Quralis™

Driving Scientific Breakthroughs into Powerful Precision Medicines Targeting Major Genetic Disease Drivers

September 2024

Driving Scientific Breakthroughs Into Powerful Precision Medicine

Groundbreaking Science

- Targeting validated major genetic disease drivers in neurodegeneration and beyond
- Next-gen precision medicines developed through relevant human disease models
- Utilizing biomarkers for patient selection, target engagement, and efficacy

First- & Best-in-Class Programs

- Two programs in the clinic; disease-relevant biomarker readouts in 2025
- Proprietary platform to enable additional therapies
- Most programs benefitting from Orphan Drug and Breakthrough designations

World-Class Team to Execute

- Supportive investor syndicate
- Raised $143.5M to date from a strong set of investors, with $88M oversubscribed Series B round in March ’23
- Validation through partnership with Lilly substantiating our approach and platform

Genetic Validation of Targets Provides Unprecedented Opportunities

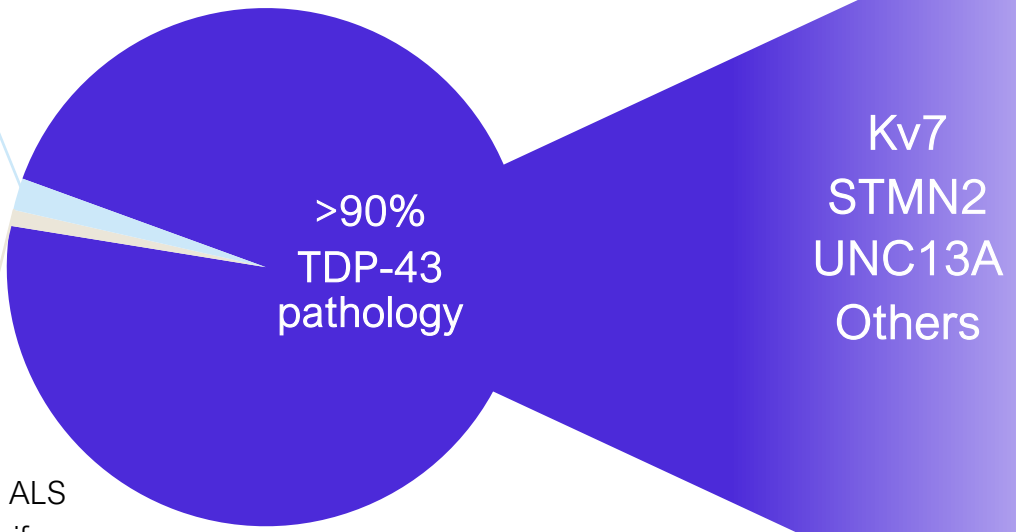
Therapeutic interventions for genetic targets for familial population have been validated

QurAlis is targeting TDP43-associated ALS using precision-medicine approaches in sporadic population

