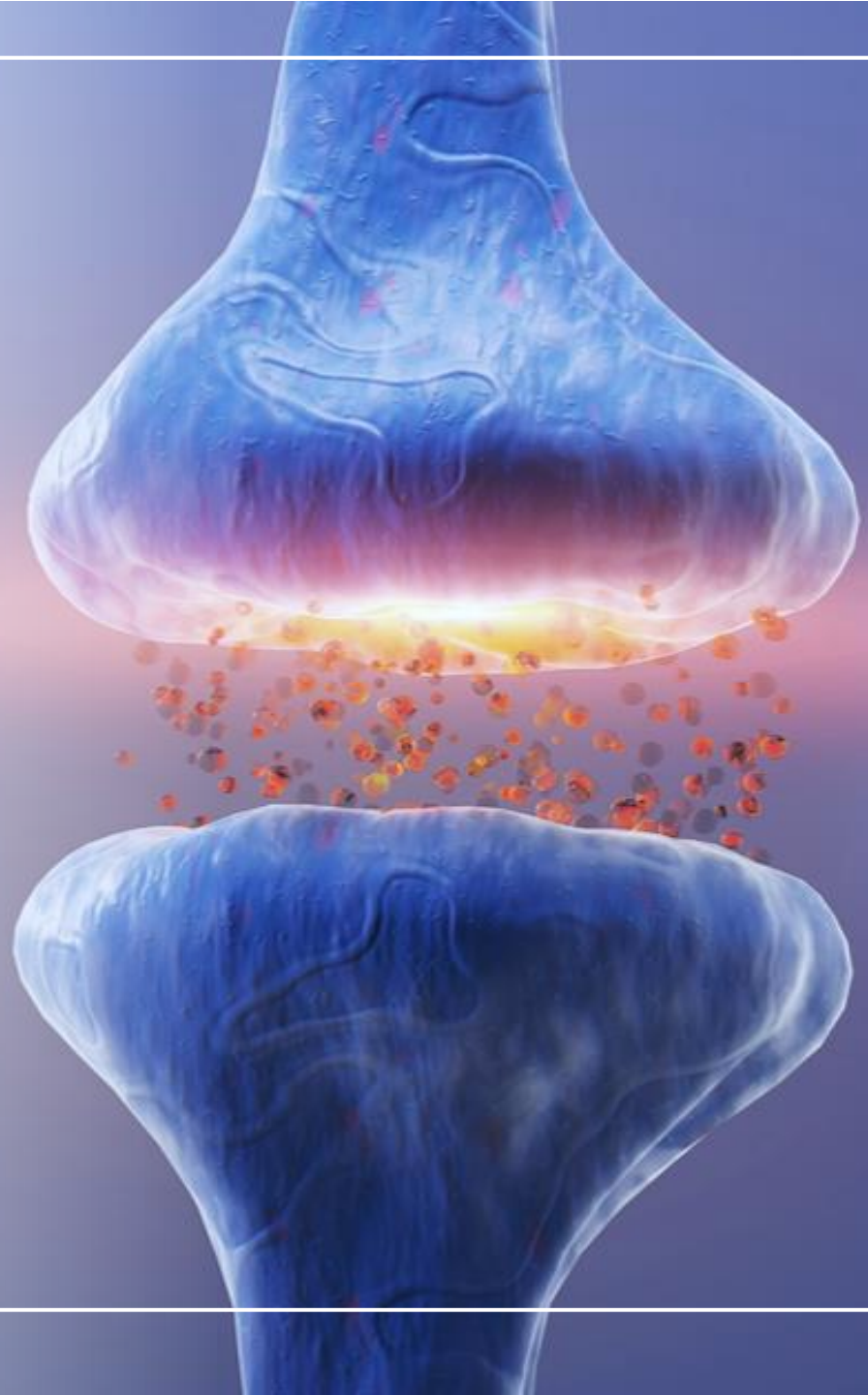
NeuroSense Therapeutics



April 2024

Nasdaq: NRSN

NeuroSense Therapeutics
Nasdaq: NRSN

Forward-Looking Statements

This presentation and oral statements made regarding the subject of this presentation contain "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements contained in this presentation other than statements of historical facts, including our business strategy and plans and objectives for future operations, including our financial performance, are forward looking statements. The words " anticipate"," believe," "continue," "estimate," "expect," "intend," "may," "will" and similar expressions are intended to identify forward looking statements. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short term and long-term business operations and objectives and financial needs.

Forward looking statements made in this presentation include statements about the timing of reporting neurofilament and biomarker results from our ALS Phase 2b clinical trial and of other clinical and regulatory milestones, including target market and opportunities for our product candidates; our expectations regarding our competitive advantages; the planned development timeline of our product candidates; and characterizations of the pre-clinical and clinical trial results of our product candidates. Forward looking statements are subject to a number of risks and uncertainties and represent our views only as of the date of the presentation. The future events and trends discussed in this presentation may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements due to, among other things, a delay in the reporting of neurofilament and biomarker results from our ALS Phase 2b clinical trial, a delay in other clinical and regulatory milestones, and the development and commercial potential of any product candidates. More information about the risks and uncertainties affecting the Company is contained under the heading "Risk Factors" in the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 22, 2023 and the Company's subsequent filings with the SEC. We undertake no obligation or duty to update information contained in these forward-looking statements, whether as a result of new information, future events or otherwise.

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NeuroSense Highlights

Developing **novel therapies for neurodegenerative diseases of high unmet need**

Significant top line results from Phase 2b study for ALS[1]

Additional catalysts expected:
Biomarker results
(H1 2024)

Patent coverage for novel formulation, method & combination

(until 2038)

Expedited and de-risked regulatory pathway

(orphan drug designation / 505(b)2 pathway)

Global opportunity in ALS

[1] ALS - Amyotrophic Lateral Sclerosis, also referred to as Lou Gehrig's Disease

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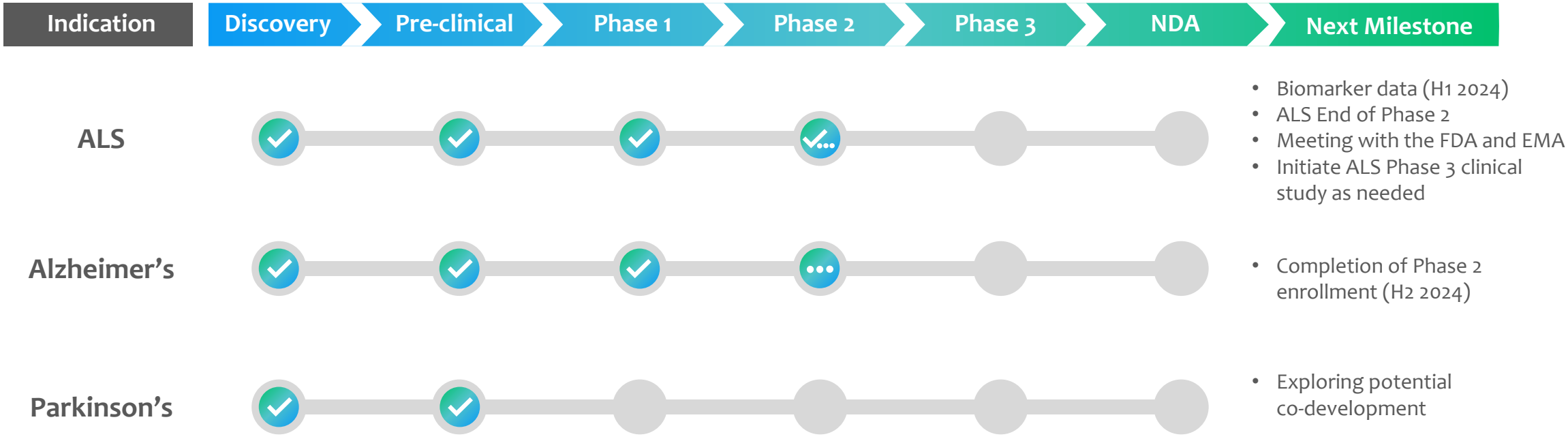
Neurodegeneration Focused Pipeline

Diseases with Significant Unmet Need and Substantial Commercial Opportunity



- Biomarker data (H1 2024)
- ALS End of Phase 2
- Meeting with the FDA and EMA
- Initiate ALS Phase 3 clinical study as needed

- Completion of Phase 2 enrollment (H2 2024)

- Exploring potential co-development

[1] NfL: Neurofilament

ALS

is an incurable neurodegenerative disease, causing complete paralysis and ultimately death within 2-5 years from diagnosis

+5,000

New cases of ALS each year (US)[1]

>80,000

ALS Patients in NeuroSense's planned target market[2]

~$3B

Annual Market Opportunity[3]

~24%

Growth in Patients by 2040 in the US and EU[2]

[1] Johns Hopkins Medicine
[2] Projected increase in amyotrophic lateral sclerosis from 2015 to 2040, Nature Communications, 2016
[3] Management estimate

PrimeC - Designed to Reduce Neuronal Cell Death

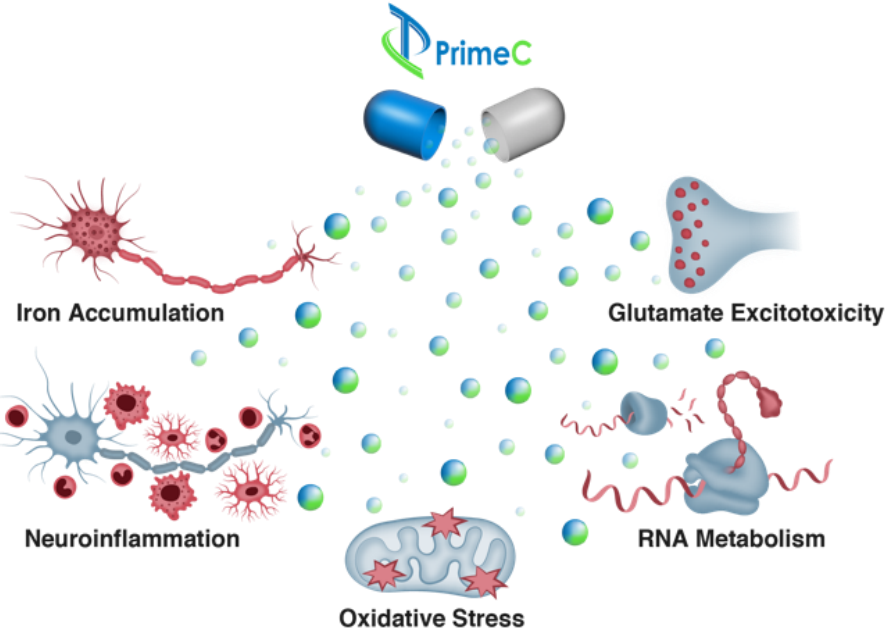
Designed to work **synergistically** on multiple targets in ALS
Novel formulation, consisting of **specific and unique doses** of two FDA-approved drugs

Celecoxib - a NSAID which reduces:

- Neuroinflammation
- Glutamate excitotoxicity
- Oxidative stress

Ciprofloxacin - a fluoroquinolone which regulates:

