Quralis™

Driving Scientific Breakthroughs into Powerful Precision Medicines for ALS and Other Neurodegenerative Diseases

Feb 2024

The QurAlis Story

- We are on the cusp of a revolution in drug development for ALS, FTD, AD and other neurodegenerative diseases largely aided through recent genetic discoveries and stem cell technologies.
- There are now ALS patients with SOD1 and FUS mutations who have stopped progressing and are even regaining function. This is changing the outlook for patients, their families, and the doctors and nurses who treat them and it is changing the whole field.
- Through its pioneering approach, QurAlis is leading in drug development for sporadic ALS and FTD following an oncology-like, precision-medicine approach focused on breakthrough genetic targets using relevant human disease models and biomarkers.
- QurAlis closed Series B financing in March 2023 to support clinical development of QRL-201 STMN2 and QRL-101 Kv7, and to support development of QRL-204 UNC13A.

Groundbreaking Science

New insights into human genetics and stem cell technology

Next-gen precision medicines using biomarkers for patient selection, target engagement, and efficacy

First- & Best-in-Class Programs

Two programs in the clinic – First efficacy biomarker readouts in 2025*

Two proprietary platforms to enable additional therapies

Most programs benefitting from Orphan Drug and Breakthrough designations

World-Class Team to Execute

Supportive investor syndicate

Strong IP positions

Raised $143.5M to date from a strong set of investors, with $88M oversubscribed Series B round in March ‘23