2% SOD1 ALS

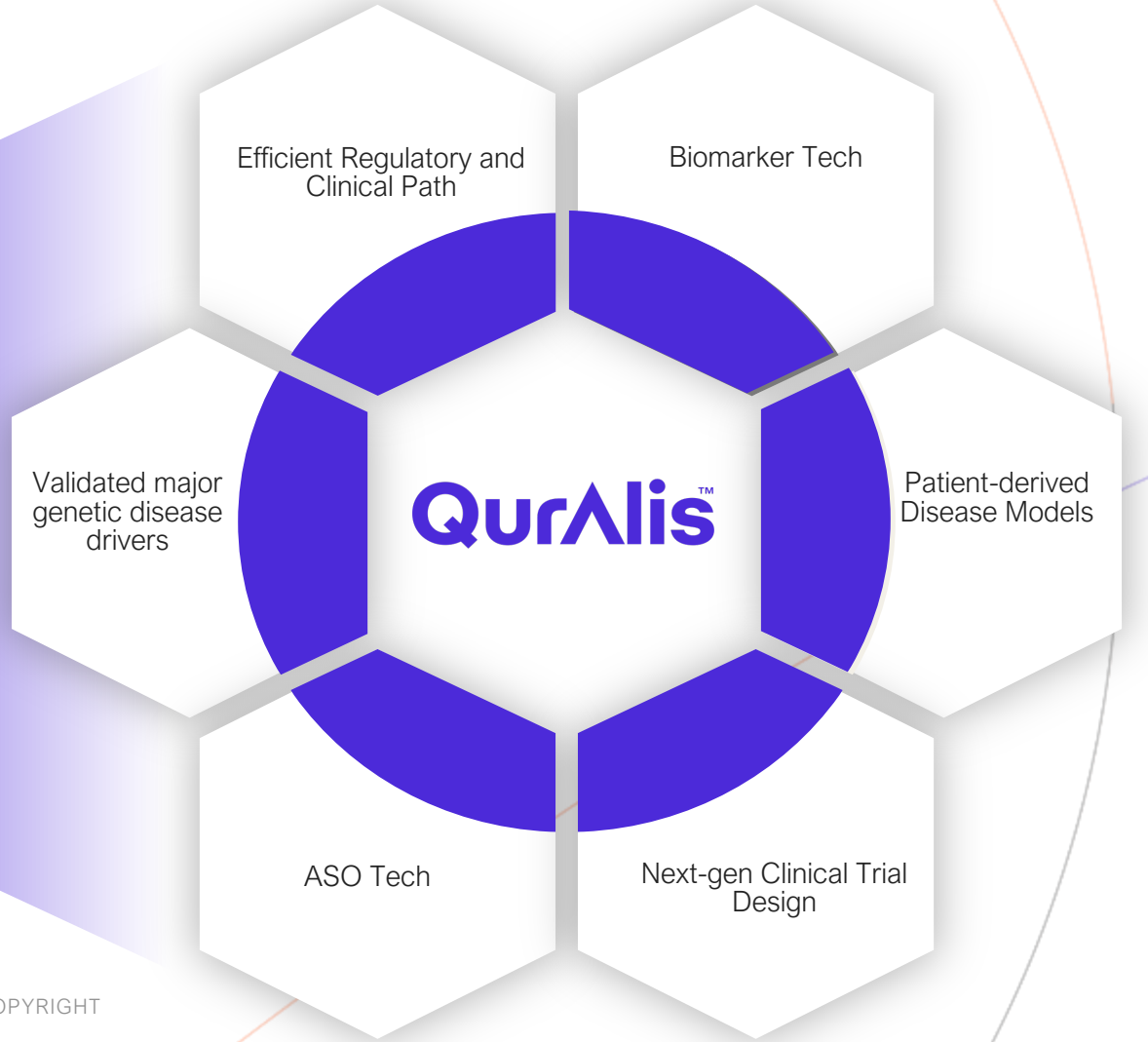
QALSODY (tofersen) 100 mg/1.5 mL injection

Approved 2023*



1% FUS ALS
ION363/jacifusen
in Phase 3**

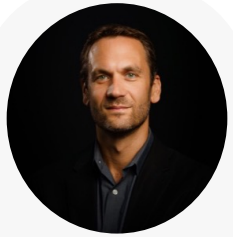
Kv7
STMN2
UNC13A
Others



*Biogen. (2023). *Qalsody (tofersen) [package insert]*. Retrieved from https://www.biogen.com

**"Jacifusen (ION363) - Investigational Antisense Therapy for FUS-ALS." *Ionis Pharmaceuticals*, 2024. Available at Ionis Pharmaceuticals.

