Quralis™

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

January 2026

Driving scientific breakthroughs into powerful precision medicines

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

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

First & best-in-class programs

Multiple programs in the clinic with near-term data readouts

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

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

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

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)

Advancing precision neuroscience pipeline across multiple clinical and preclinical programs

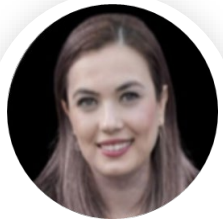
Program	MOA	Indication	Upcoming Milestone(s)	Discovery	IND-Enabling	Ph1 Safety / PoM[1]	Proof of Concept	Registration Studies
QRL-201	STMN2	ALS	ANQUR interim readout Q1 2026					
QRL-101	Kv7.2/7.3	DEEs	KCNQ2 PoC[2] initiation H2 2026					
		ALS	PoC planning under way					
		Pain	PoM[1] study initiation H2 2026[3]					
QRL-204	UNC13A	ALS / FTD	In partnership with Lilly					
QRL-TBA	FMR1	Fragile X	DC[4] nomination 2026					
QRL-TBA	Undis.	PSP	DC[4] nomination 2026					

1. PoM = Proof of Mechanism; 2. PoC = Proof of Concept; 3. Pending Series C funding; 4. DC = development candidate

Pioneers with unrelenting commitment to patients

Kasper Roet, PhD
CEO
Co-founder

HARVARD MEDICAL SCHOOL
Johnson & Johnson



Guzide Adhikari, PhD
SVP CMC Operations & Strategy

TranslateBIO
Takeda
Shire

Jason Brown, MBA
CFO & COO

KARUNA THERAPEUTICS
PURETECH GIVING LIFE TO SCIENCE
NOVARTIS

Hagen Cramer, PhD
CTO

Avecia
Girindus Solvay Organics
Ridgeway Biosystems Inc.
WAVE LIFE SCIENCES

Dan Elbaum, PhD
CSO

Retrophin
Pfizer
AMGEN
CRITICAL Therapeutics
FoldRx
VERTEX
Ra Pharma

Manoj Malhotra MD
CMO

abbvie
Ovid Therapeutics
Eisai
Mallinckrodt Pharmaceuticals
Takeda
NOVARTIS
Cleveland Clinic

Vikas Sharma, PhD
CBO

bioxcel therapeutics
MACROGENICS
AstraZeneca
MedImmune
rexahn PHARMACEUTICALS
CH

Robin Wojcieszek, RPh
SVP Regulatory Affairs & Drug Safety

Lilly
FibroGen
Pfizer
Lundbeck
FDA

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 WINNER
THE TERMEER FOUNDATION

Collaborators

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

UMass Chan MEDICAL SCHOOL
Fragile X

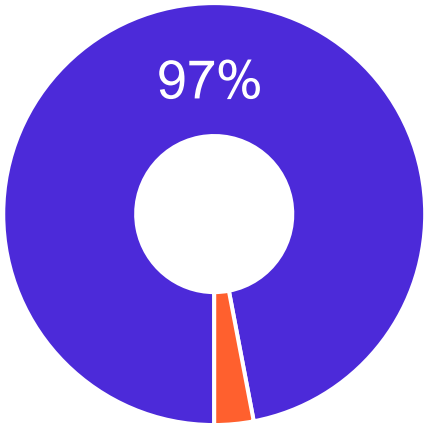
RNA Restoration: STMN-2 Program

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

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

STMN2 is the most consistently downregulated gene in sporadic ALS patients

- 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
- Two approved ASO therapies for motor neuron diseases (Spinraza® for SMA and Qalsody® for SOD-1 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 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 2040 plus potential PTE, pending issuance

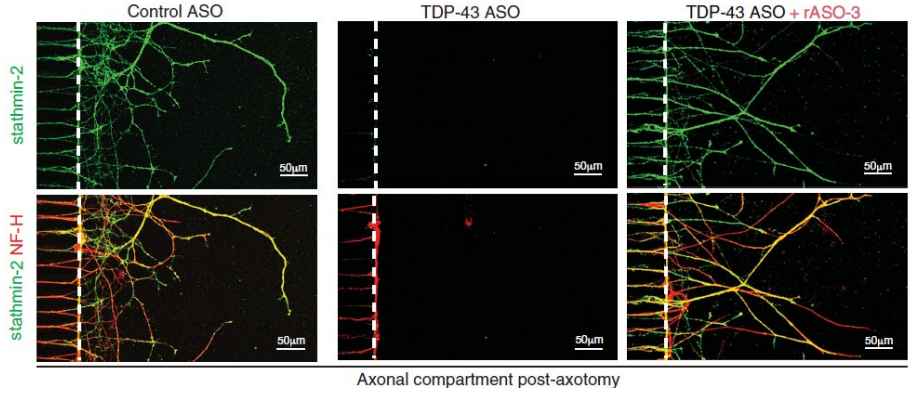
Restoration of STMN2 levels by ASO is a promising therapeutic strategy for the majority of ALS patients

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

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

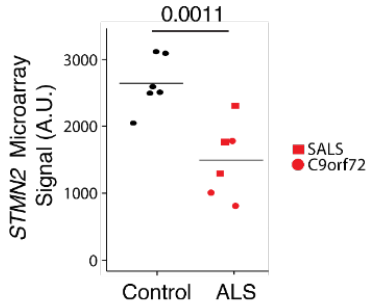
Loss of TDP-43 from the nucleus (ALS hallmark) leads to loss of STMN2