- MicroRNA synthesis
- Iron accumulation



PrimeC's effect on pathways which lead to neuronal cell death in ALS

PrimeC Demonstrates Synergies *In-Vitro* & *In-Vivo*

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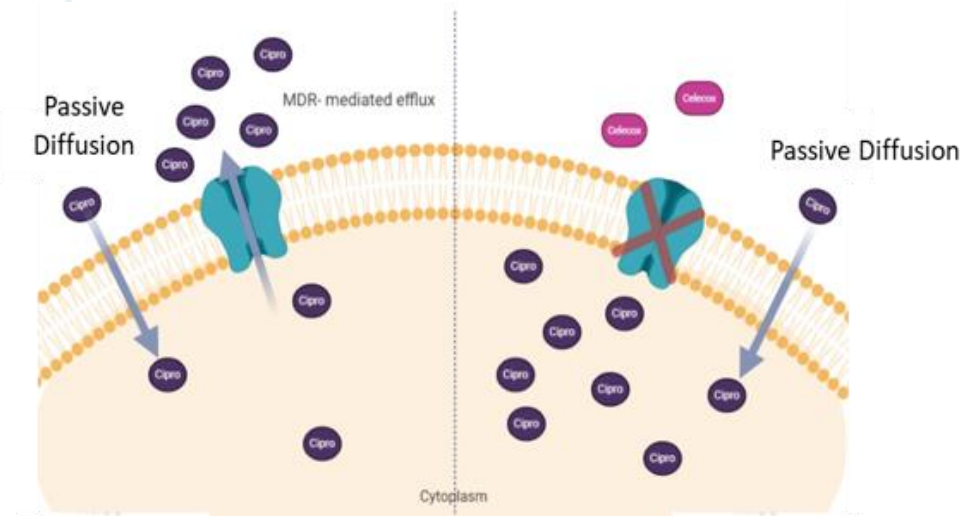
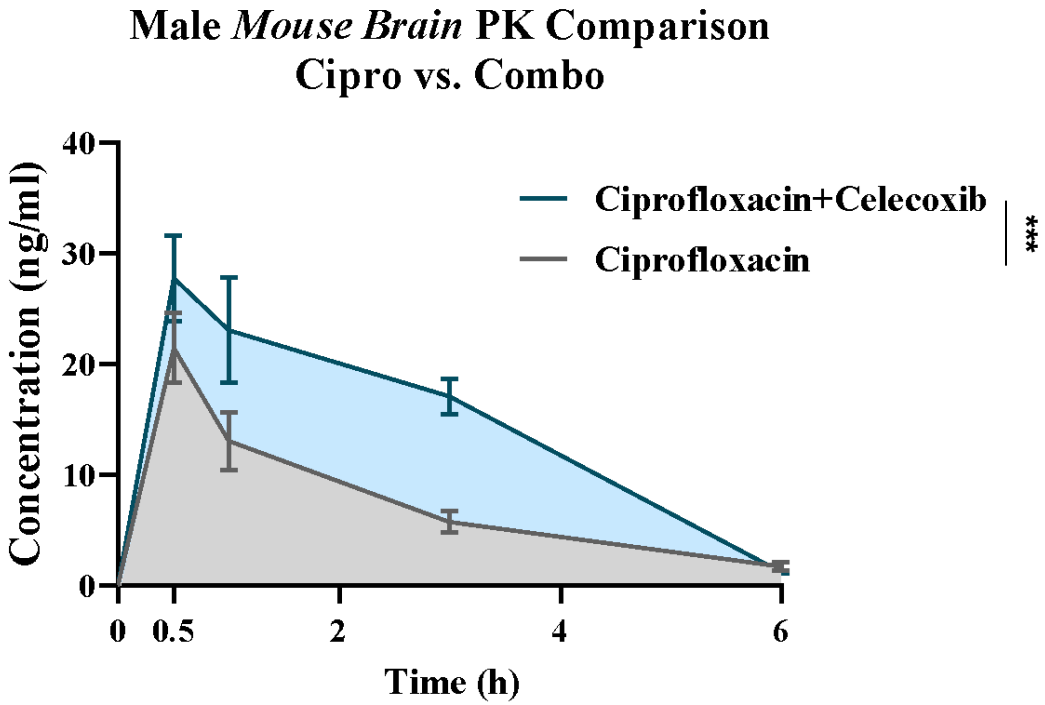
Synergistic Mode of Action



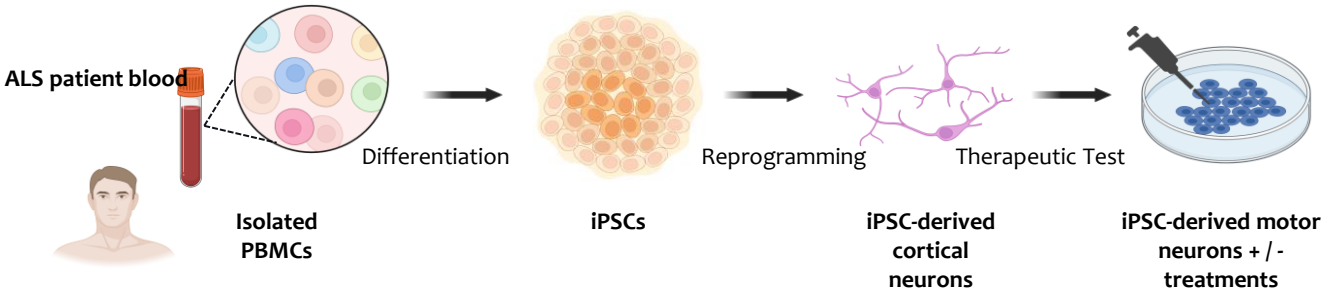
Celecoxib is blocking efflux of **Ciprofloxacin,** thus increasing its concentration in the neurons

Improved Pharmacokinetic (PK) Profile

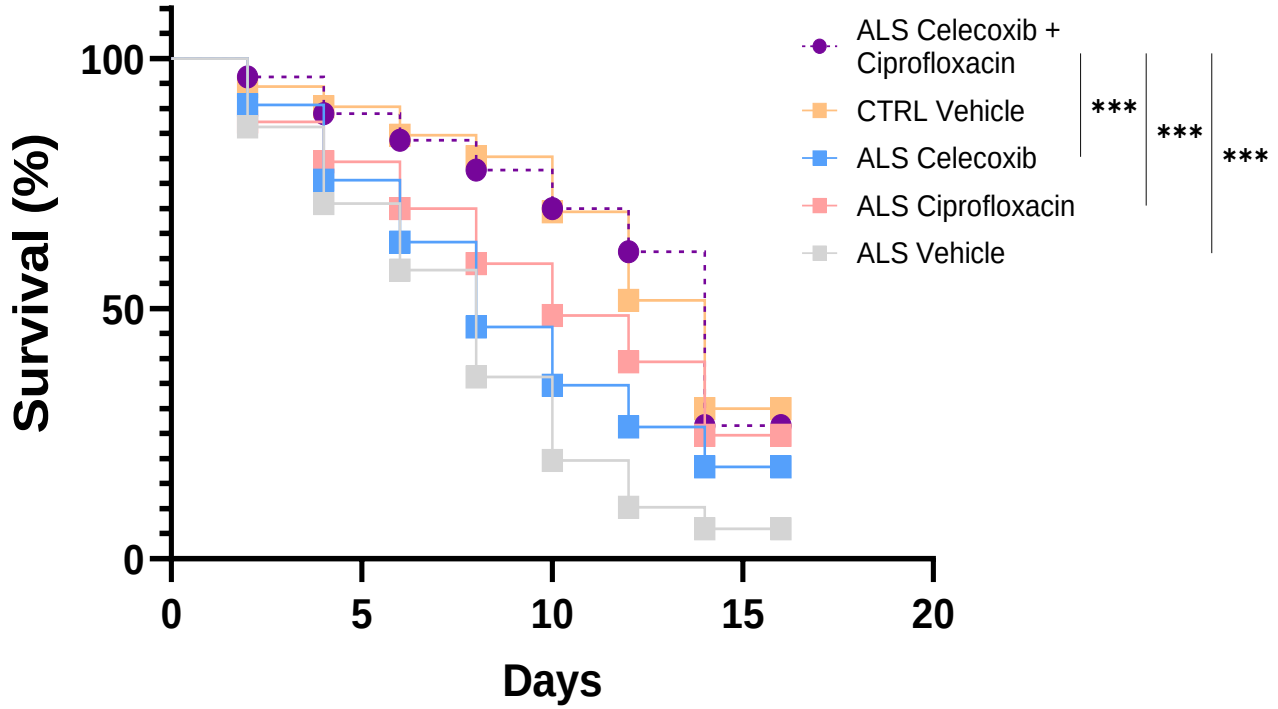


PrimeC's combination (**Celecoxib** + **Ciprofloxacin**) **remained at a higher concentration in rodent brain tissue for longer,** when compared to administration of **Ciprofloxacin alone**

Efficacy in Well Established ALS Model



Combination Showed Superior Cell Survival



Studies from Prof. Justin Ichida's lab, USC, induced Pluripotent Stem Cells (iPSCs) Generated from blood of People Living with ALS

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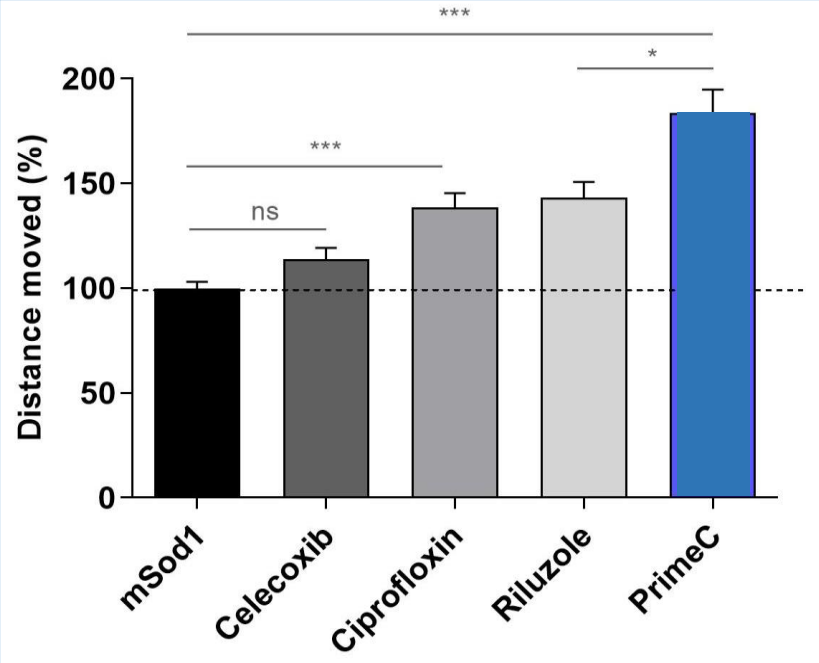
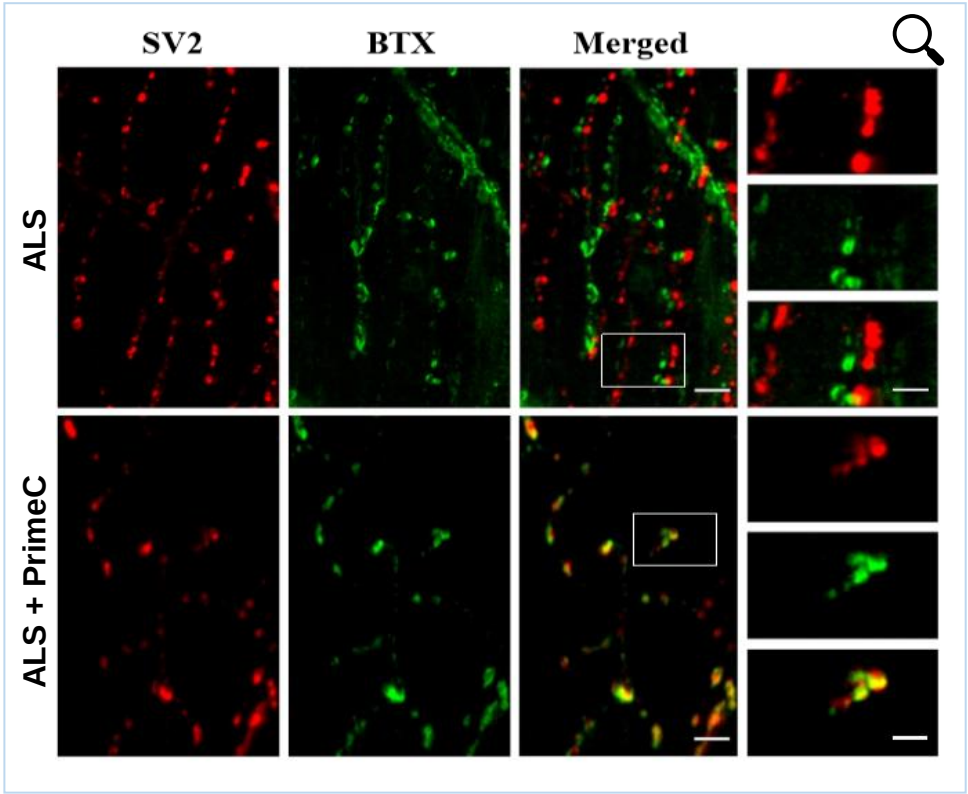
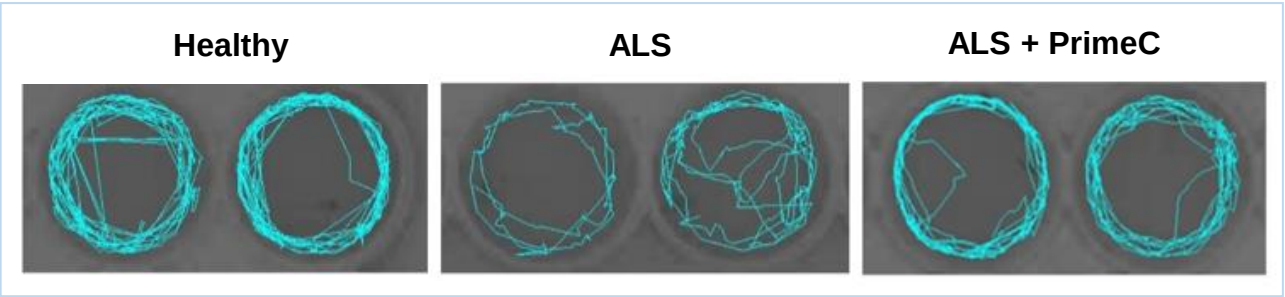
PrimeC Demonstrated Statistically Significant Efficacy *In-Vivo*

