Pain/ALS	Stimulus-Response\Slope	0.0128	0.0001
Pain/ALS	Subexcitability (%)	0.0091	0.0002
Pain/ALS	Accommodation Half-Time (ms)	0.03	0.0011
Pain/ALS	Refractoriness at 2 ms (%)	0.0001	0.0019
Pain/ALS	Rheobase (mAmp)	0.3858	0.0068
Pain/ALS	TEd40-60 (%)	0.3991	0.0221
Pain/ALS	Resting I/V-Slope	0.3635	0.0237
Pain/ALS	Motor Stimulus for 50% max response or Threshold Current (mAmp)	0.6093	0.0285
Epilepsy/ALS	TMS-EMG Intracortical Facilitation (ICF) at 15 ms (%)	0.0071	0.0486
Epilepsy	TMS-TEP 0-300ms	0.001	0.03
Epilepsy	TMS-TEP N100	0.02	0.002
Epilepsy	TMS-TEP P180	0.002	0.06
Epilepsy	EEG Beta-power Fz-Cz eyes closed (dB)	0.0318	0.0067
Epilepsy	EEG Gamma-power Pz-O2 eyes closed (dB)	0.0154	0.0083

p-value <0.05

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

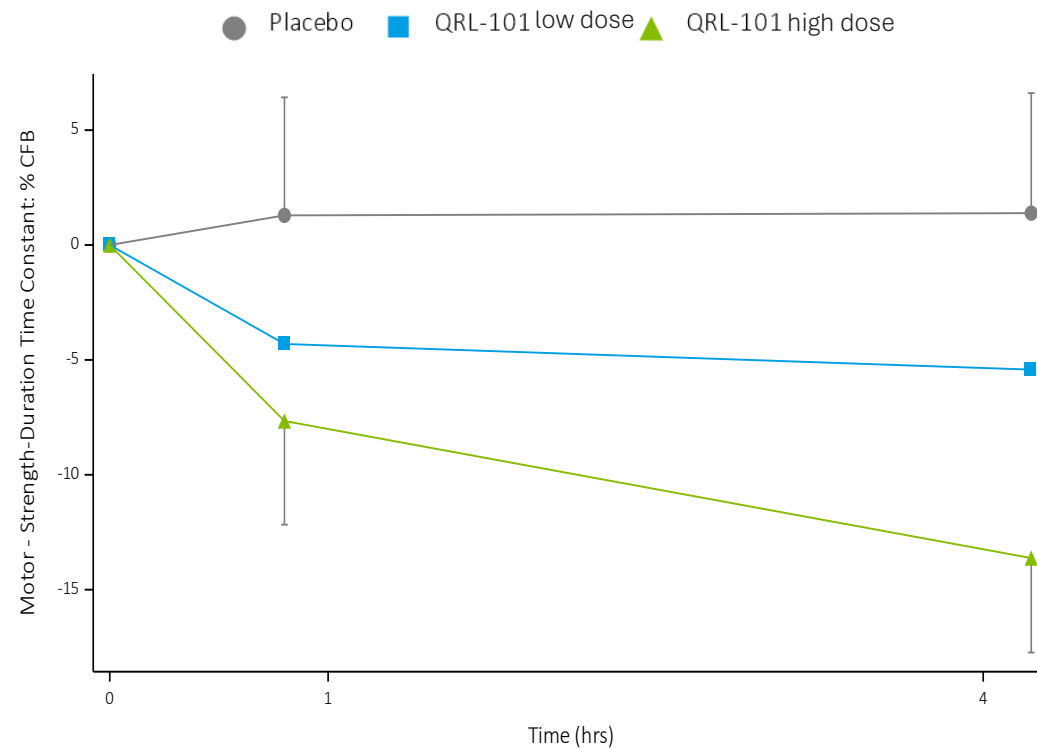
QRL-101



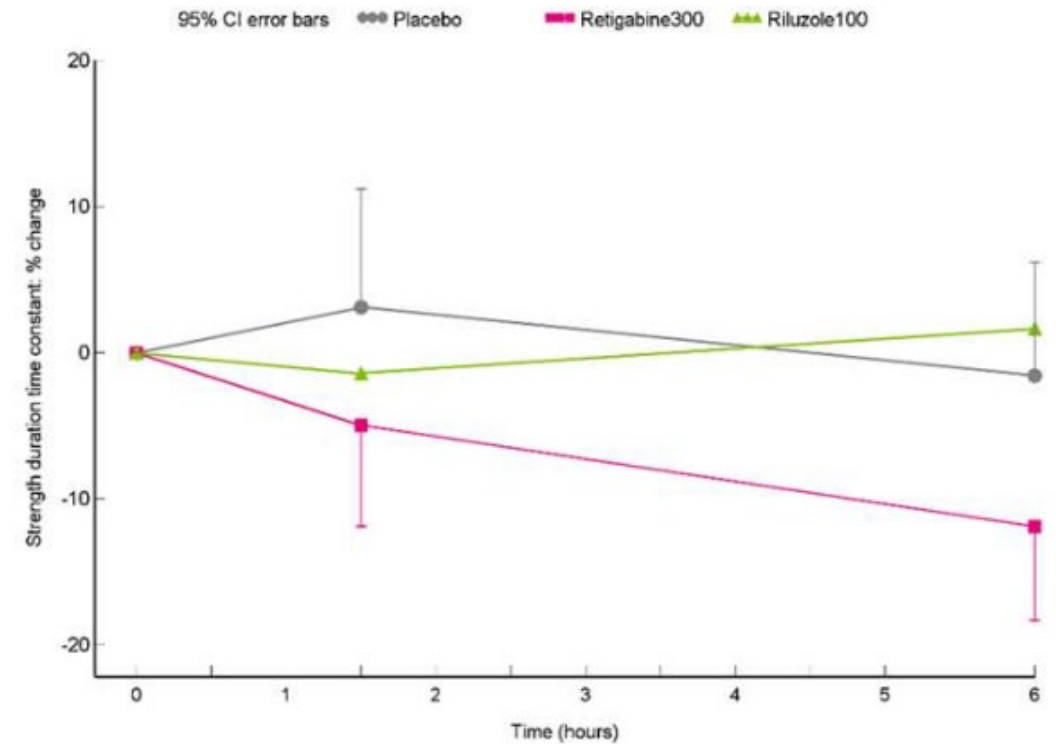
QRL-101 is ~50% more potent than retigabine/ezogabine on peripheral excitability biomarker SDTC in humans

QRL-101

Strength-Duration Time Constant (% CFB)



Strength-Duration Time Constant (% CFB)

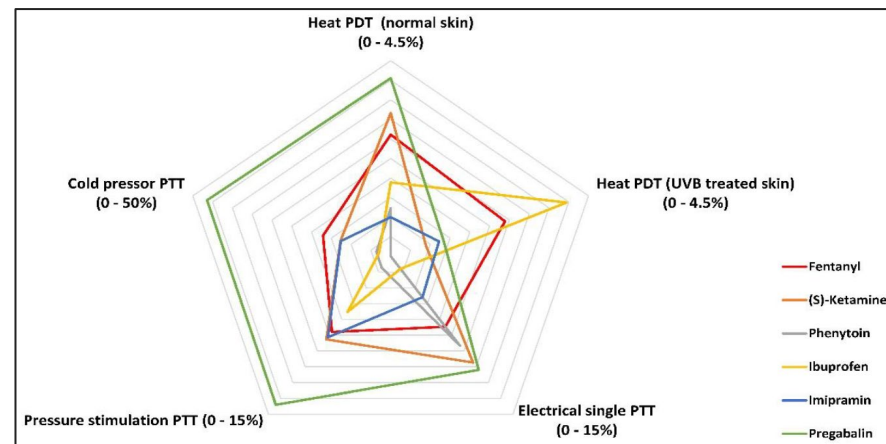


300mg retigabine is single dose, equivalent to 900mg total daily dose in POTIGA FDA label