*Dependent on funding decisions

QurAlis' Comprehensive Approach to Tackling ALS


Kevin


Clifford

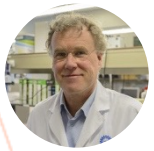

Sandy

Patient-derived Disease Models

Efficient Regulatory and Clinical Path


Angela


Merit


Leonard


Kevin


Chris

Genetic Understanding

QurAlis™

Biomarker Tech


Matthew


Brian


Michelle


Hagen


Sudhir

ASO Tech

Structure-based Drug Design


Manuel

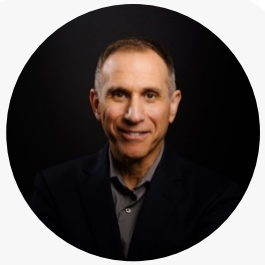

Dan

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

biocad therapeutics

MACROGENICS

AstraZeneca

MedImmune

rexahn PHARMACEUTICALS

Hagen Cramer, PhD
CTO

Avecia

Girindus
Solvay Organics

GeminiBio

WAVE LIFE SCIENCES

Emma Bowden, PhD
Head of Clinical Development

Lilly

Sangamo THERAPEUTICS

MedImmune
A member of the AstraZeneca Group

ThermoFisher SCIENTIFIC

GEORGETOWN UNIVERSITY

Supported and Recognized by Investors, Pharma, and Industry

Investors

EQT Life Sciences

sanofi ventures

DROIA ventures

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

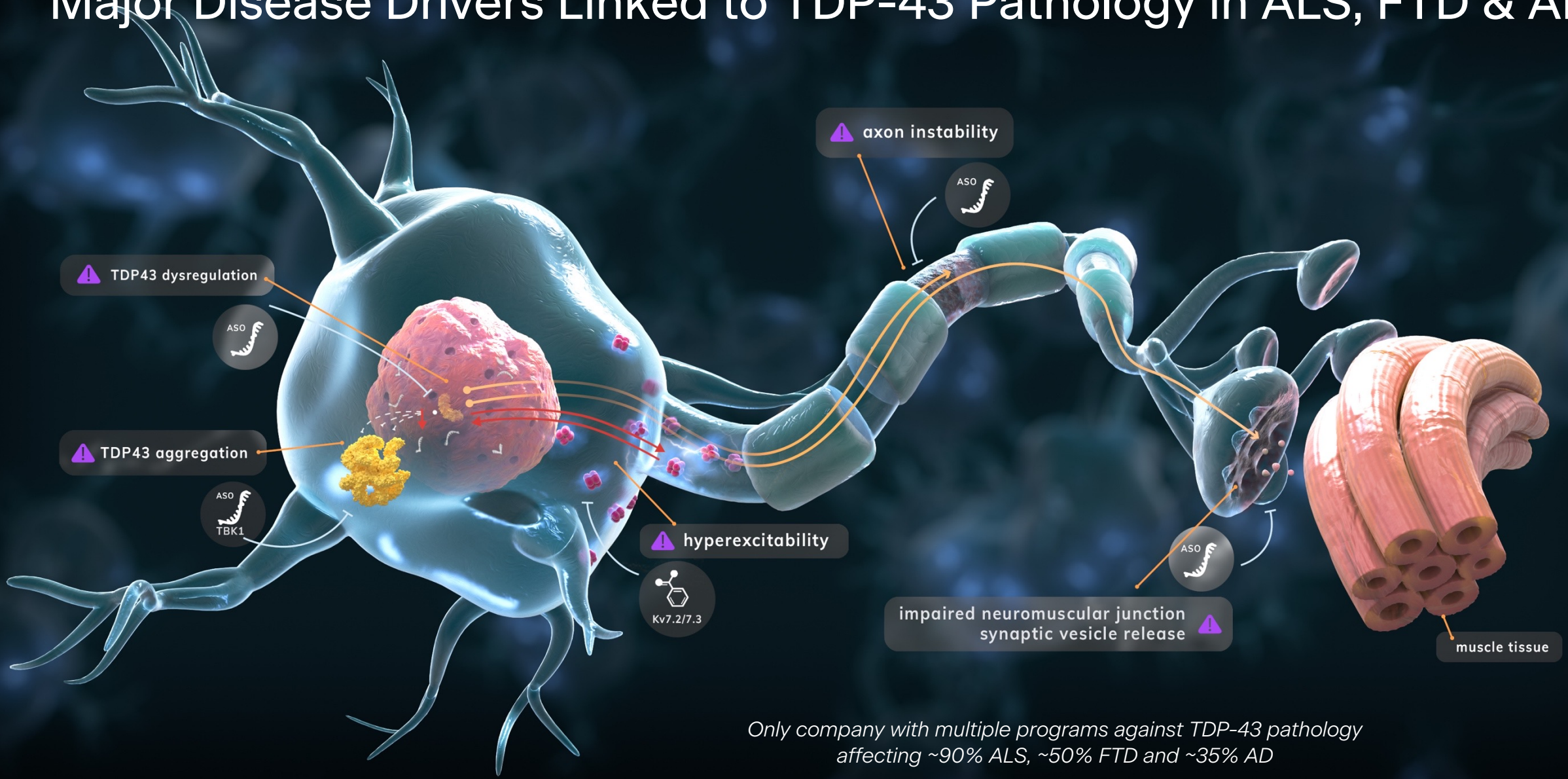
NEVY AWARDS
PRESENTED BY DELL Technologies
WINNER

THE TERMEER FOUNDATION

Partner

Lilly

Major Disease Drivers Linked to TDP-43 Pathology in ALS, FTD & AD



Only company with multiple programs against TDP-43 pathology affecting ~90% ALS, ~50% FTD and ~35% AD

QA™

Double Genetic Validation of Targets Provides Unprecedented Opportunities

Highly compelling market opportunity

TDP-43 pathology underlie neurodegenerative diseases including ALS, FTD, and Alzheimer's

ALS

~30K US ALS patients

90% addressable

FTD

~50-60K US FTD patients

50% addressable

Alzheimer's

~6MM US AD patients

35% addressable

Multiple causes of neuronal death and dysfunction

- TDP-43 dysfunction
- TDP-43 aggregation
- Axon instability
- Neuronal hyperexcitability
- Impairment of vesicle release at the neuromuscular junction

QurAlis approach

Double genetic target validation

Broad strategy centered

on TDP-43 pathology

Mutations in Familial Forms of Disease

Programs (Targets)

STMN2

UNC13A

TDP-43

Others

Loss in Sporadic Forms of Disease

Precision Biomarkers

Precision Therapies

QurAlis' Advantage – Two Proprietary Platforms

QR43 platform™: proprietary & investigative TDP-43 platform

Stem cell model systems

In vitro neuronal functional readouts

TDP-43 loss of function animal model

Clinical TDP-43 biomarkers

The only company with a TDP-43 LOF animal model

Flex ASO™ proprietary anti-sense oligonucleotide splice modulator platform

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

Potential to overcome modality-specific, dose-limiting toxicities observed with 'traditional ASO'