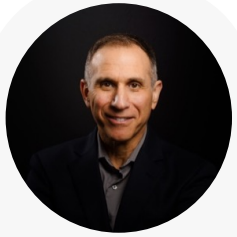
Pioneers with Unrelenting Commitment to Patients



Kasper Roet, PhD
CEO

HARVARD MEDICAL SCHOOL

Johnson & Johnson

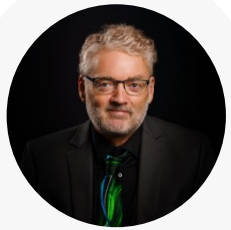


Dan Elbaum, PhD
CSO

Ra Pharma
Retrophin
Pfizer
AMGEN
CRITICAL Therapeutics
FoldRx
VERTEX

Vikas Sharma, PhD
CBO

biocel therapeutics
MACROGENICS
AstraZeneca
MedImmune
rexahn PHARMACEUTICALS



Hagen Cramer, PhD
CTO

Avecia
Girindus
Solvay Organics
Ridgeway Biosystems Inc.
WAVE LIFE SCIENCES

Emma Bowden, PhD
Head of Clinical Development

Lilly
Sangamo THERAPEUTICS
ThermoFisher SCIENTIFIC

Doug Williamson, MD
CMO

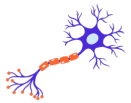
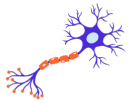
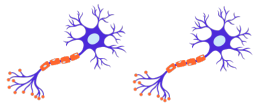
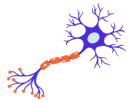
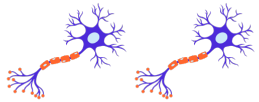
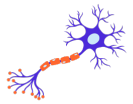
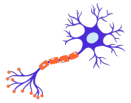
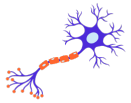
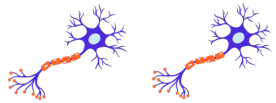
Lilly
parexel
Lundbeck

Jason Brown, MBA
CFO

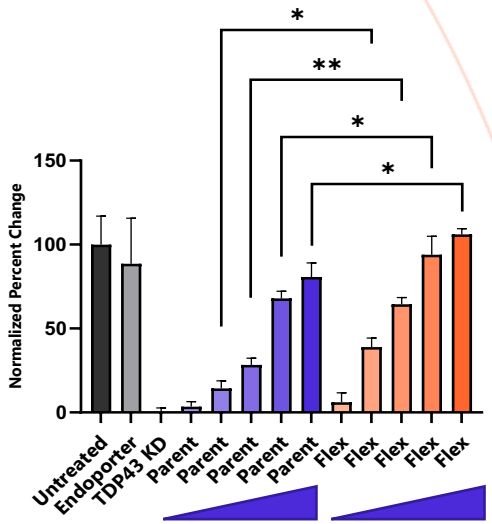
KARUNA THERAPEUTICS
PURETECH GIVING LIFE TO SCIENCE
NOVARTIS

Leading Splice Modulation Through Validated Proprietary FlexASO™ Platform

Flex ASO™ is a proprietary anti-sense oligonucleotide splice modulator platform that incorporates a unique backbone, providing advantages over traditional ASOs

ATTRIBUTES	FLEX ASO	TRADITIONAL ASO
Size		
Efficacy		
Safety		
CMC		
Distribution		Known for spinal cord and frontal cortex

Potential to overcome modality-specific, dose-limiting toxicities



QurAlis™

QurAlis Grants Lilly Exclusive Global License for QRL-204, a Potentially First-in-Class Precision Therapy That Restores UNC13A Function in ALS and FTD

QRL-204 is a splice-switching ASO generated through QurAlis' FlexASO™ Platform; represents Lilly's first program targeting UNC13A in ALS and FTD

Parties to also collaborate to leverage QurAlis' ALS and ASO development expertise to advance QRL-204 and next-generation compounds

UNC13A is an essential regulator of neurotransmitter release at synapses; mis-splicing is a critical RNA alteration occurring in up to 63 percent of all ALS patients and up to one-third of all FTD cases

CAMBRIDGE, Mass., *June 3, 2024* – QurAlis Corporation ("QurAlis") today announced that it has entered into an exclusive license agreement with Eli Lilly and Company ("Lilly") in which QurAlis is granting Lilly global rights to develop and commercialize QRL-204, a potentially best-in-class splice-switching antisense oligonucleotide (ASO) designed to restore UNC13A function in amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD), and other neurodegenerative diseases.