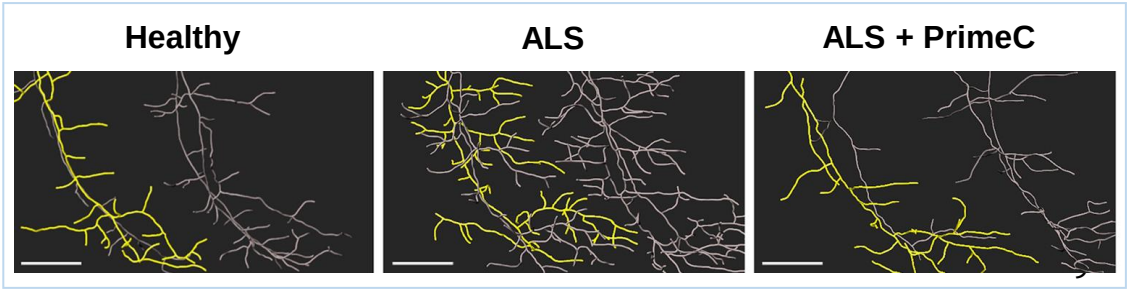
Improved Motor Performance



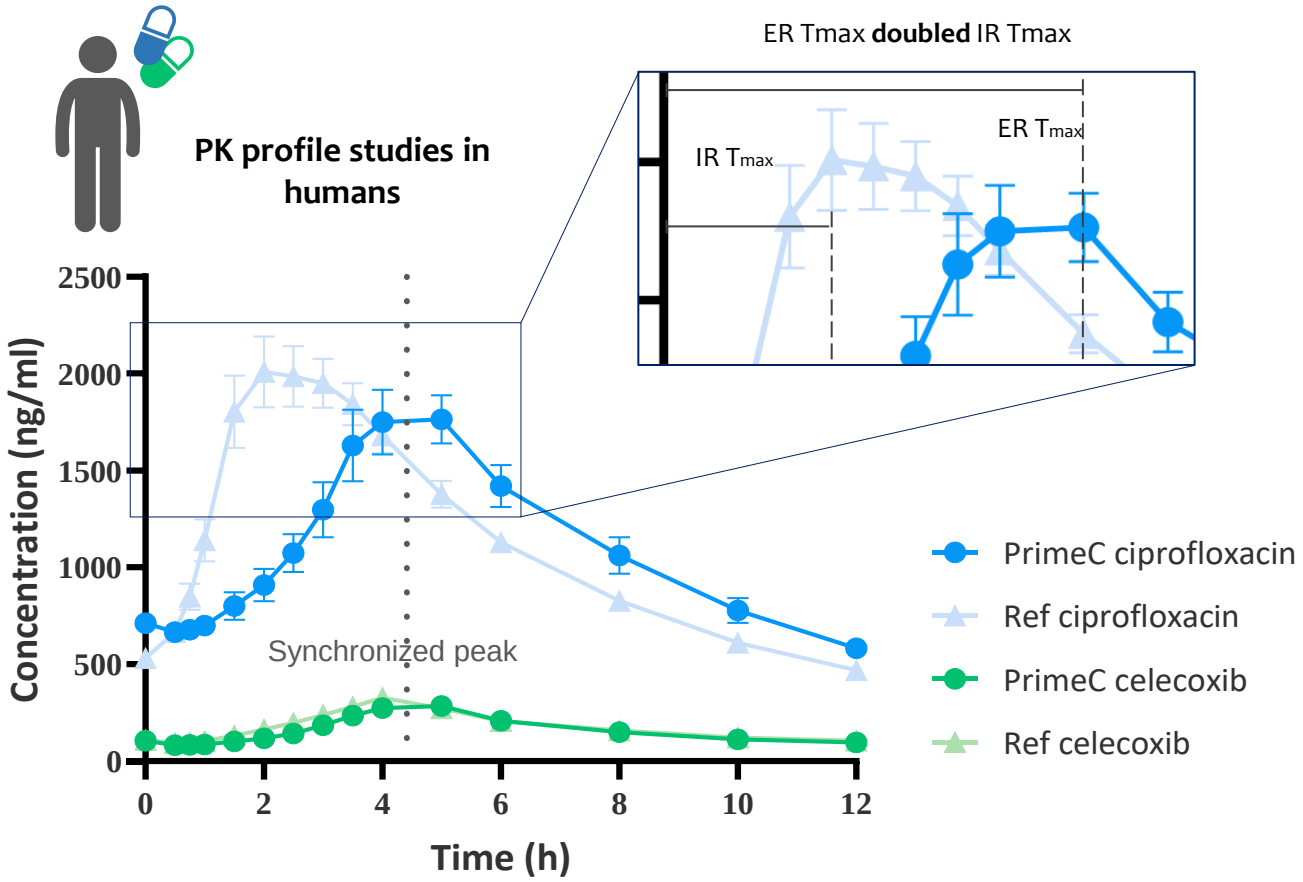
Recovered Neuronal Structures







PrimeC Unique Formulation Induces a Synchronized PK Profile



The **synchronized PK** profiles of the two compounds, potentially **maximizes synergies**

PrimeC Met Primary and Exploratory Endpoints in a Phase 2a Study

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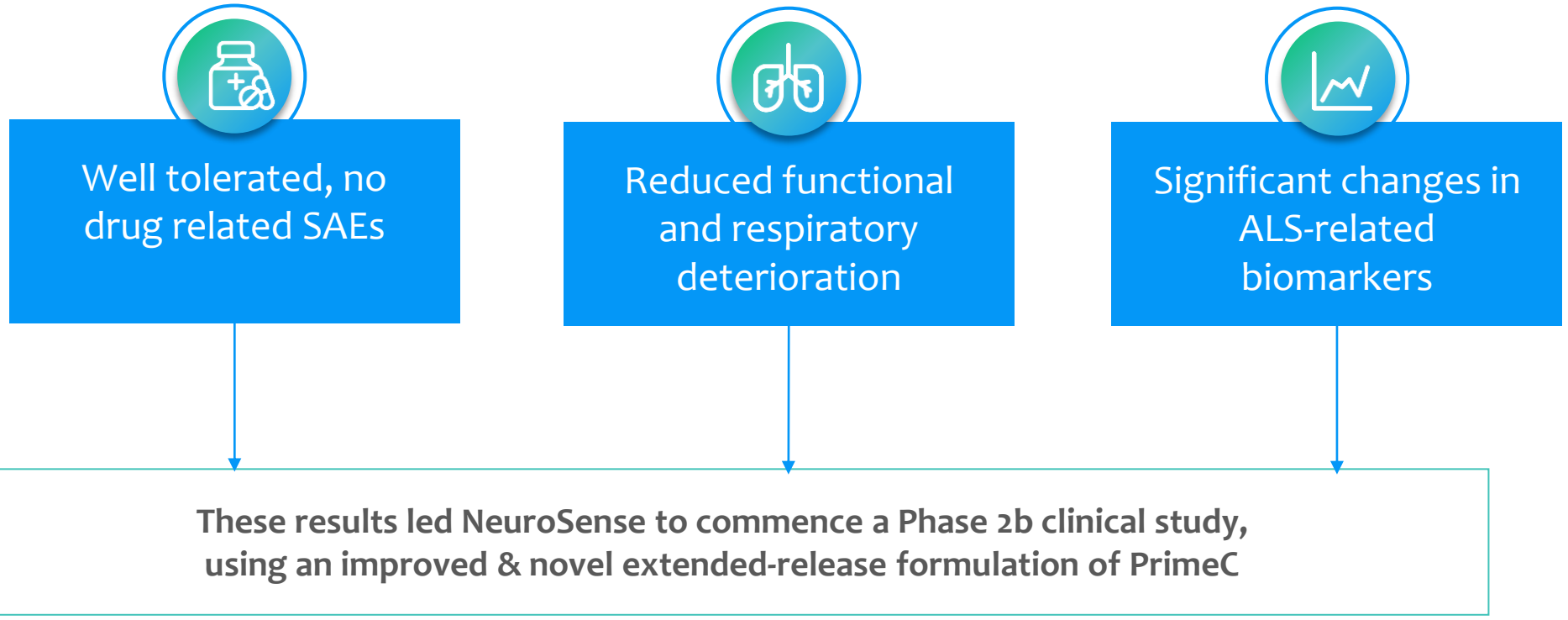
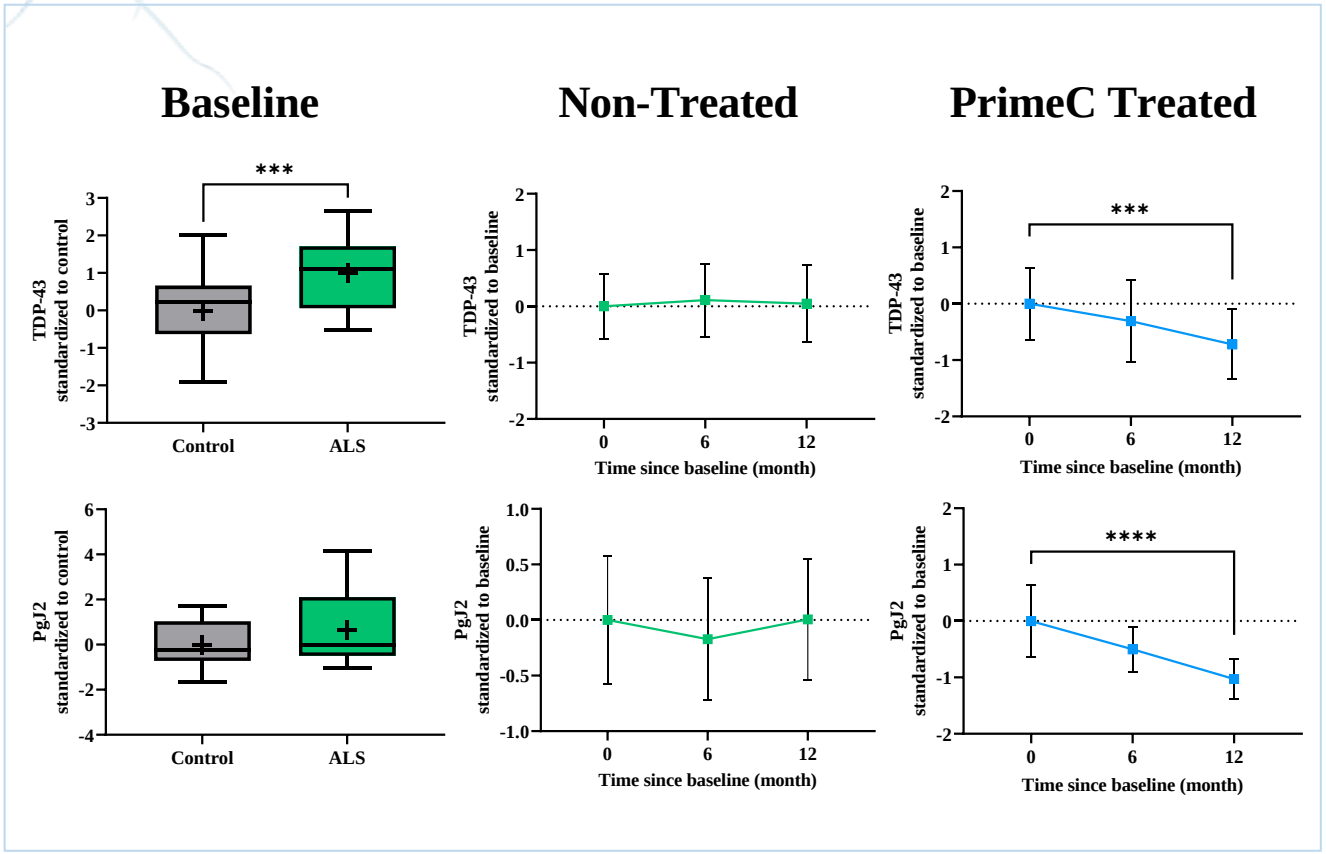
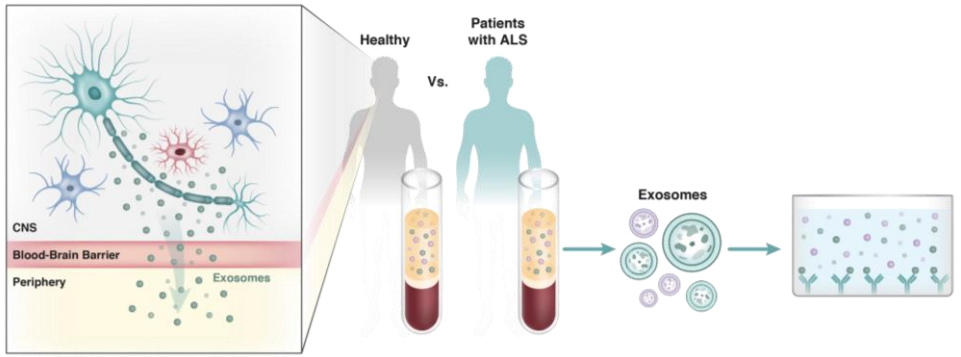
NST002

- **15** patients
- Open-Label
- **Intermediate formulation** of PrimeC
- **12**-month dosing
- Clinic visit every **3** months
- Phone visit every **1.5** months
- **Location:** Tel Aviv Sourasky Medical Center