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

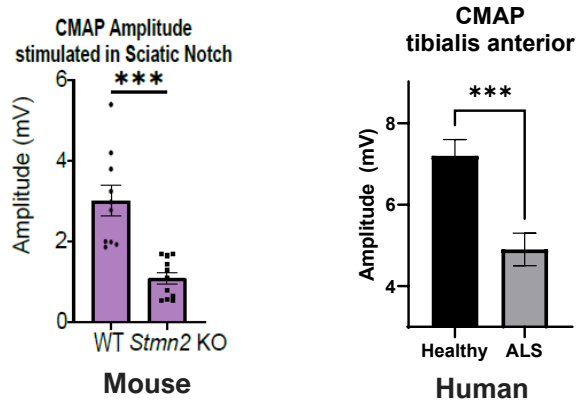


STMN2 is downregulated in ALS patients

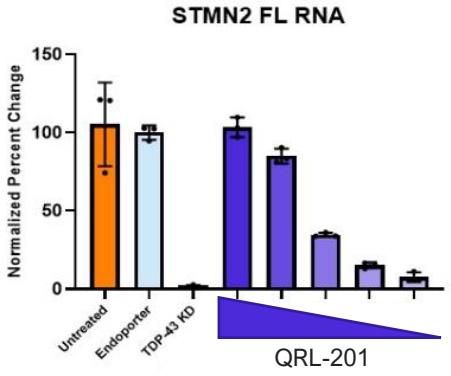
Microarray Laser Capture Motor neuron (Highley et al 2014)



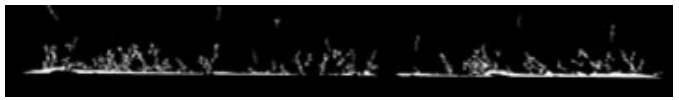
Loss of STMN2 leads to denervation of muscles as measured by CMAP Amplitude



QRL-201 restores STMN2



QRL-201 restores neuronal processes



TDP-43 Pathology

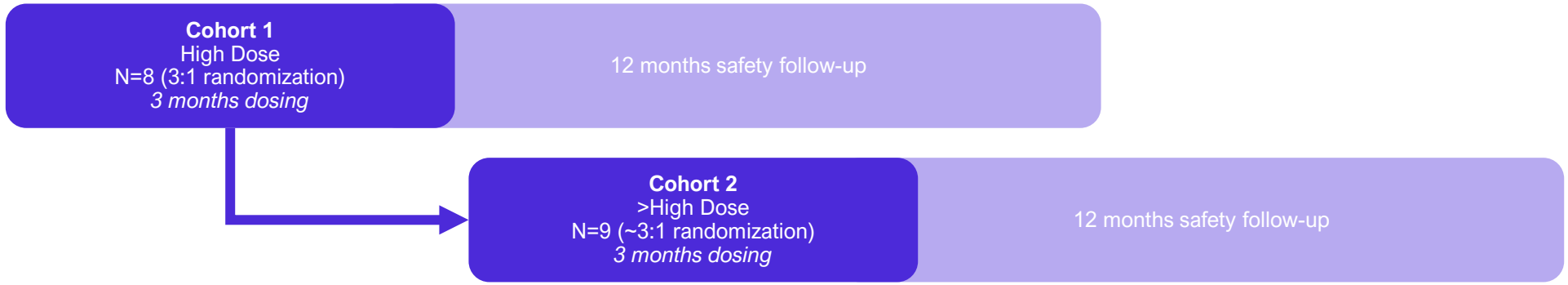
TDP-43 Pathology
+QRL-201 (STMN2 Rescue)

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 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



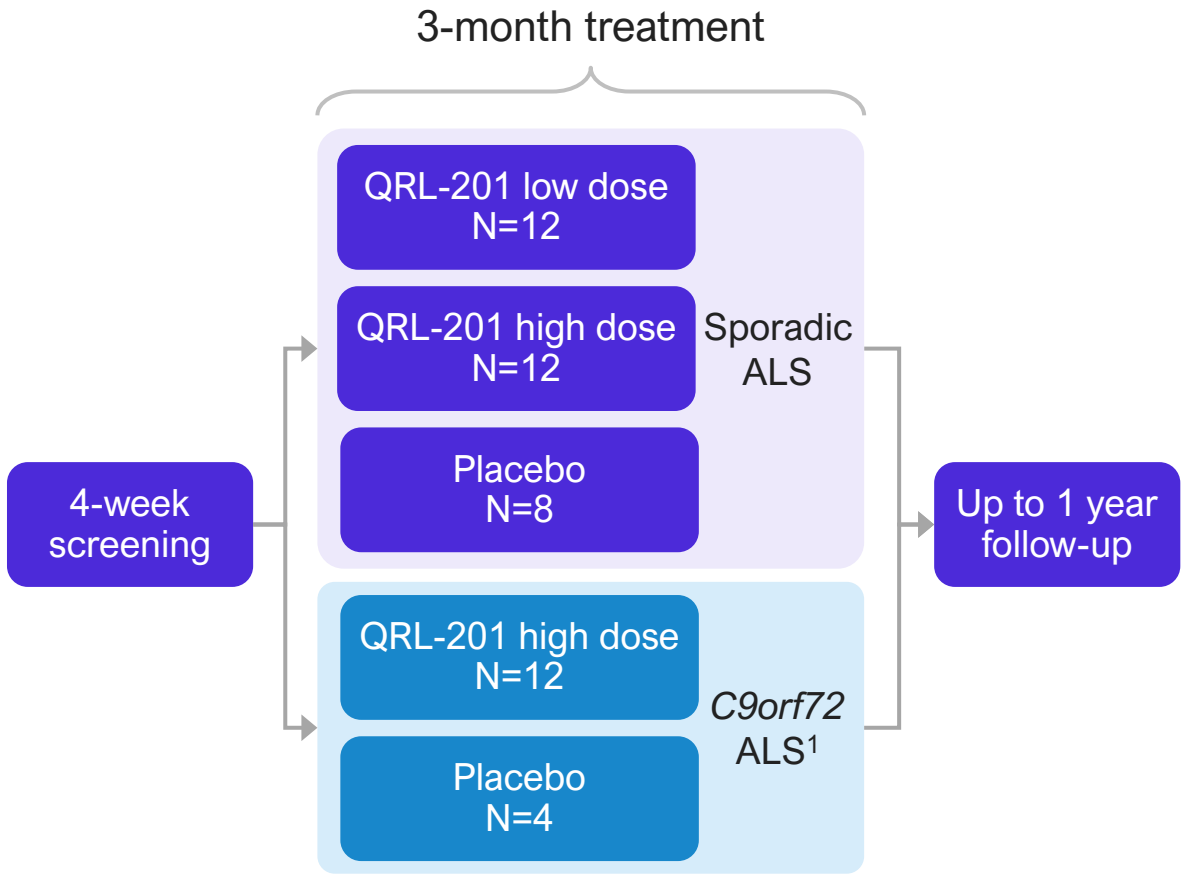
Dose escalation results

- Total of 17 patients (randomized ~3:1) dosed with QRL-201
- DSMB recommended continuing with dosing after both cohorts
- Inclusion criteria updated to only enroll patients who are <24 months from symptom 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 dose-range finding safety follow-up on-going