Pipeline Targeting Major Disease Drivers in Neurodegeneration

Targeting Major Disease Drivers in Patients

PROGRAM	POPULATION	MODALITY	MOA	INDICATION	PRECLINICAL	CLINICAL
QRL – 201		ASO	STMN2	ALS		
				FTD (non-Tau)		
				PLS		
QRL - 101		Small Molecule	Excitatory (Kv7)	ALS		
				FTD		
QRL -204		ASO	UNC13A	ALS/ FTD		
				FTD		

QRL-101 Excitotoxicity Program

QRL-101 Program Overview

Candidate	Potential best-in-class Kv7 opener
Function/MOA	Reduction of hyperexcitability through K+ channels (>50% of ALS patients)
Patient Selection	Excitability biomarker
Indications	Disease modification of sporadic ALS subgroup
Development & Status	Clinical trials initiated in healthy volunteers
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

Kv7 is a Clinically Validated Target in ALS

EFFICACY: CLINICAL BENEFITS OBSERVED IN 65 PATIENTS

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

- Significant dose dependent effects on biomarkers that predict patient survival
- Significant correlation between effect size on excitability biomarker and efficacy biomarker CMAP

ADVERSE EVENT: 97% PARTICIPANTS IN THE RETIGABINE TRIAL 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

QRL-101 is More Potent and Selective Than Previously Marketed Retigabine

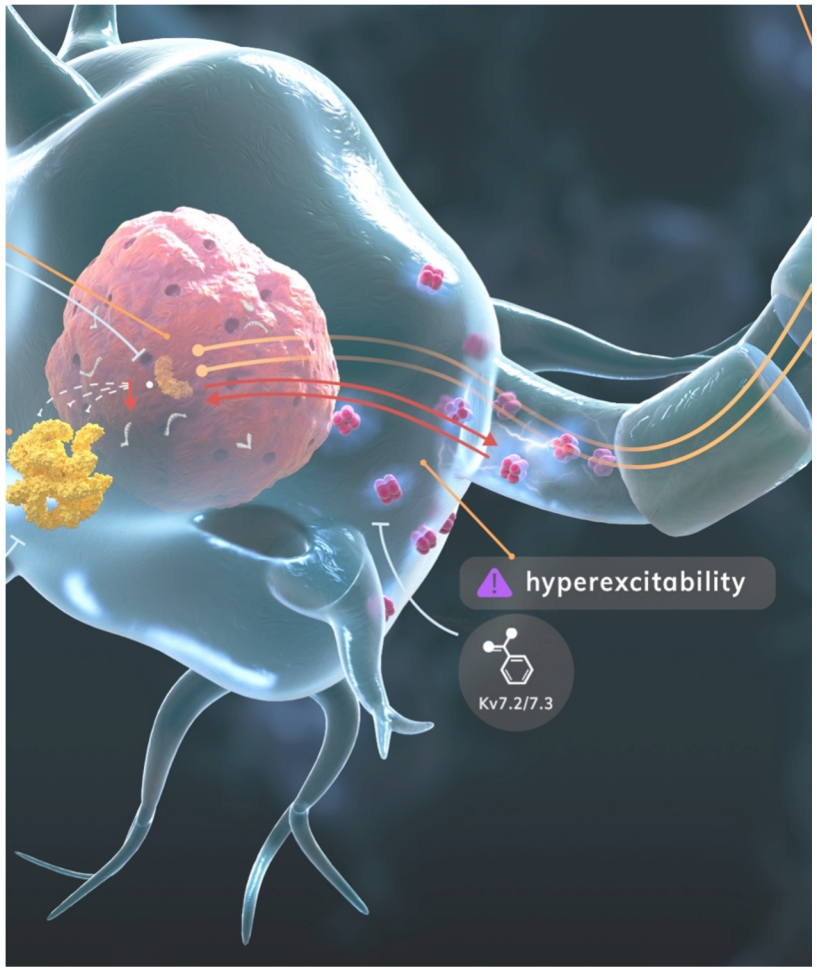
Retigabine has a problematic adverse event profile in the clinic due to lack of selectivity

QRL-101 in preclinical studies has demonstrated lack of same liabilities as retigabine

QRL-101 IND enabling studies ongoing

	EFFICACY	SIDE EFFECTS (AE PROFILE)				
		FATIGUE / SOMNOLENCE		DIZZINESS	URINARY RETENTION	PIGMENTATION
TEST	Kv7.2/7.3 activity	GABAa receptor activity / binding	REM / non-REM sleep	Rotarod	Bladder strip test	Compound specific photo-reactivity
RETIGABINE	EC_{50}=1.2uM	+++	Liability (10mg/ kg)	Liability (10mg/ kg)	Liability (1uM)	Liability
QRL-101	EC_{50}=0.06uM	--	No Liability	No Liability	No Liability	No Liability