PrimeC Reduces Neuroinflammation and TDP-43 Levels



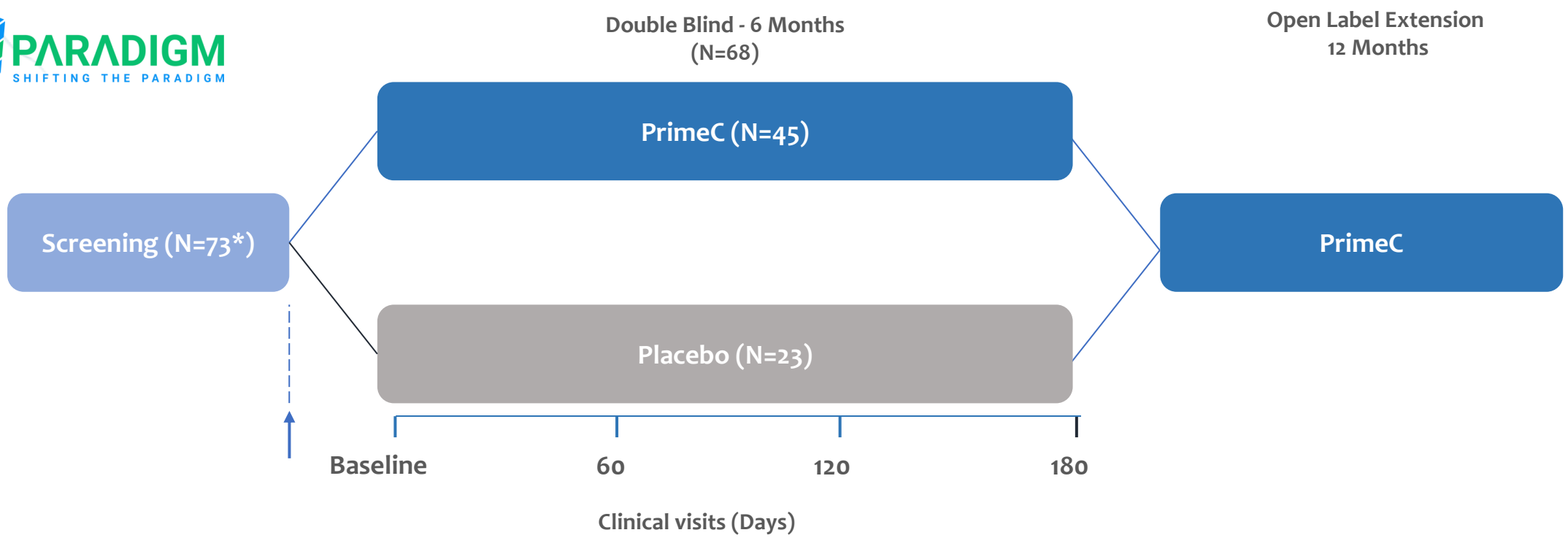


NST002 study

The effect of PrimeC on selected biomarkers was tested in samples from an open-label Phase 2a study

PARADIGM Phase 2b Trial Design

Randomized, Prospective, Double-Blind, Placebo-Controlled Study



PARADIGM used PrimeC's novel extended-release formulation

~90% of patients in PrimeC and Placebo groups were co-treated with Riluzole

** 4 Screen Failures, 1 participant misdiagnosed for ALS*

PARADIGM Trial Endpoints

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Primary Endpoints

1

- Safety and Tolerability Measures
- ALS-Hallmark Biomarker Measures of TDP-43 and ProstaglandinJ2 (results expected H1 2024)

Secondary Efficacy Endpoints

2

- ALSFRS-R (ALS Functional Rating Scale)
- SVC (Slow Vital Capacity)
- PROMIS-10 quality of life questionnaire
- Complication Free Survival

Exploratory Endpoint

- King's/MiToS
- Neurofilament-Light Chain

PARADIGM Inclusions / Exclusions Criteria

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Inclusion Criteria

- Males or females between the ages of 18 and 75 years of age
- Diagnosis of familial or sporadic ALS
- Disease duration less than 30 months prior to screening
- Pre-enrollment ALSFRS-R slope from disease onset ≥ 0.3 points per month
- ALSFRS-R at screening ≥ 25
- Item 3 (swallowing) in ALSFRS-R ≥ 3
- Subjects may be treated in parallel with Riluzole and/or Edaravone and/or Sodium Phenylbutyrate/TUDCA
- Upright slow vital capacity (SVC) ≥ 60%
- 18 < BMI < 30

Exclusion Criteria

- Patients with known hypersensitivity to celecoxib or ciprofloxacin and related exclusions derivative from the celecoxib and ciprofloxacin labels

ITT and PP Pre-specified Analyses

Intent to Treat (ITT) and Per Protocol (PP) are both pre-specified analyses within the study

ITT assesses the effect of the treatment on all patients enrolled in the study while PP analysis includes only patients who strictly adhered to the study protocol[1]

Both analyses are valid, yet PP best answers the question of what is the effect of receiving the treatment on a group of patients versus the effect of assigning the treatment to a group of patients

Analysis

Pre-defined populations

	ITT (N=68)	PP (N=62)
PrimeC	n=45	n=43
Placebo	n=23	n=19

PARADIGM Well Balanced Baseline Characteristics

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	PrimeC n=45	Placebo n=23
Male	60.0%	60.9%
Female	40.0%	39.1%
Age	59.1	54.9
Height (cm)	170.8	171.2
Weight (kg)	70.6	71.1
BMI (kg/m2)	24.1	24.0
TRICALS Risk Profile	-4.2	-4.4
Patients on background ALS therapy	91%	87%
PP Analysis (PrimeC=43; Placebo=19)		
ALSFRS-R at baseline	37.9	37.9
% Predicted SVC at baseline	89.4	83.9

PARADIGM Achieved Primary Endpoints with a Safety and Tolerability Profile Comparable to Placebo

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Summary of All Adverse Events	PrimeC (N=45)	Placebo (N=23)
Adverse Events (AE)	68.9%	65.2%
Treatment-Emergent AEs (TEAE)	68.9%	65.2%
Study Drug Related Treatment-Emergent AEs (TEAE)	20.0%	4.3%
Serious Treatment-Emergent AEs (TEAE)	8.9%	8.6%
Subject death	4.4%	4.3%
TEAE leading to Study Drug Discontinuation	6.7%	4.3%
TEAE leading to Study Drug Reduction	0.0%	0.0%
TEAE leading to Study Drug Interruption	15.6%	8.6%

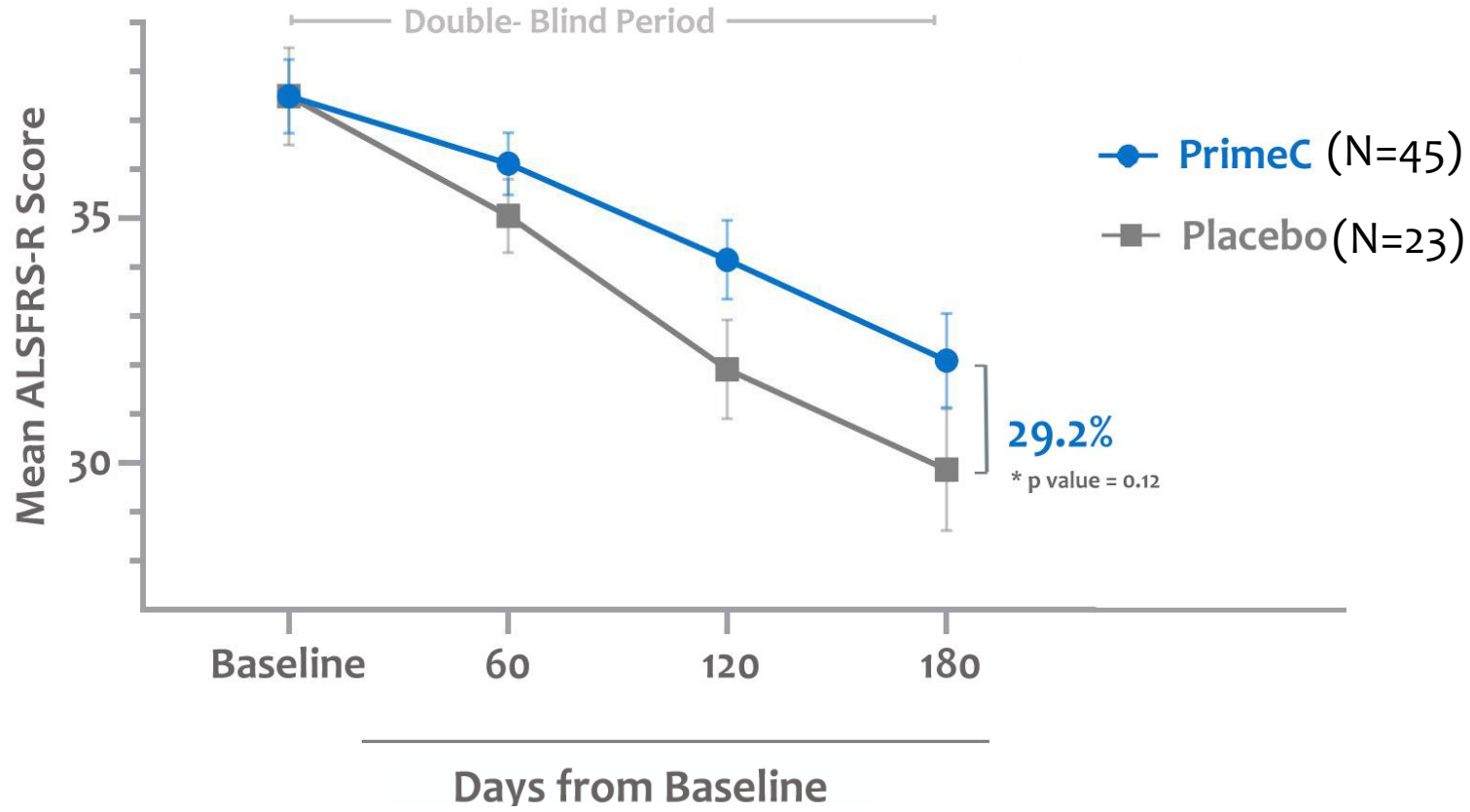
All Adverse Events Were Transient and Expected

PARADIGM Achieved Primary Endpoints with a Drug Tolerability Profile Comparable to Placebo

Tolerability is defined as time-to-discontinuation or completion of assigned study medication during the double-blind period since randomization

PrimeC Attenuated Disease Progression By 29.2% Difference in ALSFRS-R

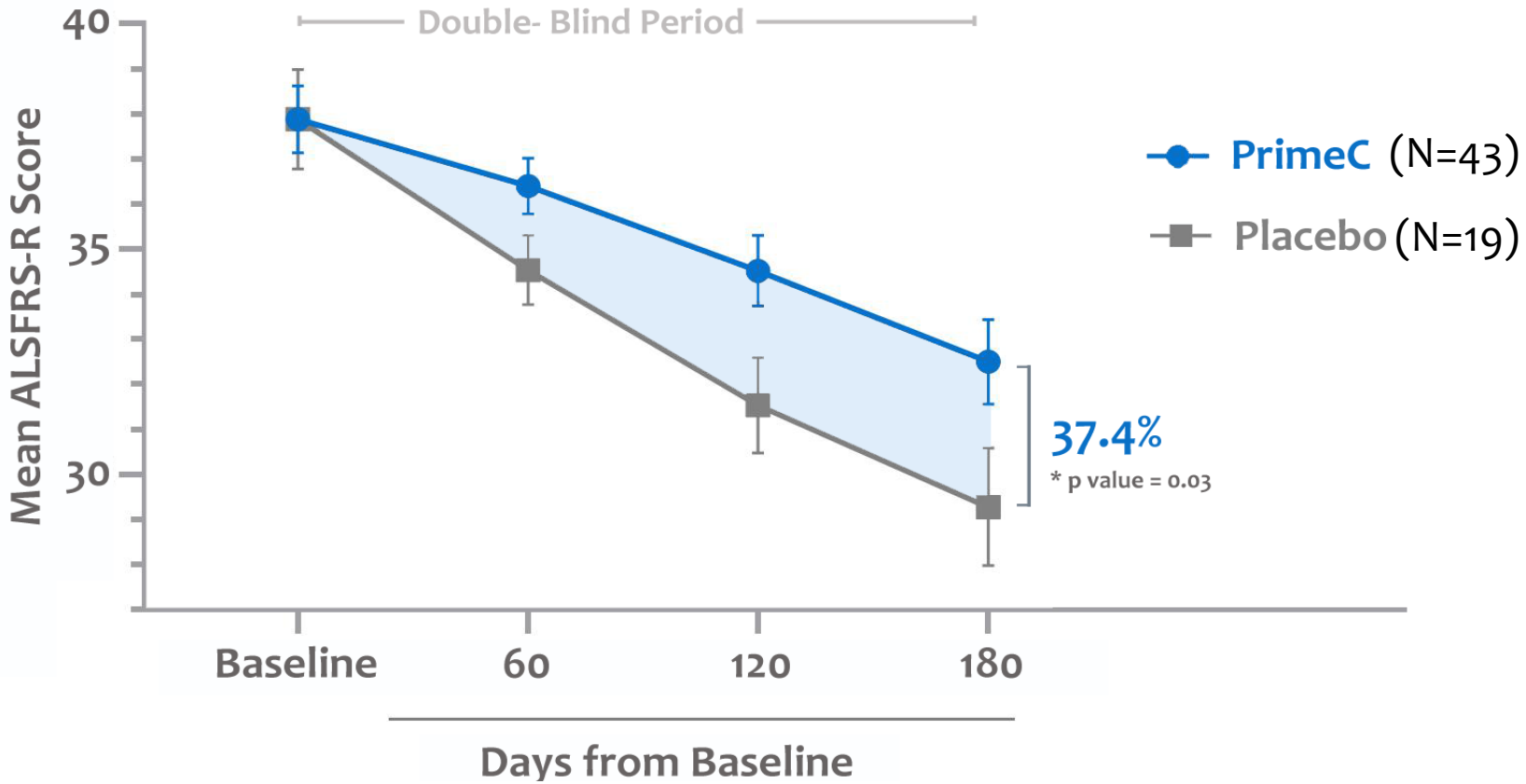
PARADIGM Results – ITT Analysis



The adjusted mean score for each treatment group, the corresponding treatment difference and p-value are analyzed using MMRM. Mean and SE.