Under the terms of the agreement, QurAlis granted Lilly an exclusive, worldwide license to develop and commercialize QRL-204 and other UNC13A-targeting compounds in exchange for an upfront payment of $45 million to QurAlis, plus an additional equity investment. QurAlis is also eligible for future milestone payments of up to $577 million and tiered royalties on net sales.

Pipeline Targeting Major Genetic Disease Drivers in Neurodegeneration

TARGETING MAJOR DISEASE DRIVERS IN PATIENTS

PROGRAM	DISEASE MECHANISM	MODALITY	MOA	INDICATION	PRECLINICAL	CLINICAL	PARTNER
QRL – 101	Splicing/ Excitotoxicity	Small Molecule	Kv7.2/3	ALS			
				Epilepsy			
QRL – 201	Splicing	ASO	STMN2	ALS			
QRL – 203				FTD (non-Tau)			
QRL – 204	Splicing	ASO	UNC13A	ALS/ FTD			Lilly
DISCOVERY PROGRAMS							
QRL – TBA	Splicing	ASO	Undisclosed	Fragile-X			
QRL – TBA				PSP			

- Disease modifying first-in-class programs for five high profile rare disease genetic splicing targets
- Portfolio expansion beyond ALS, to other rare and large indications creating additional growth opportunities
- FlexASO™ platform, validated by Lilly, provides unique opportunities for splice modulation targets

Supported and Recognized by Investors, Pharma, and Industry

Investors

EQT Life Sciences

sanofi ventures

DROIA ventures

LS POLARIS INNOVATION FUND

Lilly

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 AWARDS
DELL Technologies
WINNER

THE TERMEER FOUNDATION

Partner

Lilly

QRL-101 Excitotoxicity Program

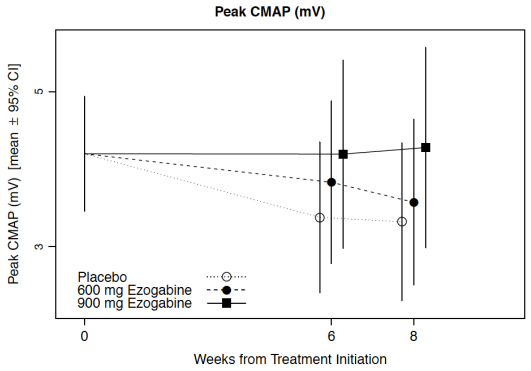
QRL-101 Program Overview

Candidate	Potential best-in-class Kv7 opener
Function/MOA	Reduction of hyperexcitability through K+ channels
Patient Selection	Excitability biomarker (>50% of ALS patients)
Indications	Disease modification of sporadic ALS subgroup; treatment of seizure disorders
Development & Status	Single ascending dose (SAD) studies completed in healthy volunteers
Rights	QurAlis retains global rights

Kv7 is a Clinically Validated Target in ALS

EFFICACY: CLINICAL BENEFITS OBSERVED

Retigabine trial in 65 patients showed Kv7 opener can lead to clinical benefits



Significant dose-dependent effects on biomarkers predicting patient survival were observed, with a notable correlation between the effect size on the excitability and the efficacy biomarker CMAP

DOSE-DEPENDENT EFFECT ON EXCITABILITY BIOMARKER AND EFFICACY BIOMARKER CMAP THAT PREDICT PATIENT SURVIVAL

RETIGABINE UNFAVORABLE AE PROFILE: 97% PARTICIPANTS REPORTED AT LEAST ONE ADVERSE EVENT

- Fatigue, dizziness and somnolence were major adverse events
- Retigabine caused blue discoloration of eyes and skin
- Retigabine interacts with the GABAa receptor
- Lack of selectivity for many Kv7 family members