Dosing complete, interim data expected Q1 2026



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

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

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

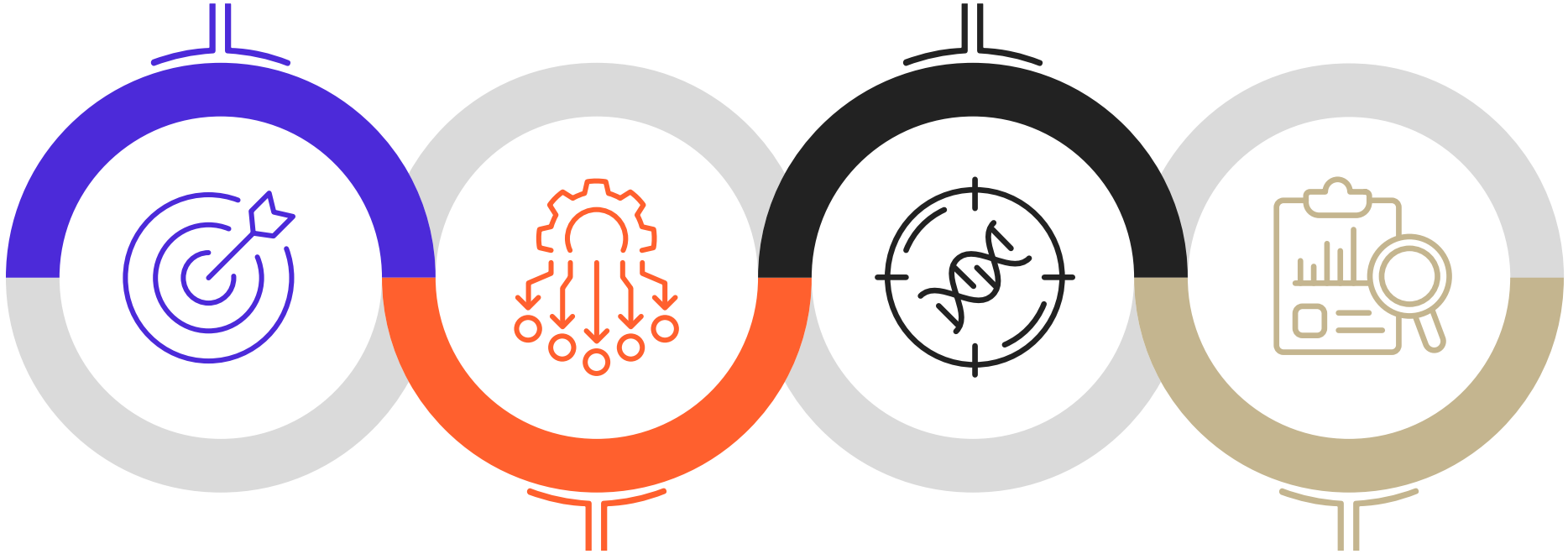
AnQur

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

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 ANQUR 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

ANQUR study is fully enrolled with interim efficacy marker & safety data expected Q1 2026
Next study is a potential registrational study

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

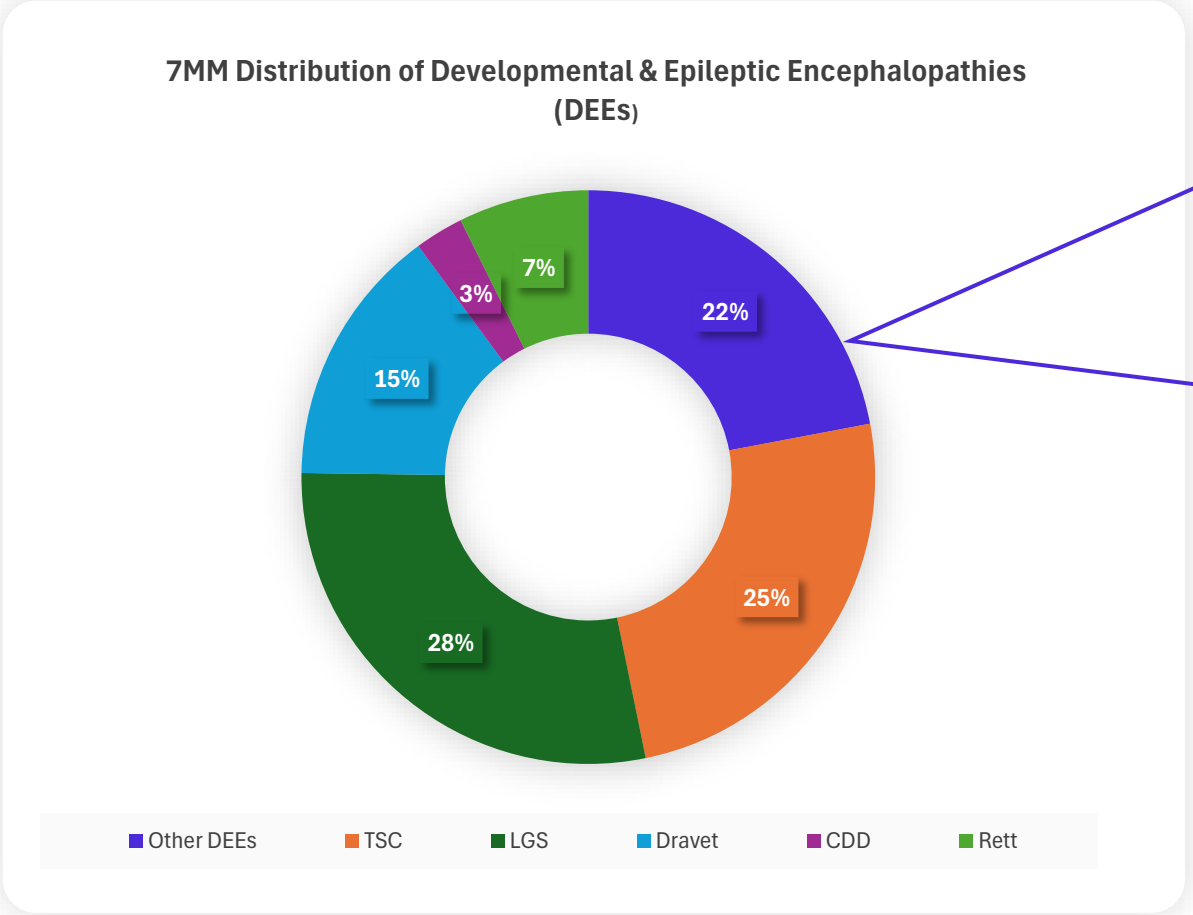
Older generation Kv7 ion channel openers exhibited safety & adverse event liabilities due to:

- 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):

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

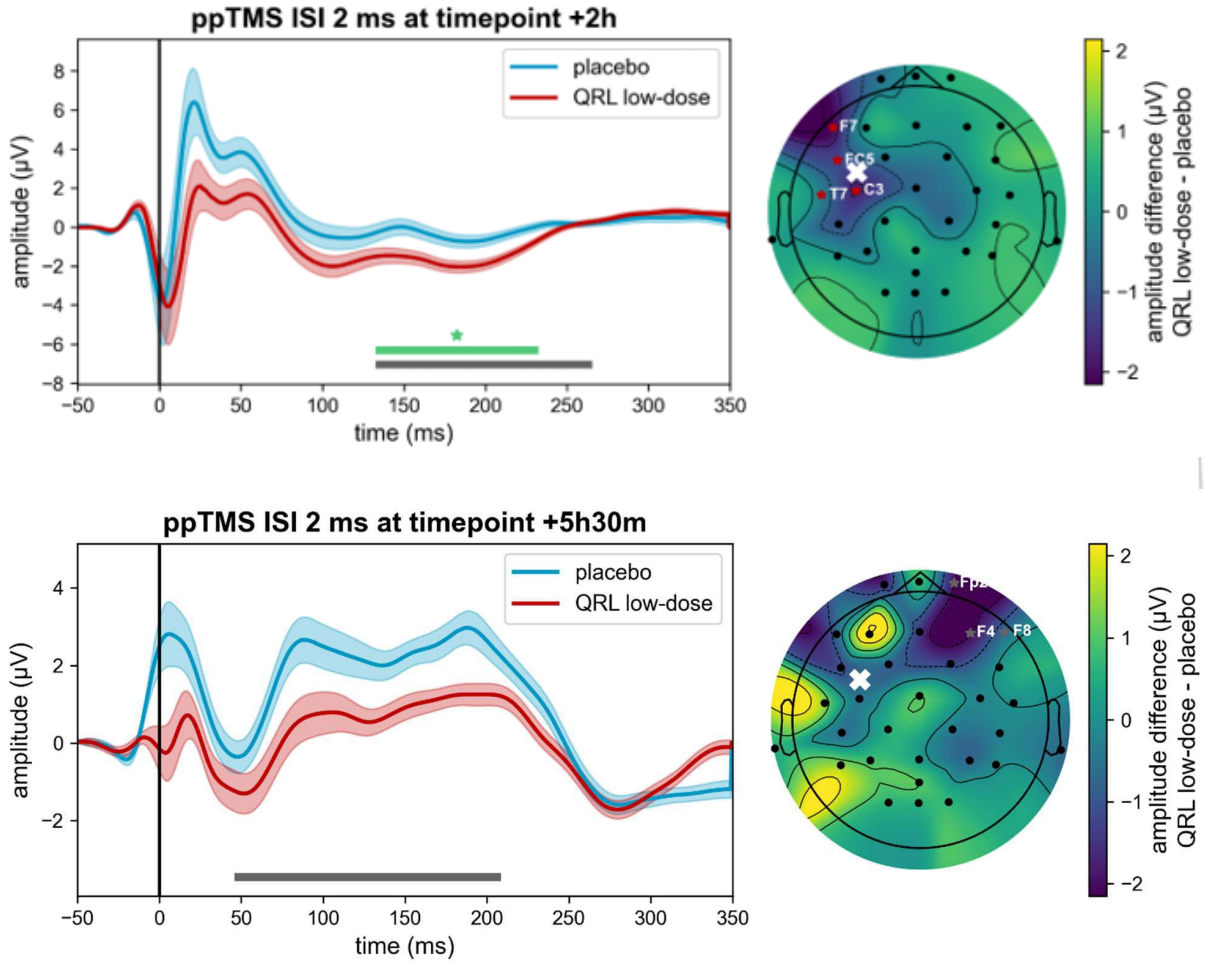
HVs: Healthy Volunteers; SAD: Single Ascending Dose; MAD: Multiple Ascending Dose; PoM: Proof of Mechanism; PK: Pharmacokinetics

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:

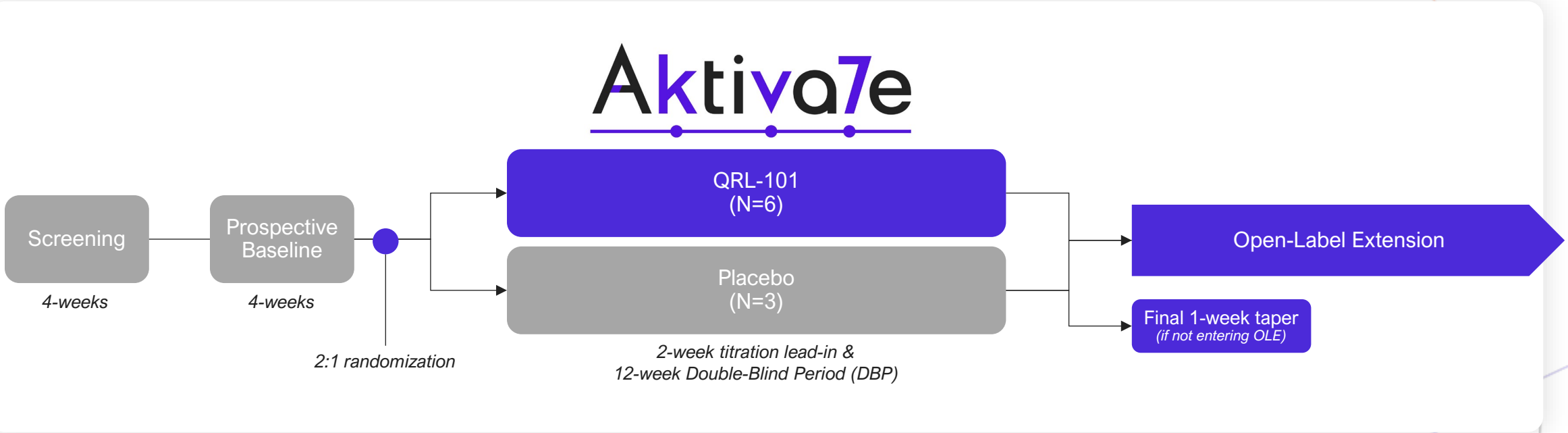
  - ☑ **TMS-Evoked Potential** (pictured right) low dose demonstrated statistically significant reductions vs. placebo at both timepoints
  - ☑ **Passive EEG** demonstrated statistically significant effects on high-frequency beta & gamma bands associated with anti-seizure activity, while not having impact 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 H2 2026



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	Safety and tolerability

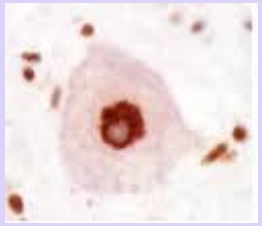
**Administered as a BID extended-release granules (SDD)*

QRL-101 Expansion Opportunities

KCNQ2 mis-splicing in ALS with TDP-43 pathology

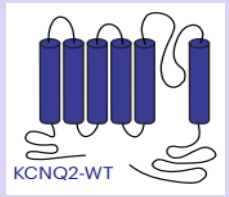
RNA mis-splicing of the voltage gated potassium channel KCNQ2 is a key hallmark of ALS related TDP-43 proteinopathy

Healthy



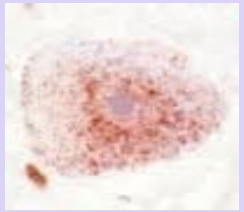
Nuclear TDP-43

KCNQ2 'normal' transcript



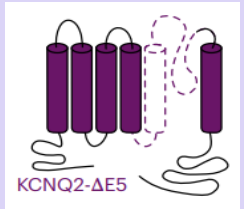
Functional KCNQ2

ALS



Cytoplasmic TDP-43

KCNQ2 mis-spliced transcript



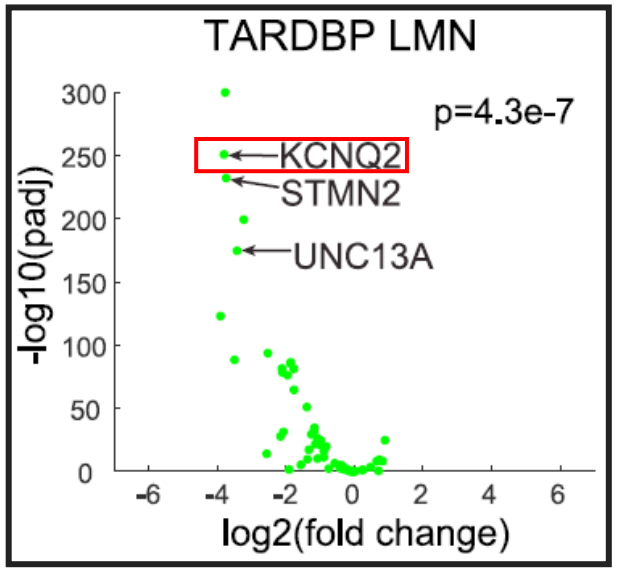
Dysfunctional KCNQ2

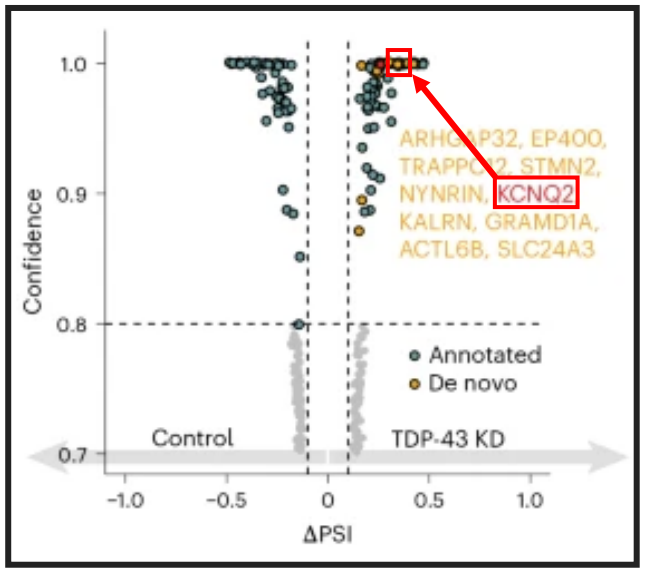
Hyperexcitability

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)