PrimeC Significantly Attenuated Disease Progression by 37% in ALSFRS-R (p=0.03)

PARADIGM Results – PP Analysis



The adjusted mean score for each treatment group, the corresponding treatment difference and p-value are analyzed using MMRM. Mean and SE.

A Single Point Change On the ALSFRS-R Has a Significant Impact on ALS Patients

A 1-point decrease in the hands' Functional Loss Score can represent a transition from independent feeding to requiring assistance.

A 1-point stumble in the legs can be the difference between walking with a cane and not being able to walk at all.

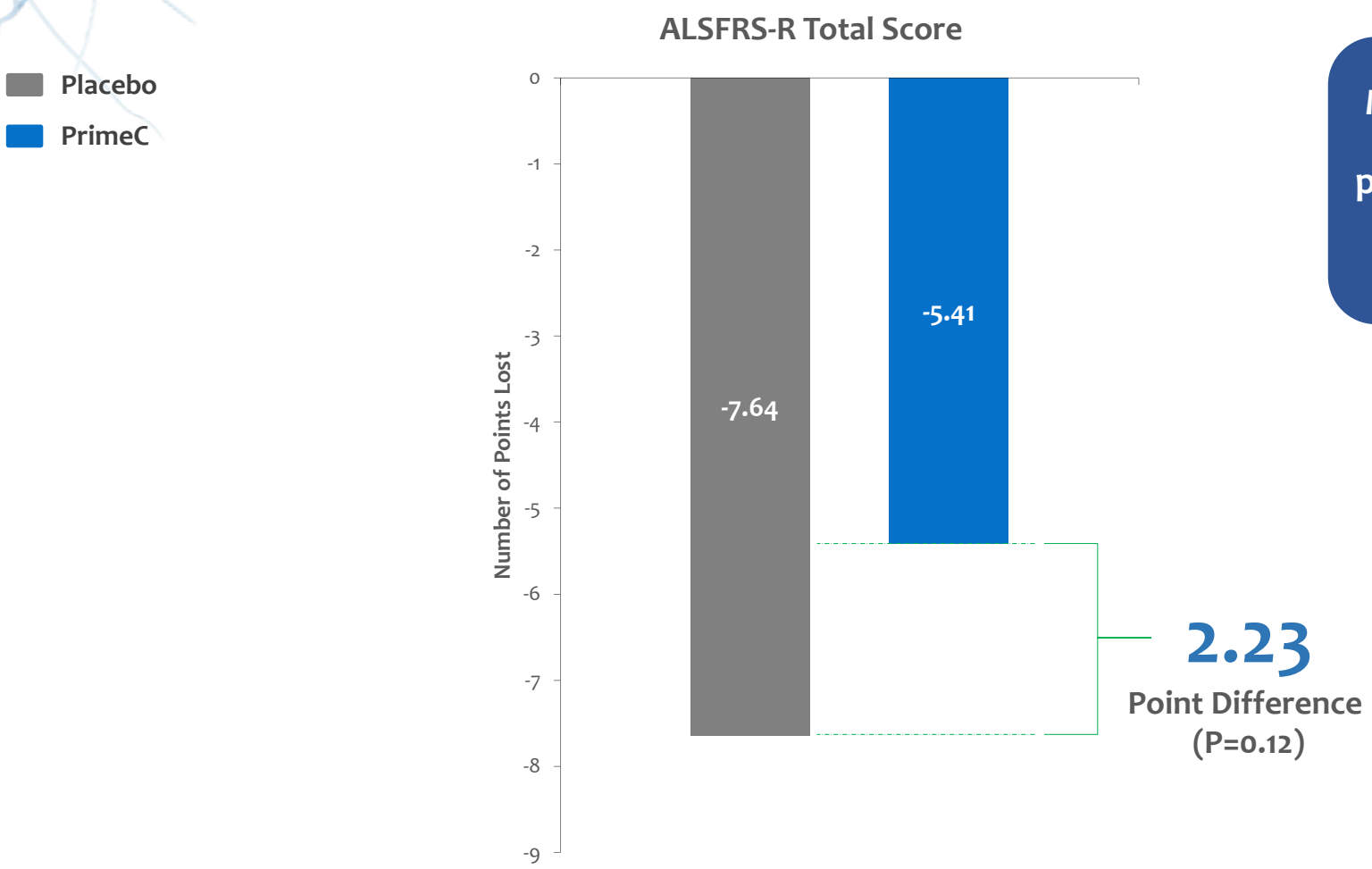
A 1-point drop on the swallowing assessment scale can mark the critical threshold between self-sufficiency and the necessity of supplemental tube feeding.

A 1-point loss in breathing can cause a transition from independent breathing to requiring the use of a machine ventilator.

Cedarbaum JM, Stambler N, Malta E, et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. BDNF ALS Study Group (Phase III). J Neurol Sci. 1999;169(1-2):13-21. doi:10.1016/s0022-510x(99)00210-5

PrimeC Slowed Decline of Physical Functions

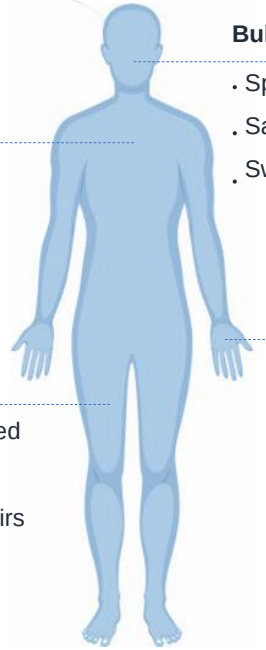
PARADIGM Results – ITT Analysis



Mean ALSFRS-R total score was 2.23 points higher at 6 months for PrimeC compared to placebo.

PrimeC Slowed Decline of Physical Functions

PARADIGM Results – ITT Analysis

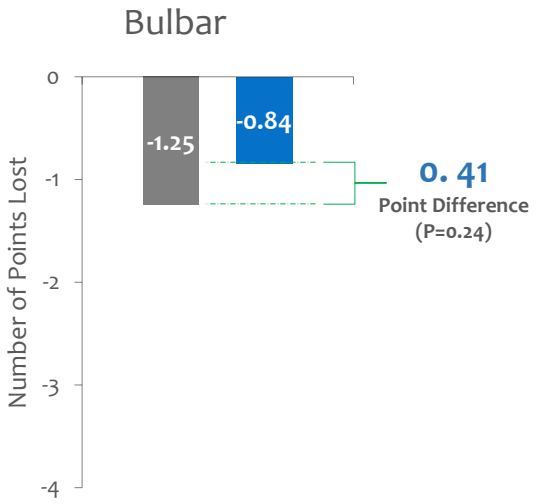


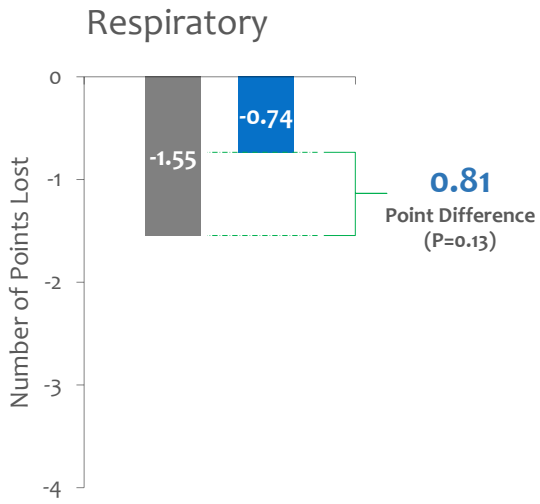
Bulbar:
- Speech
- Salivation
- Swallowing

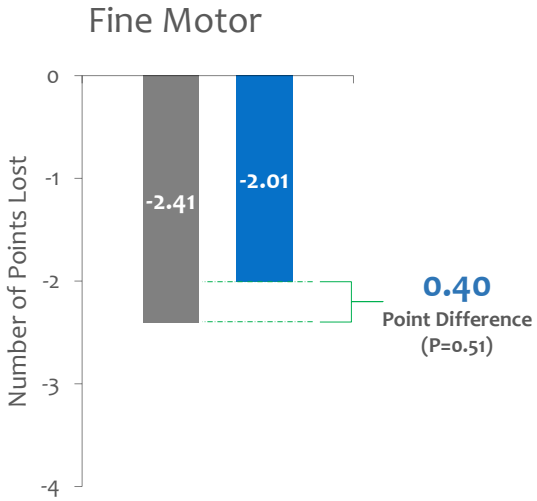
Respiratory:
- Dyspnea
- Orthopnea
- Respiratory insufficiency

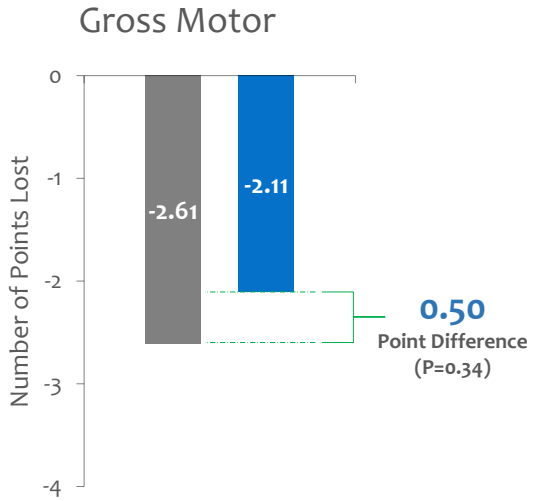
Fine Motor:
- Handwriting
- Cutting Food
- Dressing and hygiene

Gross Motor:
- Turning in bed
- Walking
- Climbing stairs









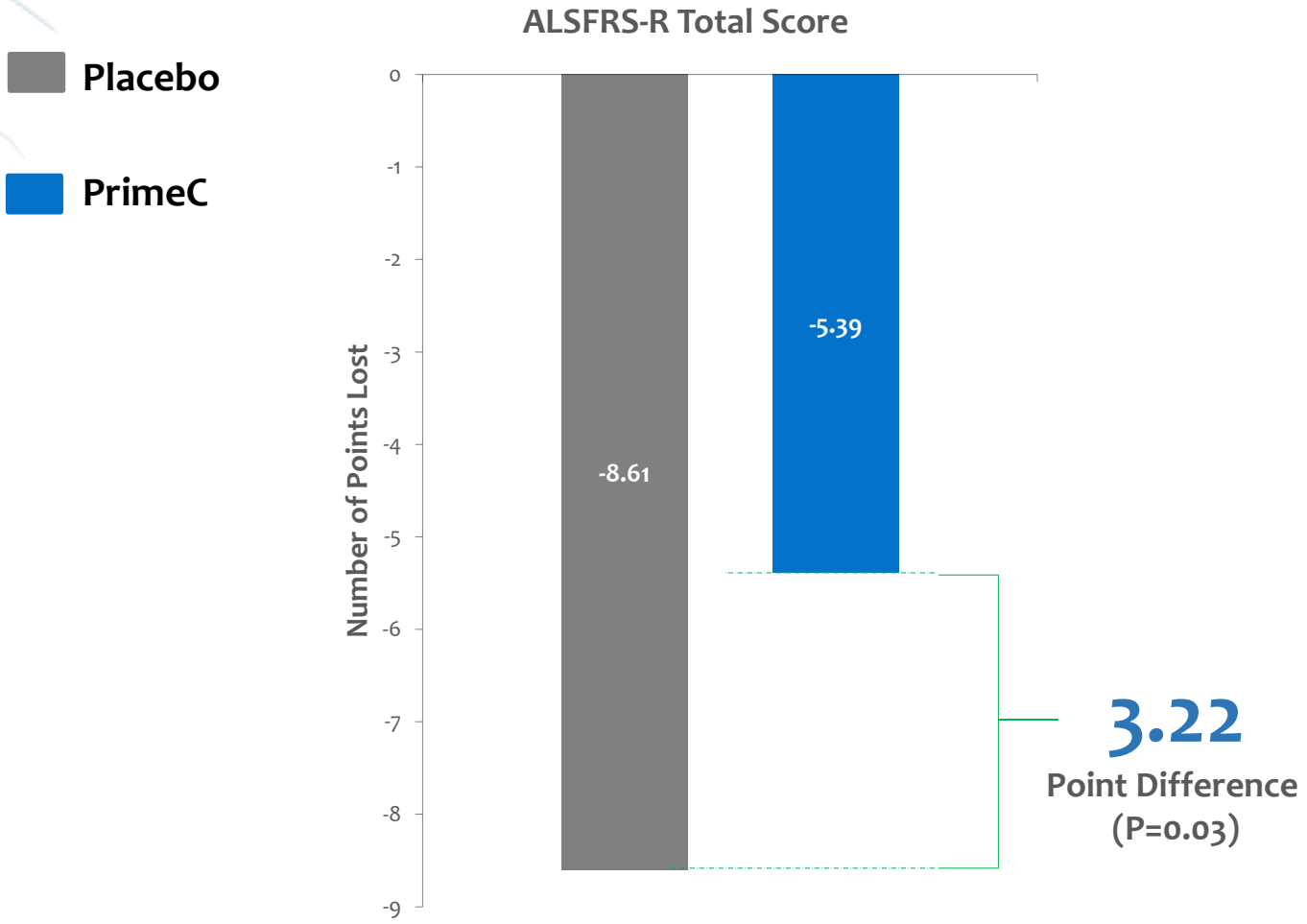
Placebo

PrimeC

Background Respiratory failure is the most common cause of death from ALS

PrimeC Slowed Decline of Physical Functions

PARADIGM Results – PP Analysis



Mean ALSFRS-R total score was 3.22 points higher at 6 months for PrimeC compared to placebo.