A MORE SELECTIVE KV7.2/7.3 OPENER IS NEEDED TO DECREASE AE RATES

QURALIS' THERAPEUTIC STRATEGY: QRL-101 IS MORE POTENT & SELECTIVE THAN PREVIOUSLY MARKETED RETIGABINE

Preclinical

Preclinical studies demonstrated a superior safety profile to retigabine

Clinical

No SAEs reported in the QRL-101 SAD studies in healthy volunteers (N>90)

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

Current Clinical Development Update

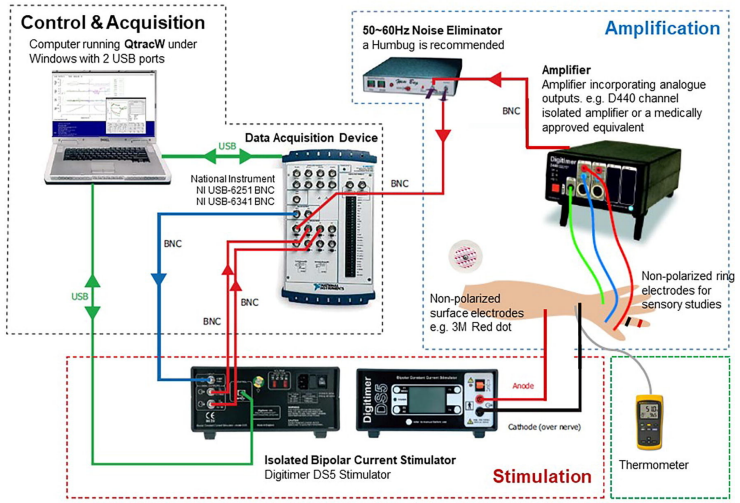
OVERVIEW	• QRL-101-01 completed a randomized, double-blind, placebo-controlled SAD, Phase 1 study to assess the safety, tolerability, and pharmacokinetics (PK) of QRL-101 in healthy participants • This study informs the subsequent multiple ascending dose (MAD) study
OBJECTIVES	• Primary: To determine the safety and tolerability of QRL-101 after multiple oral doses in healthy participants • Secondary: To determine the PK profile of QRL-101 after multiple oral doses in healthy participants
DESIGN	• Study design includes five dose escalation cohorts
ENDPOINTS	• Safety (AEs, SAEs) • PK: $AUC_{0\text{-}24;}$ $C_{max;}$ T_{max}

No SAEs reported in healthy subjects treated in the SAD studies (N>90)

Comprehensive Biomarkers and Phenotypic Assessments to Measure Activity

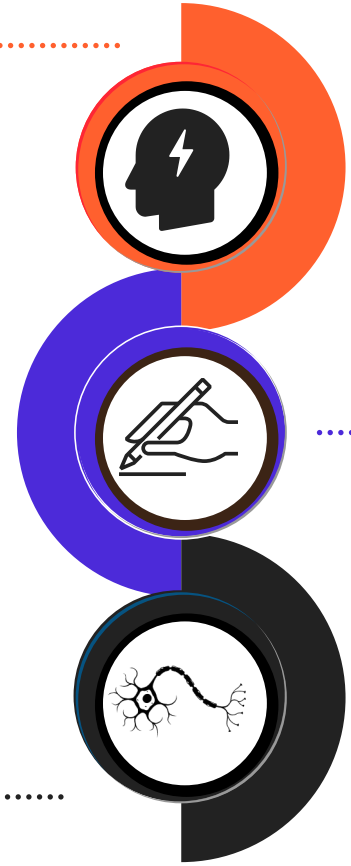
Electrophysiology

- Motor excitability recordings (CMAP, M-Scan)