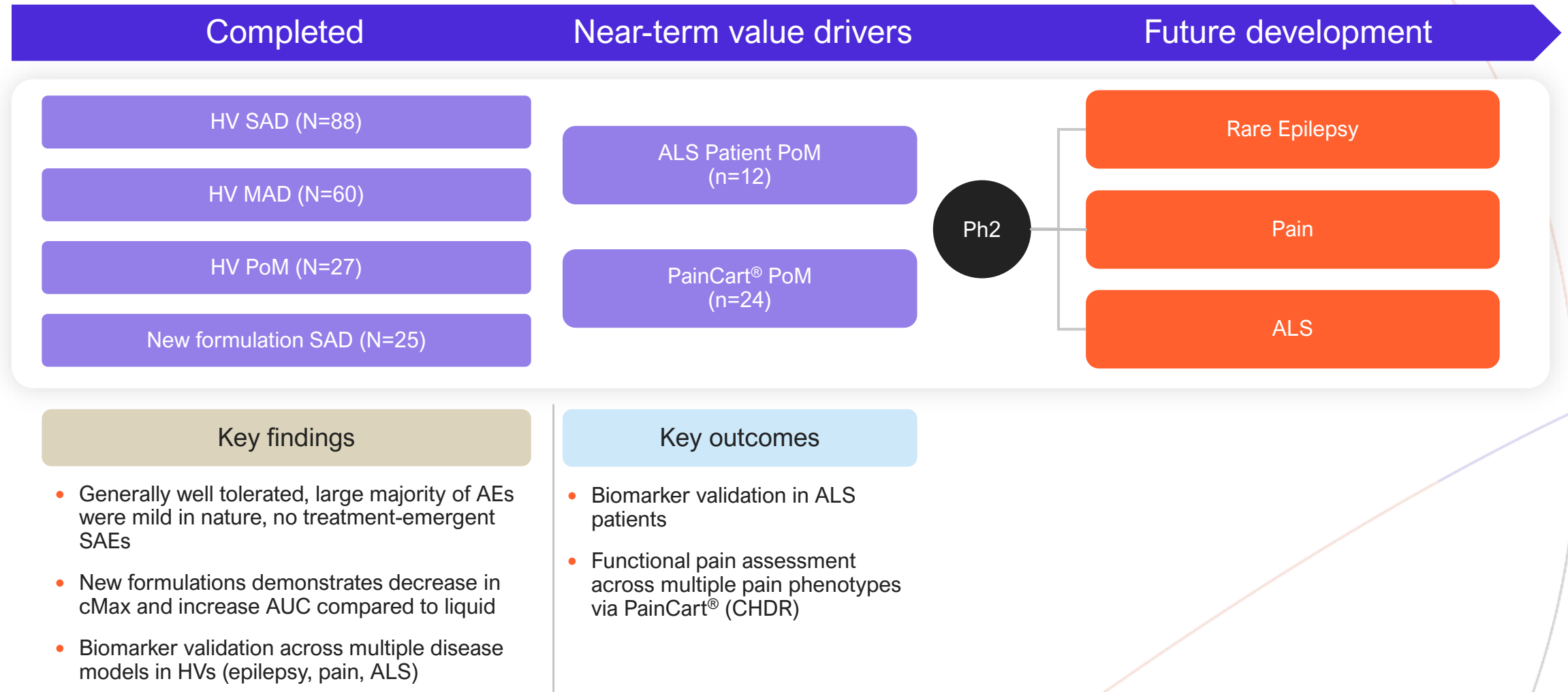
PainCart® Phase 1 study to assess analgesic effect of QRL-101 in healthy volunteers for PoC indication selection

Topline data expected H1 2026

- 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 new SDD formulation to further characterize PK / PD profile
- Outcome provides unique profile per analgesic which can be compared to standard of care / generics



Phase 1 data package supports advancement into epilepsy, pain, and ALS



SAD: Single Ascending Dose; MAD: Multiple Ascending Dose; PoM: Proof of Mechanism; PoC: Proof of Concept; PK/FE: Pharmacokinetics / Food Effect; HVs: Healthy Volunteers