PrimeC Slowed Decline of Physical Functions

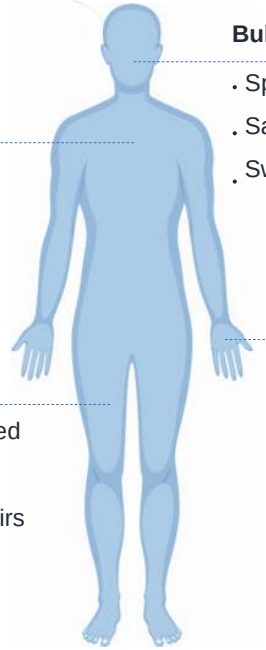
PARADIGM Results – PP Analysis

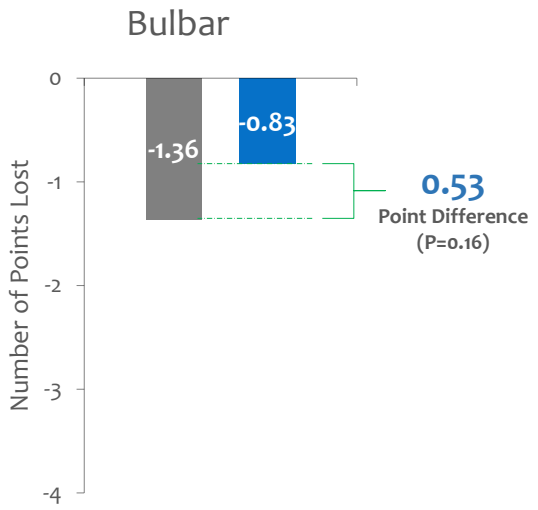
Bulbar:
- Speech
- Salivation
- Swallowing

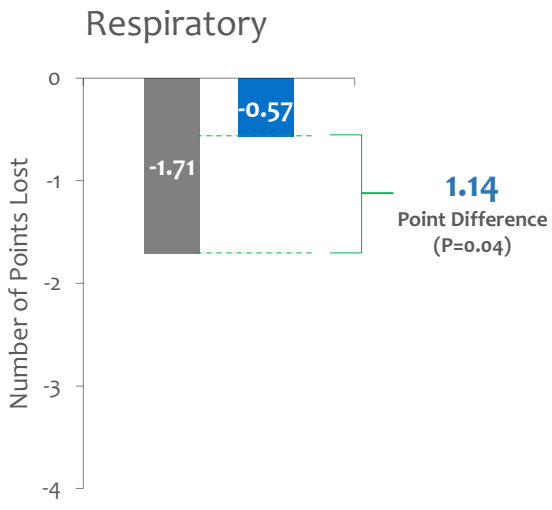
Respiratory:
- Dyspnea
- Orthopnea
- Respiratory insufficiency

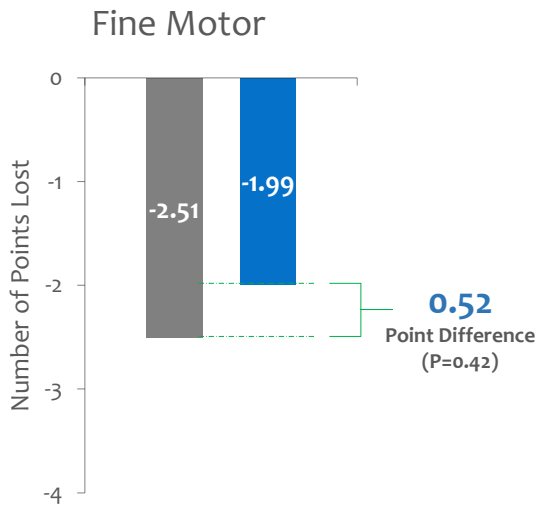
Fine Motor:
- Handwriting
- Cutting Food
- Dressing and hygiene

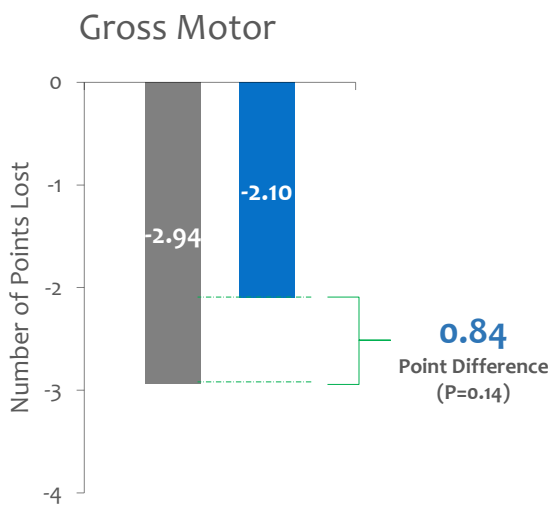
Gross Motor:
- Turning in bed
- Walking
- Climbing stairs











Placebo

PrimeC

Background
Respiratory failure is the most common cause of death from ALS

Effect of Treatment on Slow Vital Capacity (SVC)

PARADIGM Results – ITT and PP Analysis

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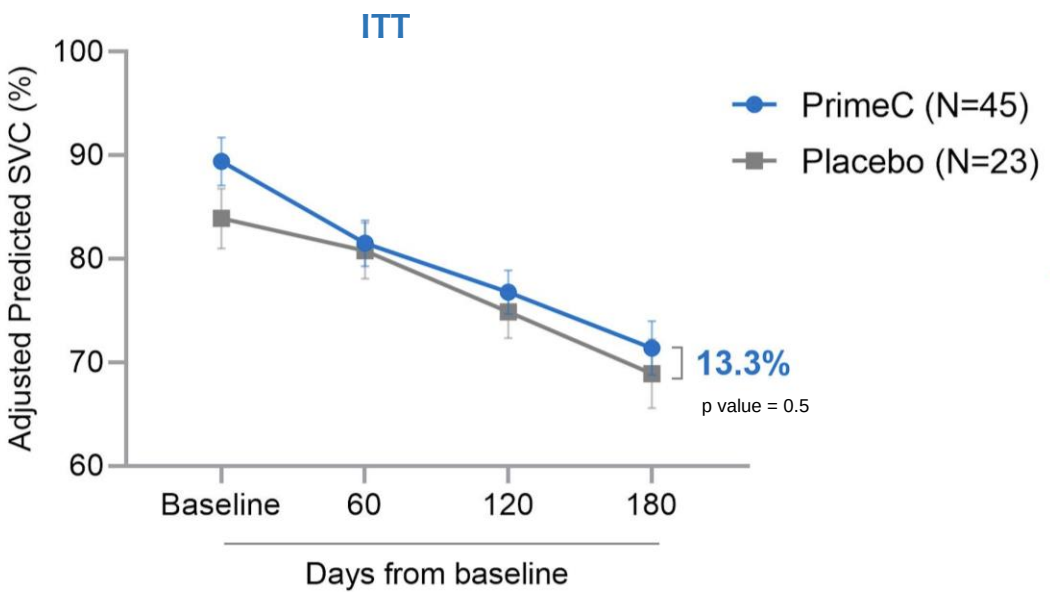
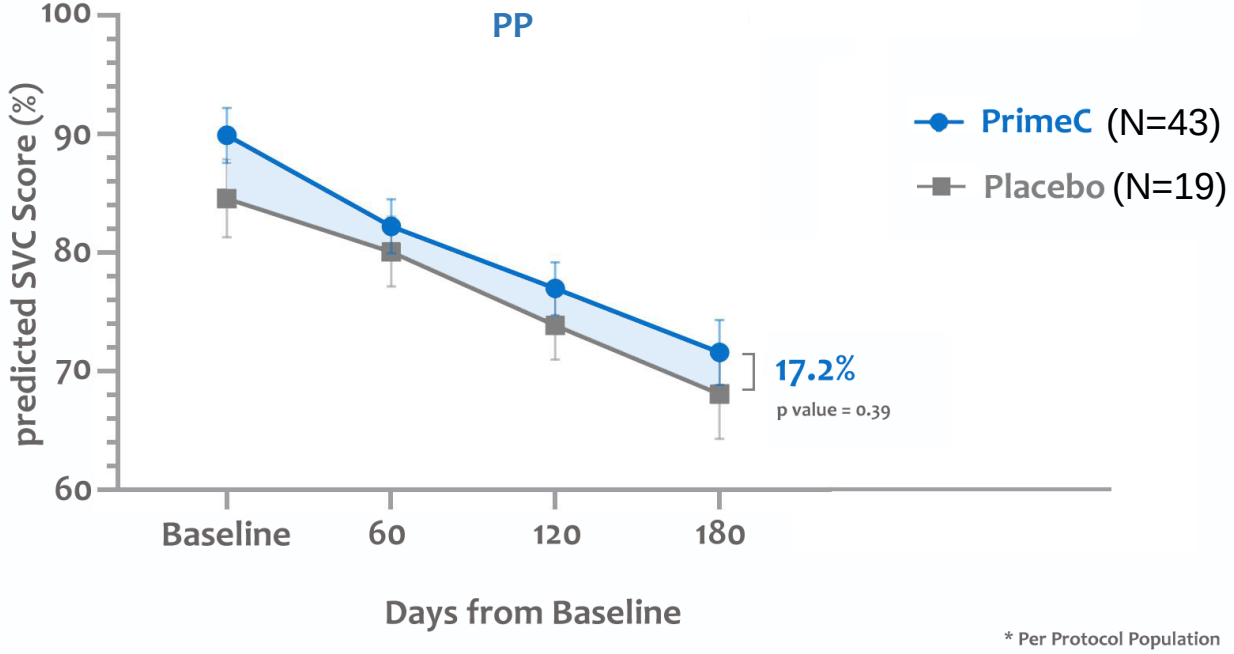




* Per Protocol Population

The adjusted mean score for each treatment group, the corresponding treatment difference and p-value are analyzed using MMRM. Mean and SE.