Biomarkers of Neuronal Loss

- NfL and other exploratory biomarkers

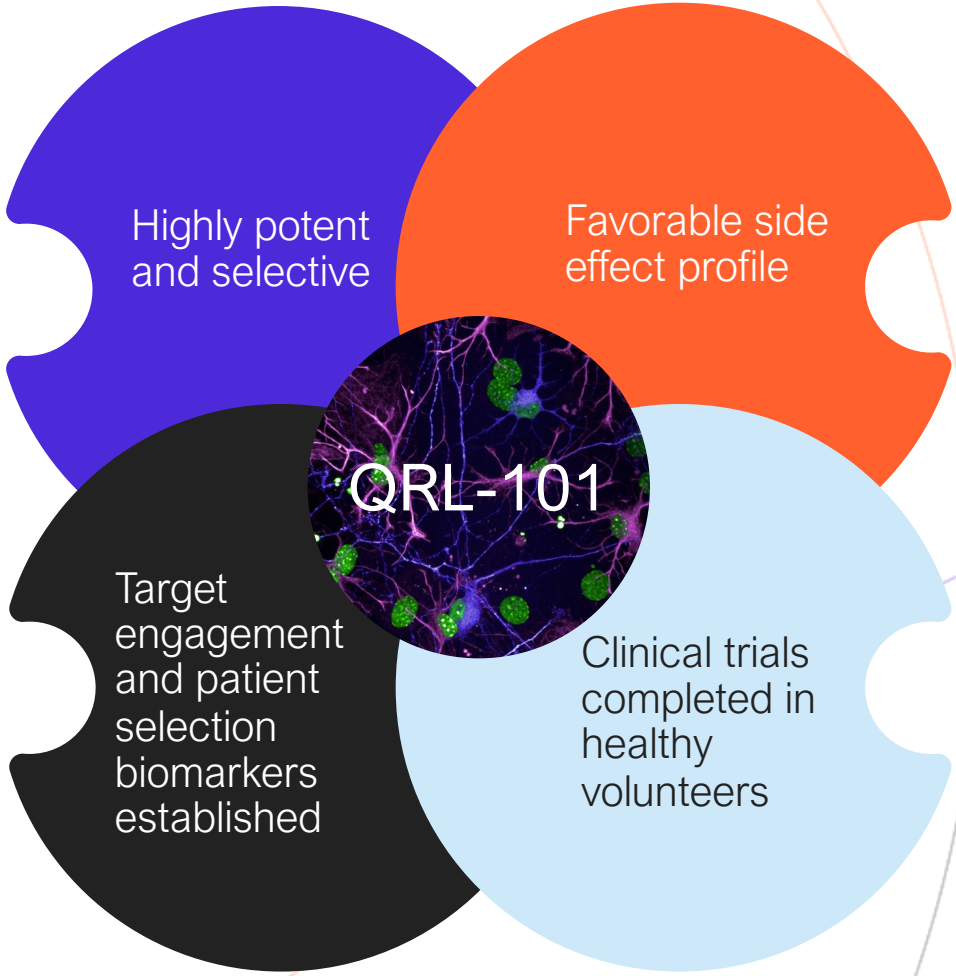


Clinical Measurements

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

QRL-101: A Potent and Validated Therapeutic in Development for ALS Patients and Hyperexcitability

- A best-in-class precision therapy to treat hyperexcitability-induced diseases
- Kv7.2/7.3 is a clinically validated target – including in seizure disorders and 50% of ALS
- Multiple clinical studies ongoing – PoM data available in 2025
- Large market opportunity



QRL-201 STMN2 ALS Program

QRL-201 Program Overview

Candidate	First-in-class ASO against STMN2 pathology
Function/MOA	Restoration of protein activity
Patient Selection	STMN2 biomarker (90% of ALS patients*)
Indications	Disease modification of sporadic ALS subgroup
Development & Status	Clinical trials ongoing in patients
Commercial & Regulatory Advantage	Precision-medicine approach | Increases probability of success
Rights	QurAlis retains global rights

*Majority of ALS and FTD patients and 30-50% of AD patients

STMN2 Levels are Consistently Decreased in Sporadic ALS Patients

BREAKTHROUGH DISCOVERY VALIDATED SIMULTANEOUSLY

EGGAN LAB[1]

STMN2 levels are consistently decreased in sporadic ALS patients

Truncated STMN2 mRNA abundant in sporadic ALS spinal cord and brain

CLEVELAND LAB[2]