RNA Restoration: FlexASO[®] Platform



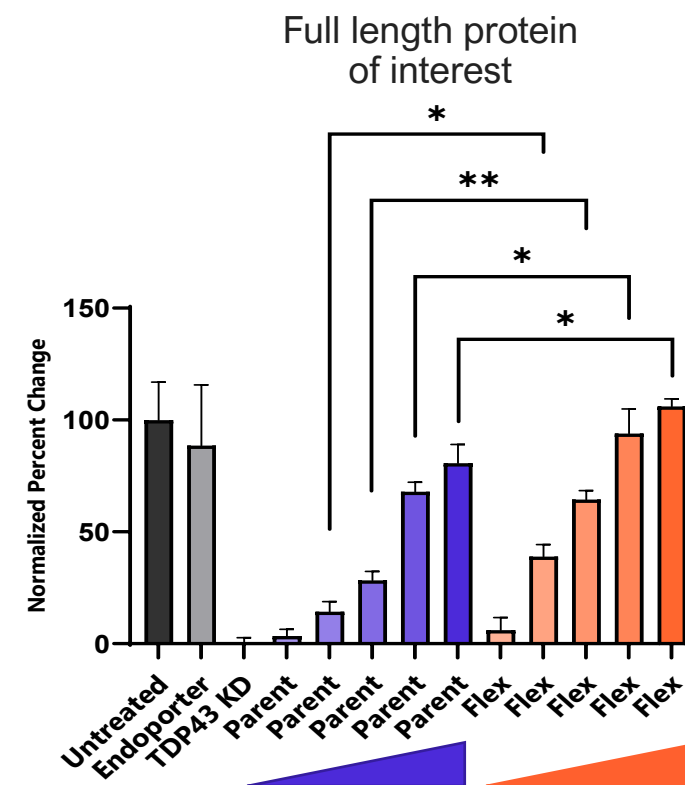
Flex ASO[®] is the leading splice-modulation platform to restore RNA

FlexASO[®] is a proprietary ASO splice-modulator platform that incorporates a unique backbone, providing advantages over traditional ASOs

Attributes	Flex ASO	Traditional ASO
Size	✓	✓
Therapeutic Effect	✓ ✓	✓
Toxicity	✓ ✓	✓
CMC	✓	✓
Distribution	✓ ✓	Known for spinal cord and frontal cortex

Potential to overcome modality-specific, dose-limiting toxicities

FlexASO[®] demonstrates statistically significant increase in RNA restoration vs. parent



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)



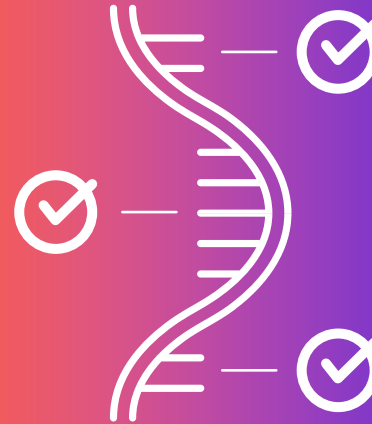
Diseases caused by haploinsufficiency (e.g., Dravet)



Previously undruggable targets for large indications



Disease-modifying RNA therapies



Driving scientific breakthroughs into powerful precision medicines

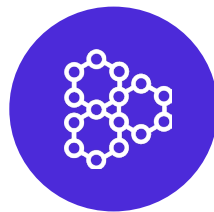


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QuralisTM

Thank you

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Advised by leading clinicians and scientists in neurodegeneration field

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DBE, MBBS, MD,
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FAAN, FANA, FAAS



Philip Van Damme
MD, PhD



Leonard van den Berg
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Amy Chappell
MD, FAAN



SAB



Clifford Woolf
MD, PhD



Kevin Eggan
PhD



Matthew Kiernan
MD, PhD



Bernhardt Trout
PhD



Brian Wainger
MD, PhD



Christopher Shaw
MD, PhD



Sudhir Agrawal
PhD



Michelle Hastings
PhD