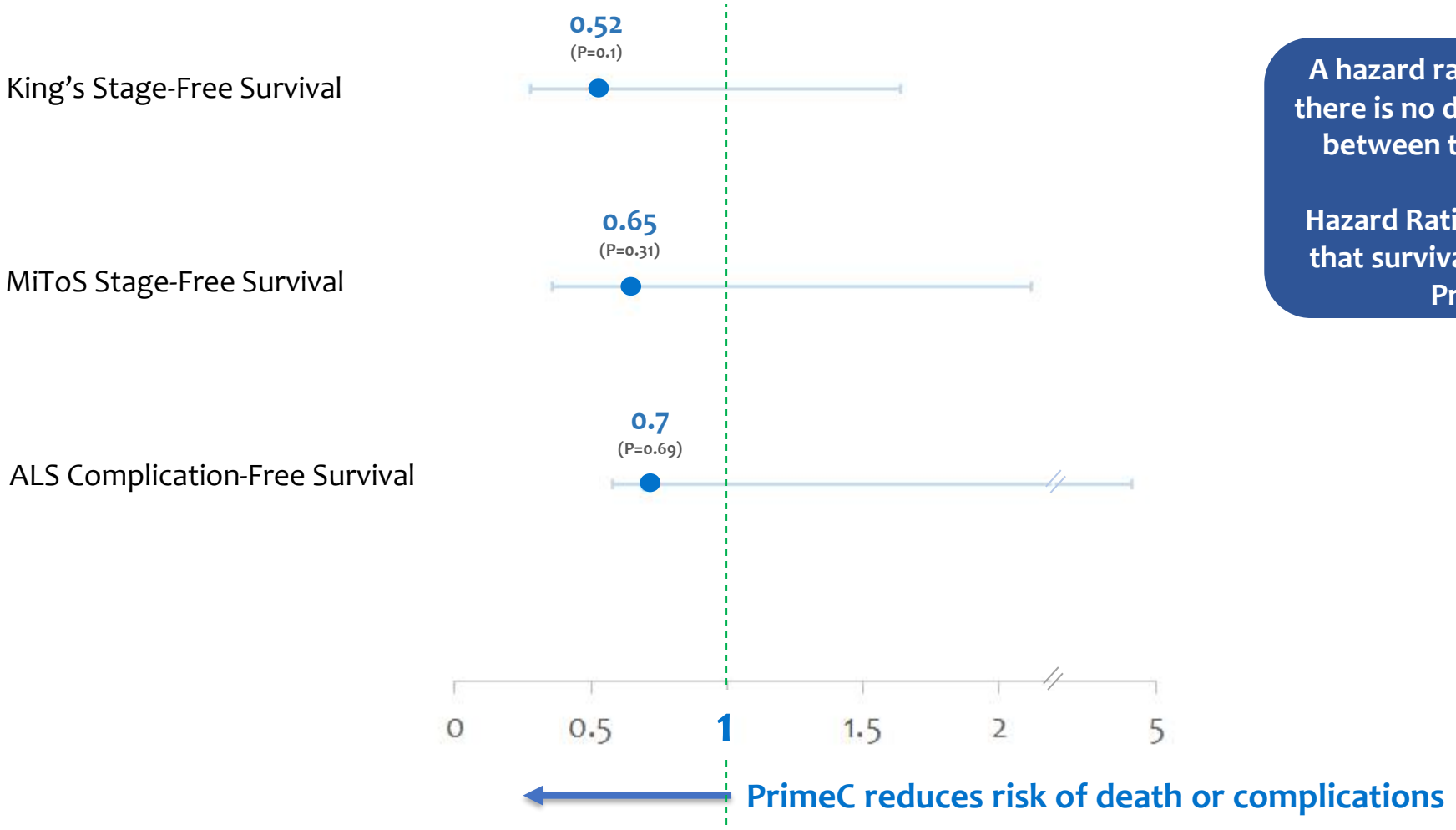
Complication free Survival Probability Measures

ALS Complications analysis includes death from any cause or respiratory insufficiency or hospitalization due to ALS-related complications

The **MiToS** system uses six stages, from 0 to 5 and is based on functional ability (ALSFRS-R)
stage 0 = normal function stage 5 = death

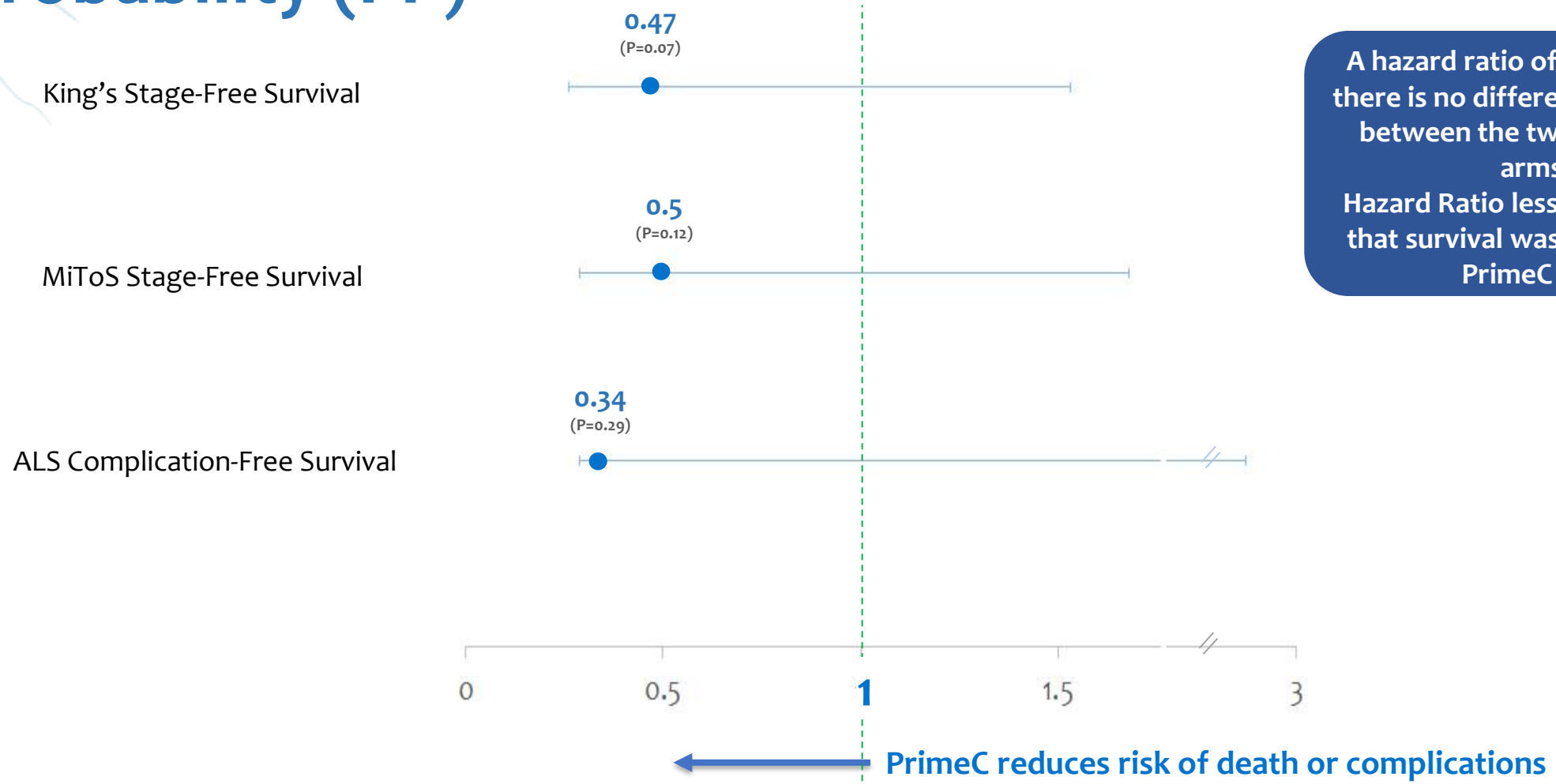
The **King's** system uses five stages from 1 to 5
based on disease burden (clinical involvement, feeding or respiratory failure)
stage 1 = symptom onset stage 5 = death

PrimeC Increases Probability of complications-free- Survival in distinct methods (ITT)



A hazard ratio of 1 means that there is no difference in survival between the two treatment arms.
Hazard Ratio less than 1 means that survival was better in the PrimeC arm

PrimeC Increases Complication- free Survival Probability (PP)



A hazard ratio of 1 means that there is no difference in survival between the two treatment arms.
Hazard Ratio less than 1 means that survival was better in the PrimeC arm

PrimeC Slowed Decline in Quality of Life (ITT)

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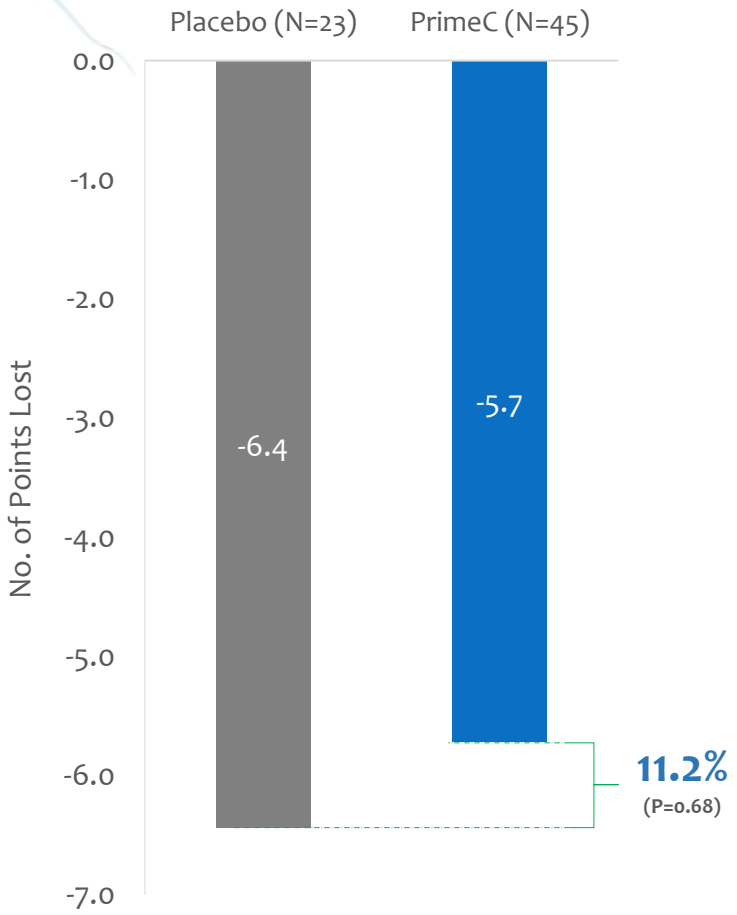
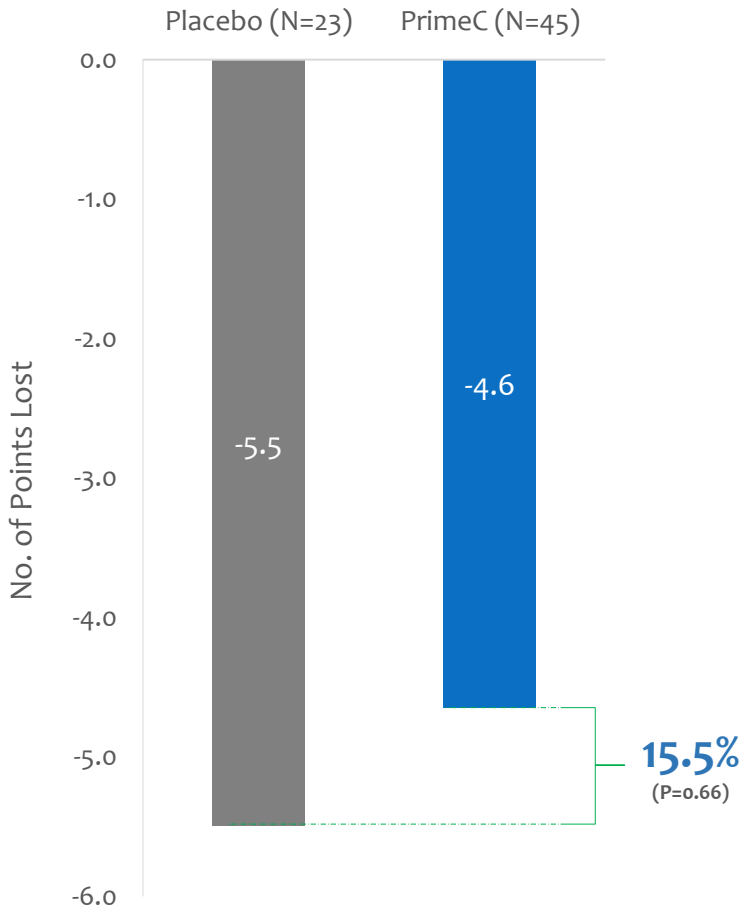
PARADIGM SHIFTING THE PARADIGM

PROMIS-10 Physical Health score



PROMIS-10 Mental Health score



PROMIS (Patient-Reported Outcomes Measurement Information System)-10 is a set of person-centered measures that evaluates and monitors physical, mental, and social health in individuals living with chronic conditions

PrimeC Slowed Decline in Quality of Life (PP)