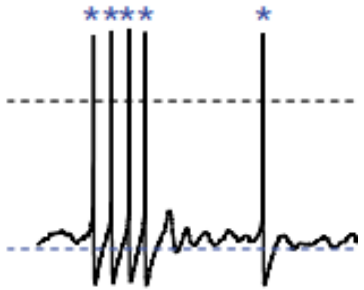


KCNQ2 mis-splicing accelerates motor neuron disease

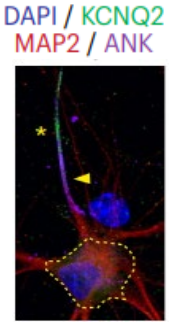
Promotes hyperexcitability, motor neuron death and accelerates ALS disease progression

Healthy

Nuclear TDP-43
Normal KCNQ2 function



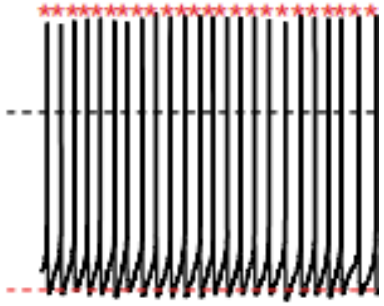
Normal neuronal activity



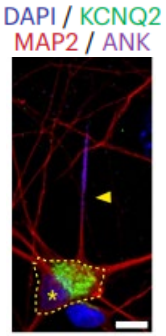
Functional KCNQ2

ALS

TDP-43 loss of function
KCNQ2 RNA mis-splicing

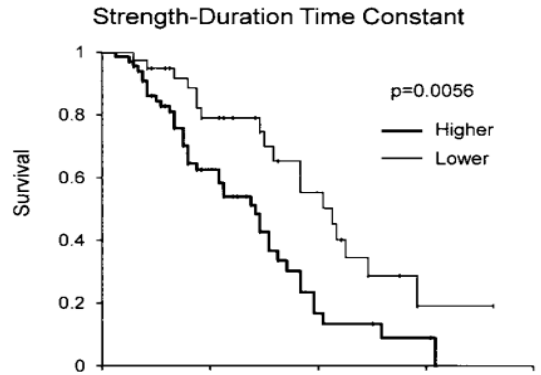


Hyperexcitability

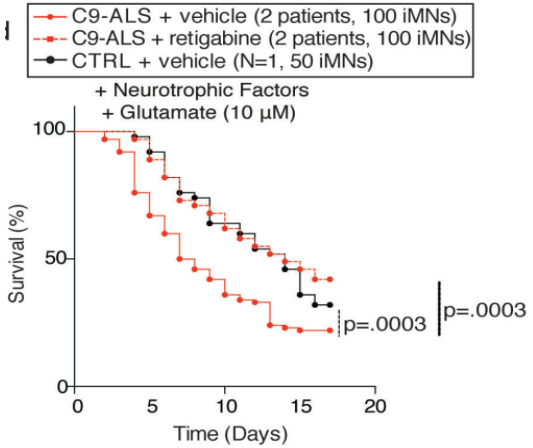


Mislocalized, Dysfunctional KCNQ2

Motor neuron hyperexcitability is correlated with accelerated ALS disease progression
(Kanai et al 2012)



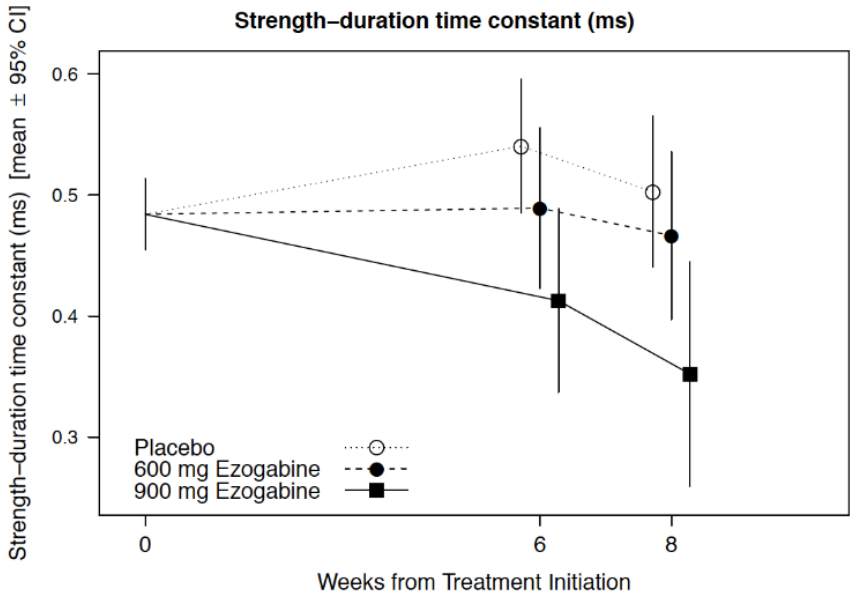
Ezogabine has been shown to improve motor neuron survival
(Shi et al 2019)