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



A first-in-class precision therapy to treat hyperexcitability-induced disease progression

50% of ALS patients provides a large market opportunity

Kv7.2 is genetically regulated in sporadic ALS

Kv7.2/7.3 is a clinically validated target

QRL-101:

- Highly potent and selective
- Favorable side effect profile
- Target engagement and patient selection biomarkers established
- Clinical trials initiated in healthy volunteers

QRL-201 STMN2 ALS Program

QRL-201 Program Overview

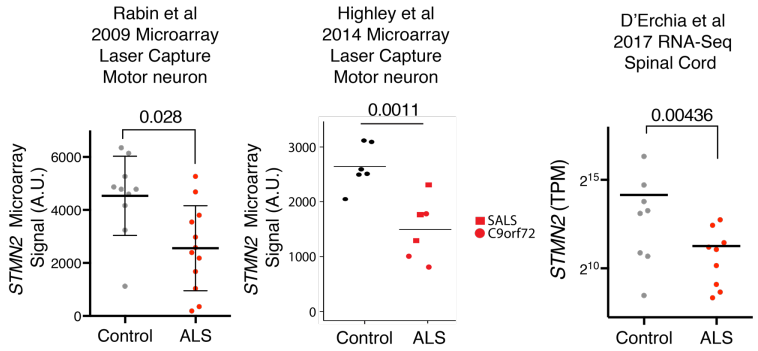
Candidate	First-in-class ASO against STMN2 pathology
Function/MOA	Restoration of protein activity
Patient Selection	STMN2 biomarker (90% of ALS patients*)
Indications	Disease modification of sporadic ALS subgroup
Development & Status	Clinical trials ongoing in patients
Commercial & Regulatory Advantage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

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

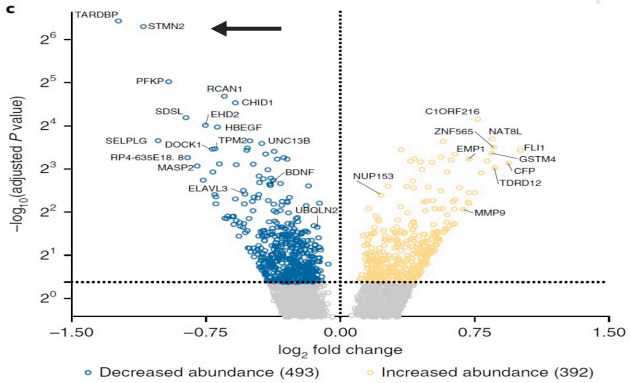
STMN2 Levels are Consistently Decreased in Sporadic ALS Patients