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

TDP-43 loss causes loss of axon repair Rescue by restoring STMN2 levels

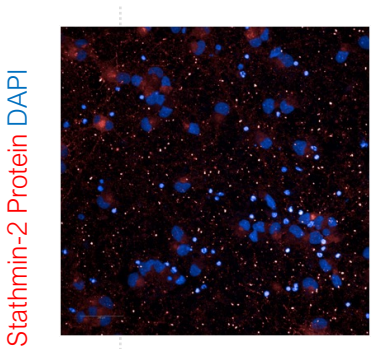
QURALIS' THERAPEUTIC STRATEGY FOR STMN2 RESTORATION

In ALS motor neurons TDP-43 leaves the nucleus

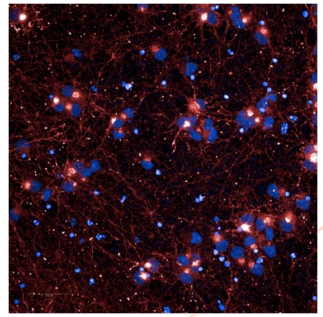
Loss of TDP-43 controlled exon splicing leads to loss of STMN2

Loss of full length STMN2 leads to axonal degeneration and damaged repair

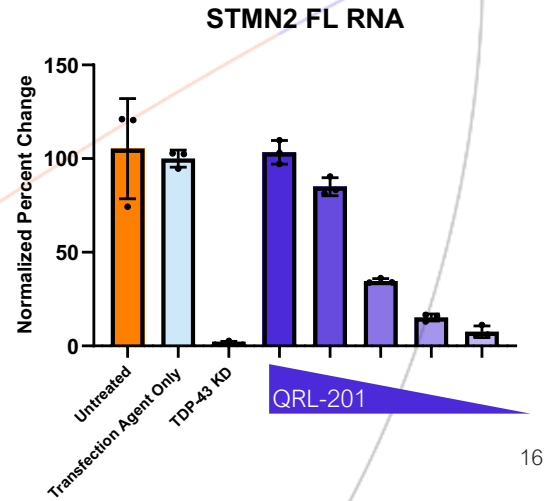
QURALIS' ASO RESTORES LEVELS OF FULL-LENGTH STMN2



Transfection Agent + TDP-43 KD ASO



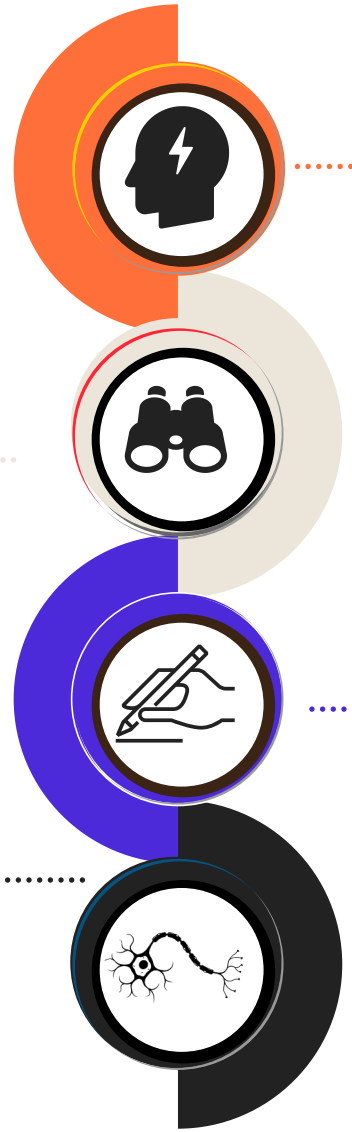
Transfection Agent + TDP-43 KD ASO + QRL-201