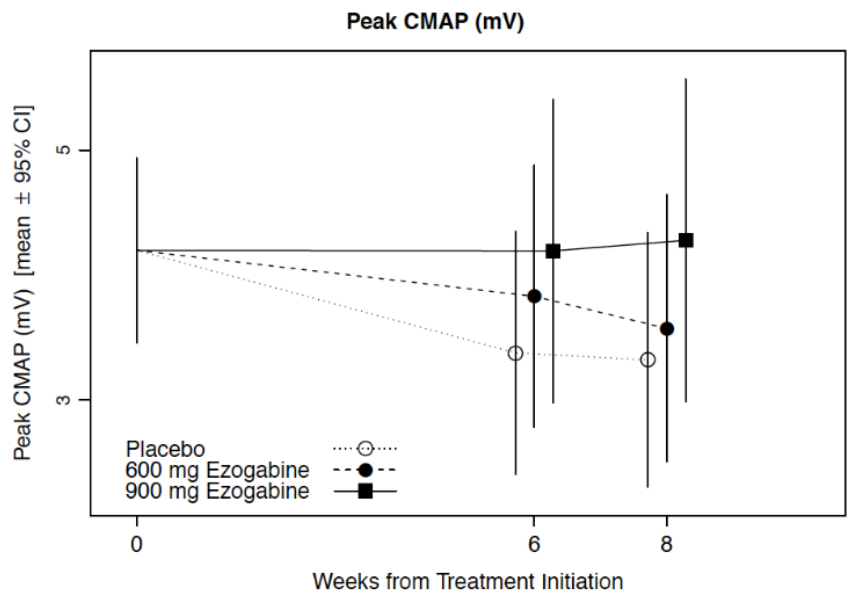
Clinical impact of Kv7 on hyperexcitability in ALS was first demonstrated by the first-generation Kv7 ezogabine[1]

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)



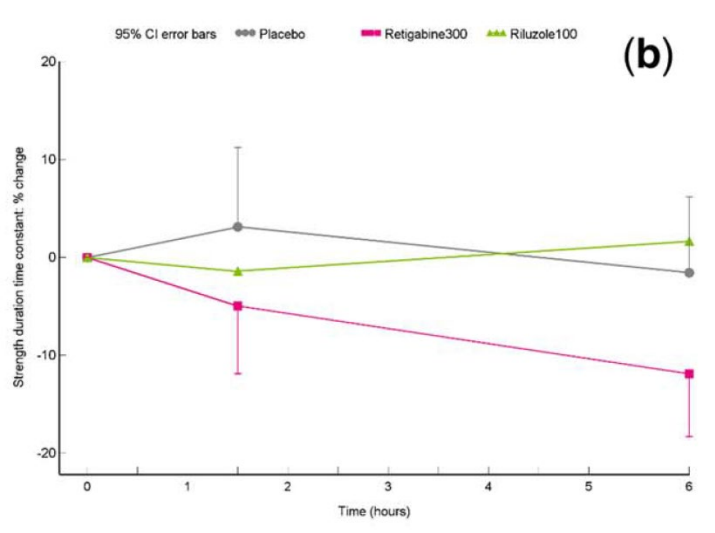
Nearly all (97%) participants in the trial reported at least one adverse event
Most frequent adverse events among participants in the ezogabine arms were fatigue and dizziness

[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

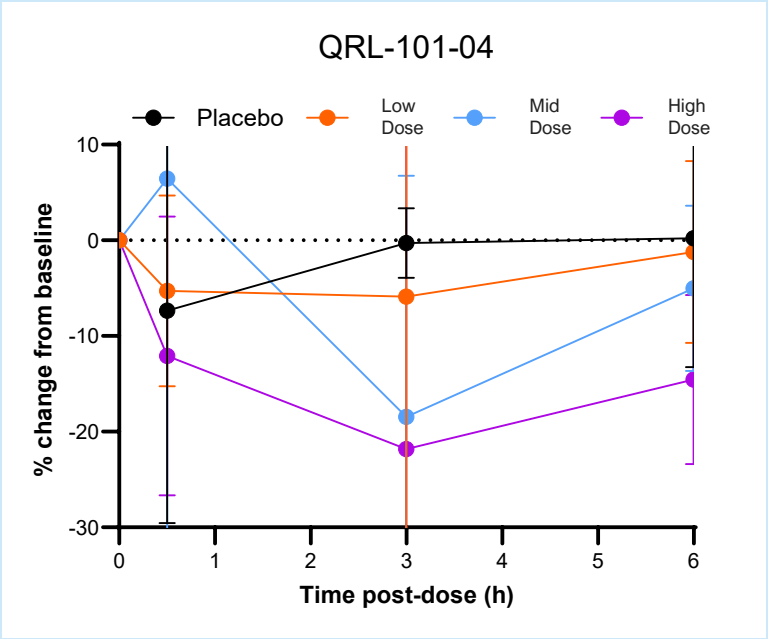
Evaluating next steps of development

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

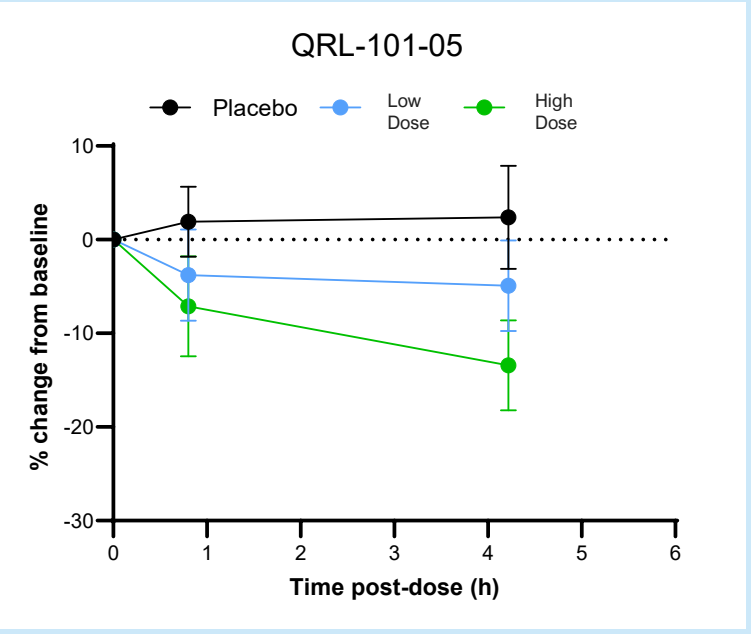


- N=18 ALS patients
- Single dose cross-over study at Utrecht, each compared to self on placebo
- Treatment v. placebo effect p=0.001