EGGAN LAB

STMN2 levels are consistently decreased in sporadic ALS patients

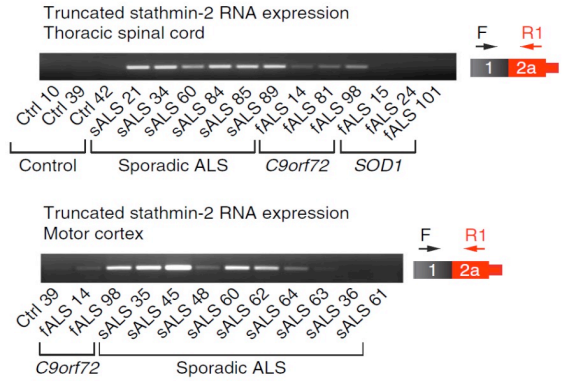


Loss of TDP-43 from the nucleus (ALS hallmark) leads to loss of STMN2

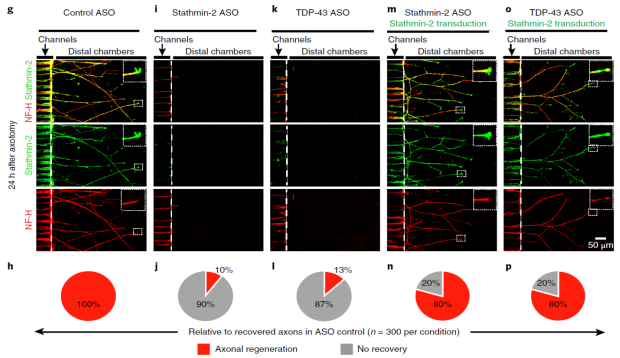


CLEVELAND LAB

Truncated STMN2 mRNA abundant in sporadic ALS spinal cord and brain



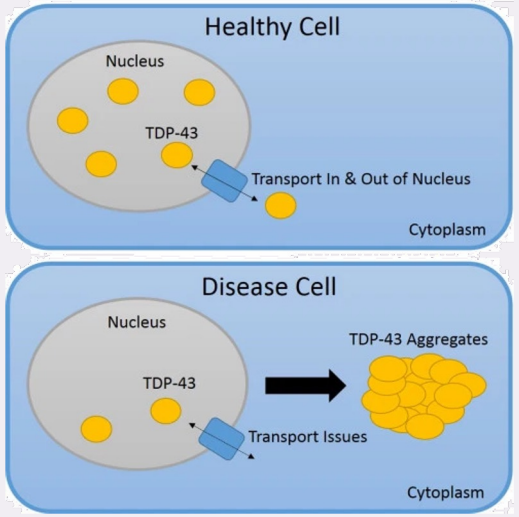
TDP-43 loss causes loss of axon repair Rescue by restoring STMN2 levels



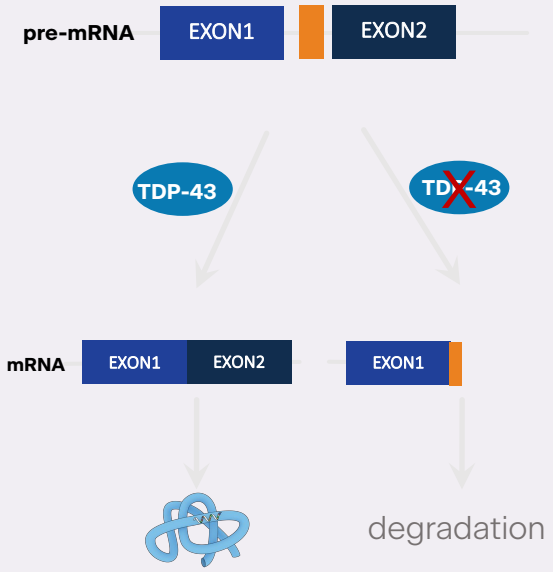
STMN2: A Genetic Target for the Sporadic ALS Population

QURALIS THERAPEUTIC STRATEGY

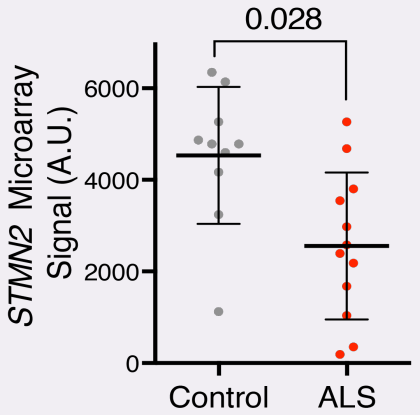
In ALS motor neurons TDP-43 leaves the nucleus



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

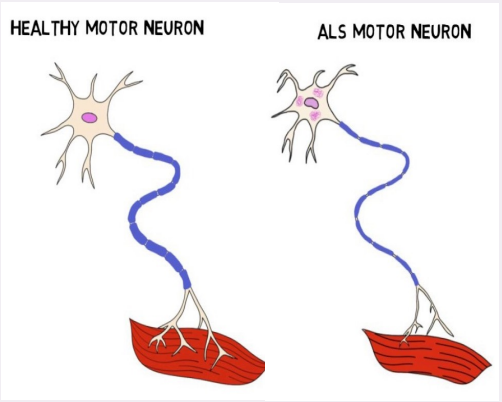


Loss of full length STMN2...