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

Comprehensive Biomarkers and Phenotypic Assessments to Measure Activity

AnQur



Electrophysiology

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

Target Engagement

- STMN2 levels

Clinical Measurements

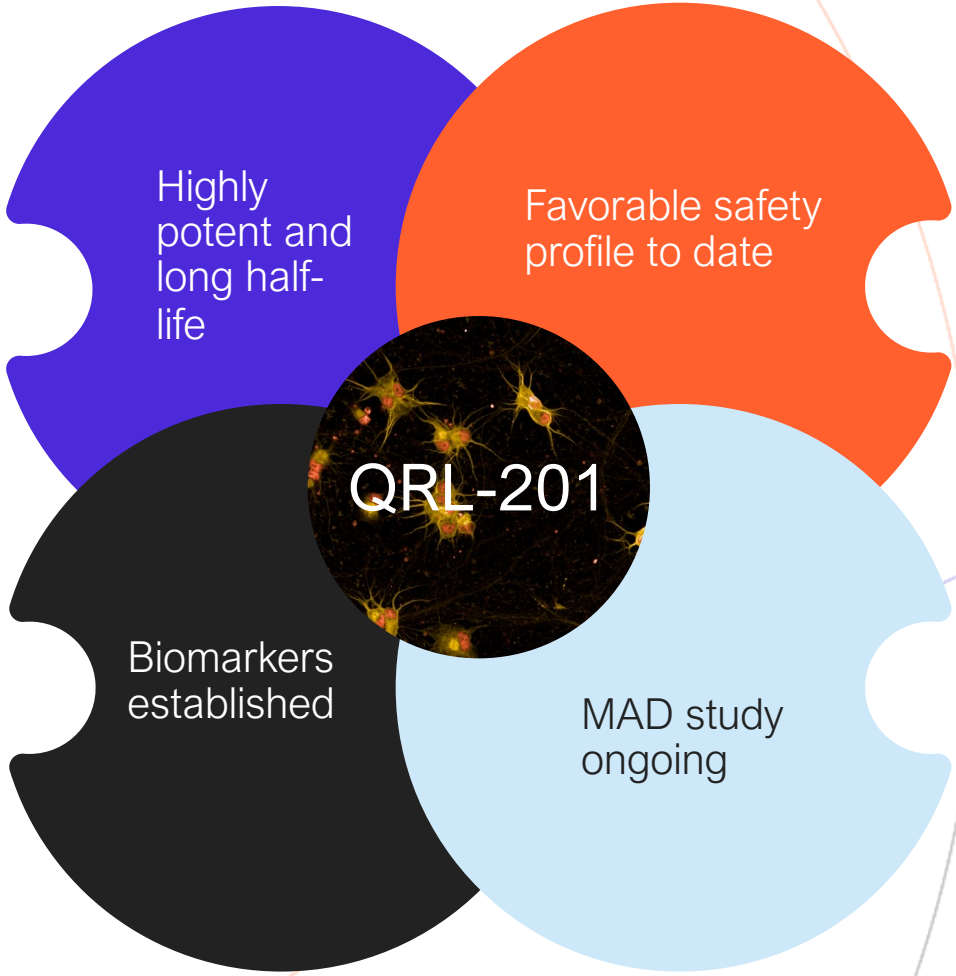
- ALSFRS-R
- ROADS
- SVC
- HHD
- Ventilation assistance-free survival
- Time to event measures

Biomarkers of Neuronal Loss

- NfL and other exploratory biomarkers

QRL-201 Protects Human Motor Neurons Against Neurodegeneration

- First-in-class therapy to treat ~90% of ALS & ~50% FTD patients
- Potent restoration of STMN2 function and TDP-43 neurodegenerative phenotypes
- Target engagement and patient selection biomarker program
- Genetic target for sporadic ALS and FTD with additional opportunities in AD and PD



Next-Gen Precision Medicine

- Approaches utilizing biomarkers for patient selection, target engagement, and efficacy

First- & Best-in-Class Programs

- Two programs in the clinic
- Biomarker readouts in 2025

Proprietary Platform/Broad Application

- Novel FlexASO™ platform for splice modulator targets
- Hyperexcitability-related diseases

Value Creation

- Expanding into additional indications
- Opportunity for accelerated regulatory path

Thank You

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