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

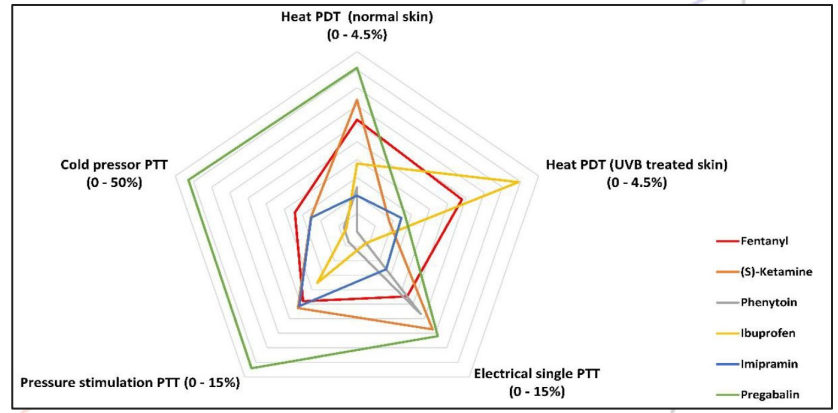
- **More than 20% of U.S. adults** reported experiencing chronic pain (pain lasting three months or more) in the past 3 months[1]
  - **8.5% of adults reported high-impact chronic pain** — pain that frequently limits life or work activities[1]
- Neuronal hyperexcitability is a central driver of pain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

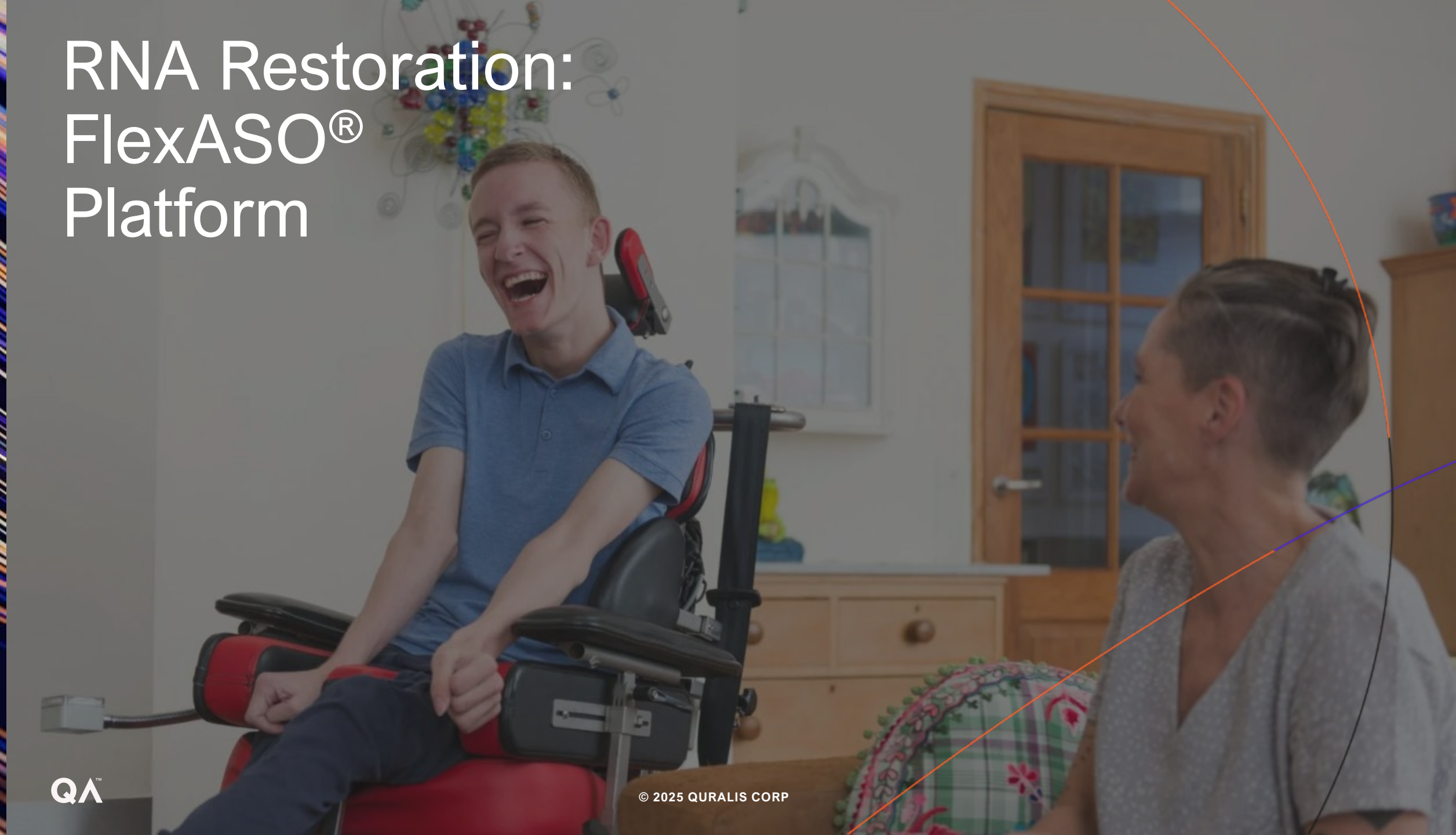
163 subjects dosed till date

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

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.

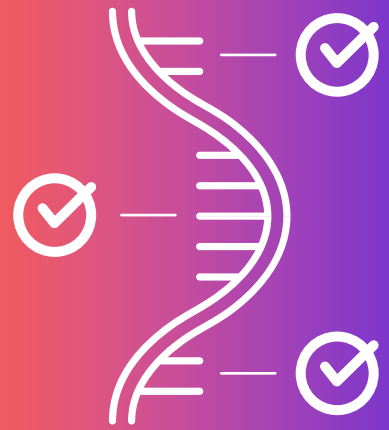
Prolonged Therapeutic Effects & Less Frequent Dosing

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)



Disease-modifying RNA therapies

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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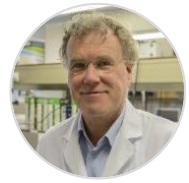

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