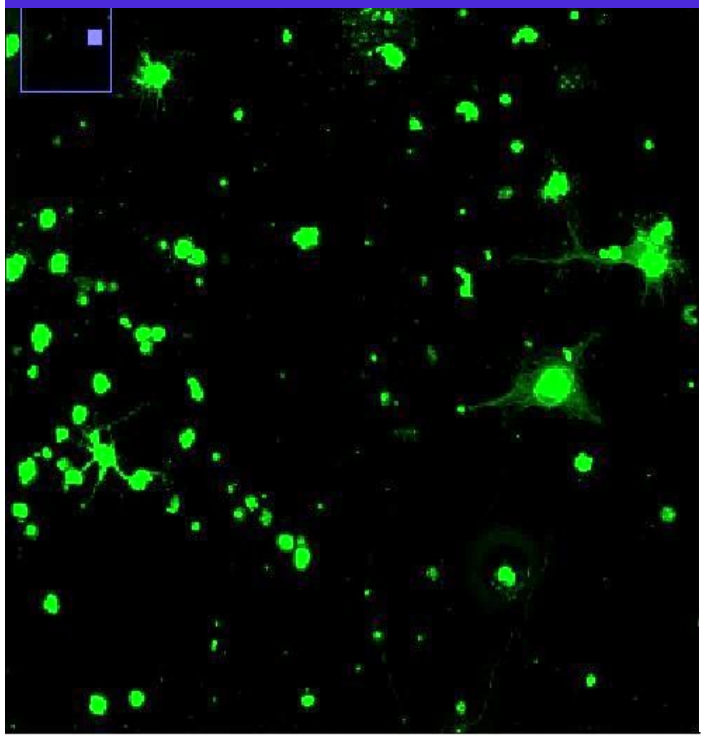
Rabin et al., 2009

...leads to axonal degeneration and impaired repair



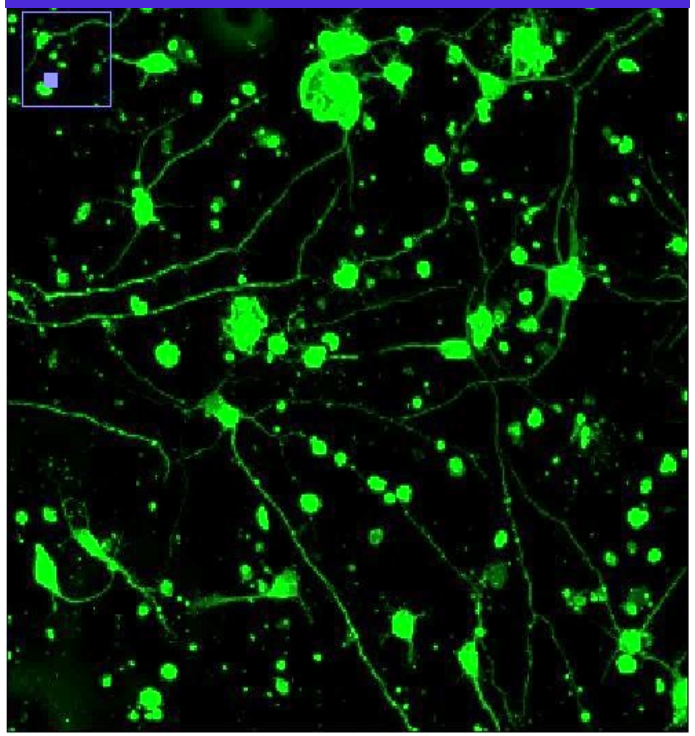
QRL-201 Protects Human Motor Neurons Against Neurodegeneration

TDP-43 TOXICITY IN HUMAN MOTOR NEURONS



Neurons Degenerate

ASO PROTECTS HUMAN MOTOR NEURONS FROM TDP-43 TOXICITY



Neurons Protected

- First-in-class therapy to treat ~90% of ALS & ~50% FTD patients
- Potent restoration of STMN2 function and TDP43 neurodegenerative phenotypes
- Target engagement and patient selection biomarker program
- Clinical trials initiated
- Genetic target for sporadic ALS and FTD with additional opportunities in AD and PD

QurAlis' Growth Strategy Beyond ALS

QurAlis™

Combinations
New Indications / Targets

FlexASO™ Platform (Next-gen ASOs, Bio-superiors)

Additional Indications (e.g., FTD, AD)

ALS (Sub-forms of the disease)

New Insights

into human genetics and stem cell technology provide genetically validated targets for ALS and other neurodegenerative diseases

Next-Gen Precision Medicine

approaches using biomarkers for patient selection, target engagement, and efficacy

First- & Best-in-Class Programs

- Two programs in the clinic
- First efficacy biomarker readouts in 2025*

Two Proprietary Platforms

- Only company with comprehensive TDP-43 platform
- Novel FlexAS™ platform for splice modulator targets

World-Class Leadership

in place for execution

*Dependent on funding decisions

Thank You

For more information contact:
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