NeuroSense Therapeutics
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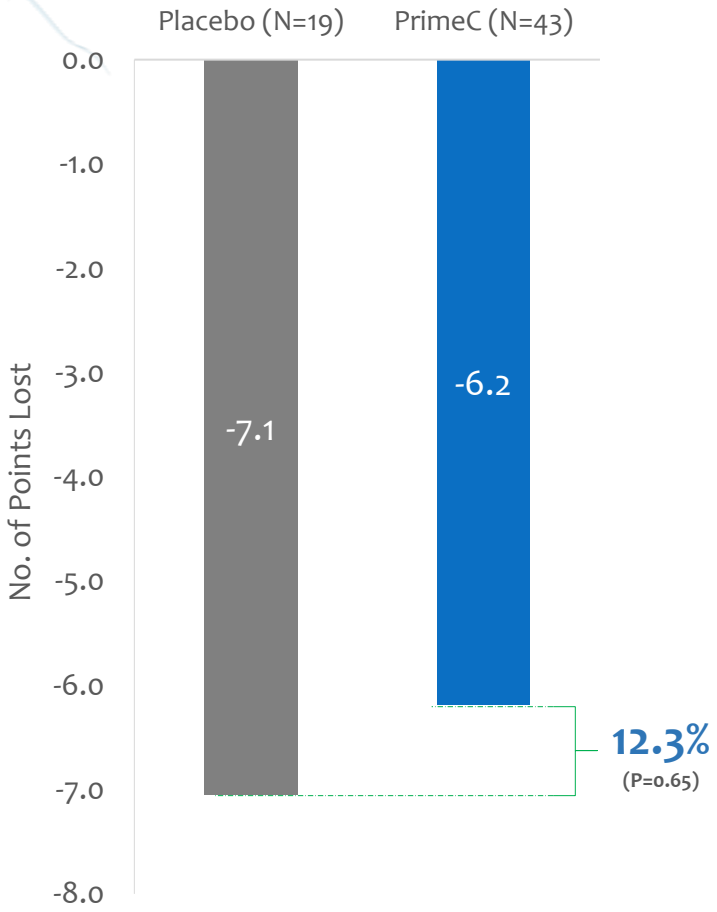
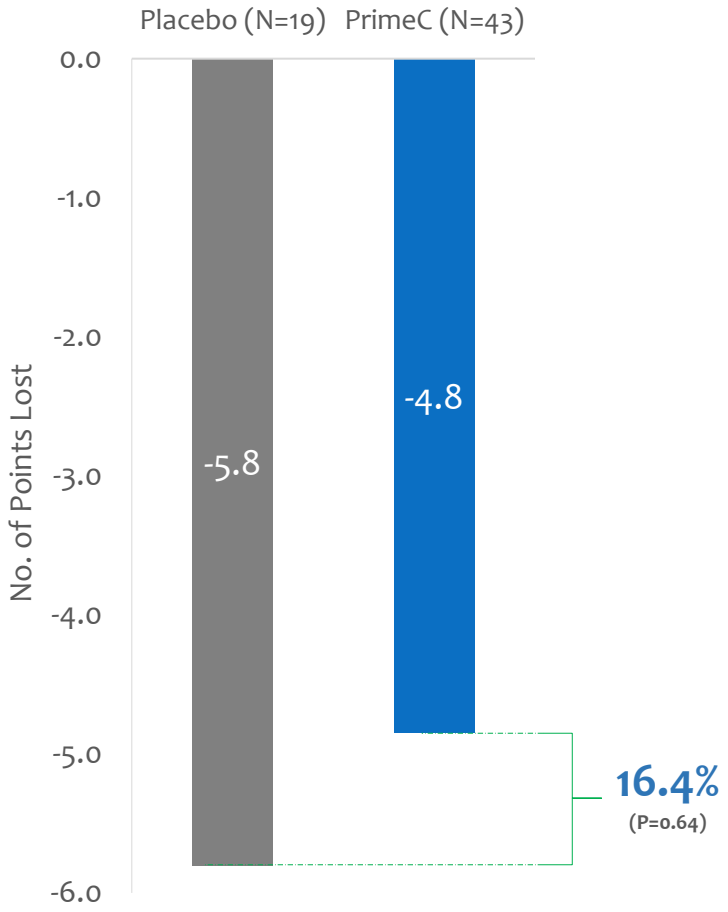
PARADIGM SHIFTING THE PARADIGM

PROMIS-10 Physical Health score



PROMIS-10 Mental Health score



PROMIS (Patient-Reported Outcomes Measurement Information System)-10 is a set of person-centered measures that evaluates and monitors physical, mental, and social health in individuals living with chronic conditions

Pioneering Approach to ALS Biomarker Research To Maximize Clinical Efforts

NeuroSense Therapeutics
Nasdaq: NRSN

NeuroSense is collaborating with leading KOLs and industry on the PARADIGM trial to elucidate PrimeC's MOA via novel methodologies

PARADIGM
SHIFTING THE PARADIGM

- Interplay Between TDP-43 and RNA Regulation
- Biomarker Driven Proteomics — inoviv
- microRNA Profiling — macrogen; TEL AVIV UNIVERSITY
- Neuronal Derived Exosomes — Lonza
- Neurofilaments
- Identification of Novel Biomarkers

PrimeC: Strong Clinical and Commercial Potential

NeuroSense Therapeutics
Nasdaq: NRSN

Novel combination therapy candidate of approved products optimized for PK and synergistic effects to address ALS and potentially other disease targets

Robust clinical efficacy and excellent safety profile observed from ALS Phase 2a and 2b clinical studies

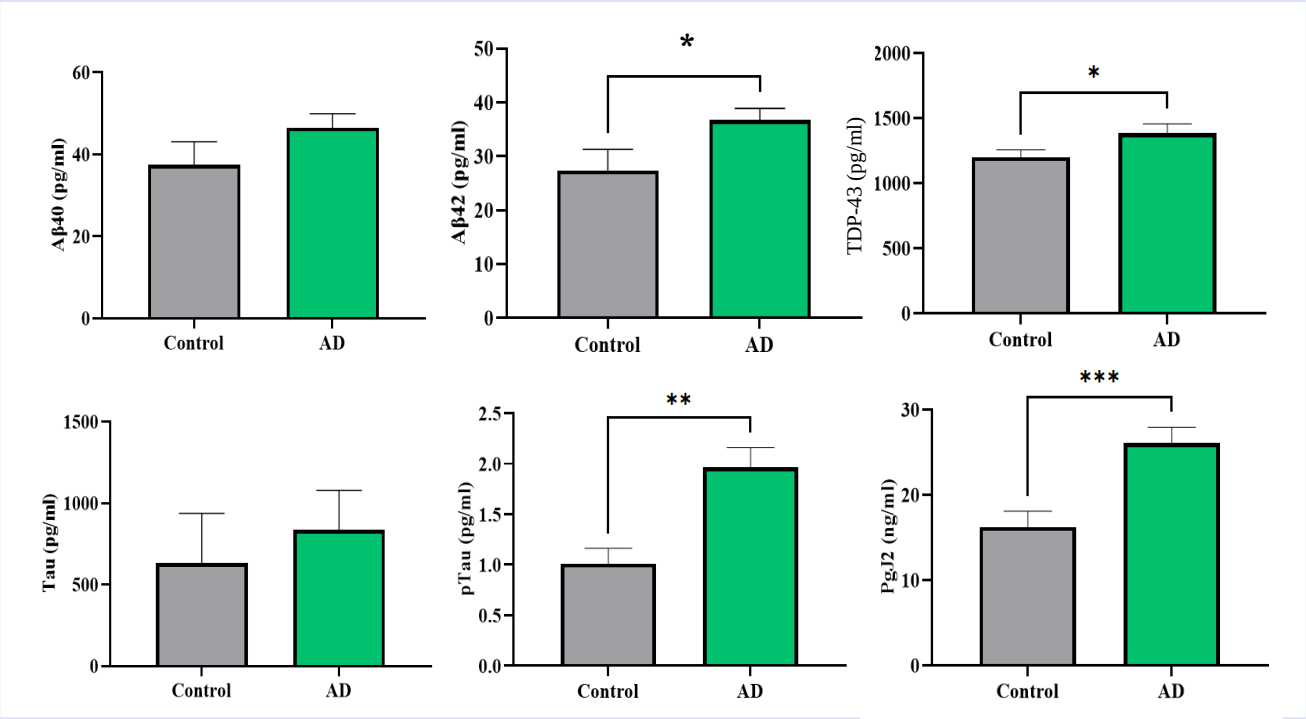
- **37% reduction in ALSFRS-R (p=0.03) in phase 2b study**

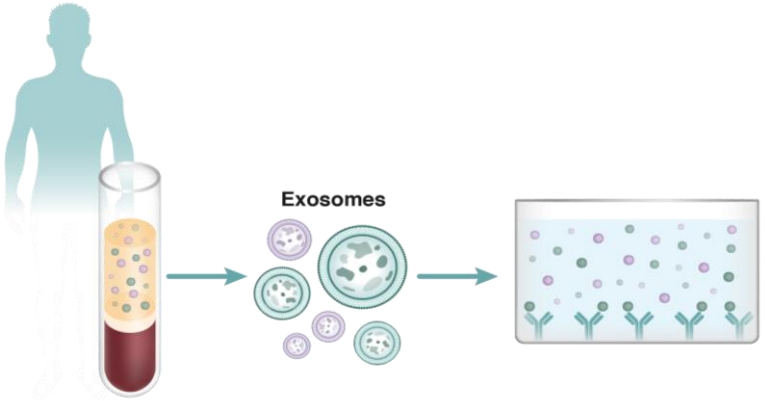
Expedited and de-risked regulatory pathway (orphan drug designation / 505(b)2 pathway)

Patent coverage for novel formulation, method & combination (until 2038)

Alzheimer's (AD) Studies Reveal Potential Effect of NeuroSense's Combination Therapy

NeuroSense Therapeutics
Nasdaq: NRSN





Biomarkers tested in Neuronal Derived Exosomes comparing Healthy vs. AD patients, **to elucidate the potential target engagement of CogniC.**

Biomarker data were analyzed using a Mann-Whitney U test comparing AD samples with controls.
*P<0.05, **P<0.01, ***P<0.001

RoAD Phase 2 Study Design

Randomized, Prospective, Double-Blind, Placebo-Controlled Study

RoAD

- **20 patients with mild to moderate AD**
- **1:1** PrimeC to Placebo
- **CogniC- intermediate formulation** (=PrimeC - ER)
- **12**-month dosing
- Clinic visit every **3** months
- Single-center

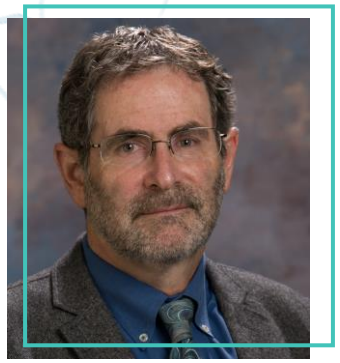
Primary Endpoint Safety & Tolerability

Secondary Efficacy Clinical Outcomes

Target Engagement Biomarkers

Exceptional Scientific Advisory Board

NeuroSense Therapeutics
Nasdaq: NRSN



Prof. Jeremy Shefner (Chair)

Senior Vice President at the Barrow Neurological Institute

Chair of the Department of Neurology

Prof. Orla Hardiman

Head of Academic Unit of Neurology at Trinity College Dublin and Consultant Neurologist at Beaumont

Co-Chair of the European Consortium to Cure ALS and Chair of the Scientific Committee of ENCALS

Prof. Merit Cudkowicz

Chief of Neurology at Mass General and Director, Sean M. Healey & AMG Center for ALS

Professor of Neurology at Harvard Medical School

Dr. Jinsy Andrews

Associate Professor of Neurology, Division of Neuromuscular Medicine, Columbia University

Director of Neuromuscular Clinical Trials

Prof. Jeffrey Rosenfeld

Professor of Neurology and Associate Chairman of Neurology at Loma Linda University School of Medicine

Medical Director of Center for Restorative Neurology at Loma Linda University

BARROW Neurological Institute
NEALS
TRINITY COLLEGE DUBLIN
ENCALS European Network to Cure ALS
CURE ALS
NEALS
HARVARD MEDICAL SCHOOL
MASSACHUSETTS GENERAL HOSPITAL
COLUMBIA UNIVERSITY
NEALS
LOMA LINDA UNIVERSITY

Experienced Leadership

NeuroSense Therapeutics
Nasdaq: NRSN

Alon Ben-Noon

Founder & CEO

Ferenc Tracik, MD

Chief Medical Officer

Or Eisenberg

Chief Financial Officer

Niva Russek-Blum, PhD

Chief Technology Officer

Nedira Salzman

VP of BD

Shiran Zimri, PhD

VP of R&D

Diana Shtossel

VP of Regulatory Affairs

Hagit Binder

Chief Operating Officer

Board of Directors

NeuroSense Therapeutics
Nasdaq: NRSN

Caren Deardorf

Mark Leuchtenberger
Chairman of the Board

Cary Claiborne

Revital Mandil-Levin

Alon Ben-Noon

Christine Pellizzari

Key Collaborations

HARVARD MEDICAL SCHOOL

MASSACHUSETTS GENERAL HOSPITAL

Tel-Aviv Sourasky Medical Center

TEL AVIV UNIVERSITY

NeuraLight

Quantalx Neuroscience

inoviv

UMC Utrecht

USC

EUPALS European Organisation for Professionals and Patients with ALS

ALS ASSOCIATION

EVERYTHINGALS CARE TO CURE

IsrA.L.S

Lonza

NeuroSense Therapeutics
Nasdaq: NRSN

Milestones Achieved and Upcoming Potential Catalysts

2022

- ✔ Initiated ALS Phase 2b PARADIGM study
- ✔ Received FDA IND Clearance for PrimeC
- ✔ Completed PK study single-dose & multi-dose successfully
- ✔ Completed In-life 90-day GLP toxicology study successfully

2023

- ✔ Completed Alzheimer's biomarker study with positive results
- ✔ Completed Parkinson's biomarker study with positive results
- ✔ Type D Meeting with the FDA
- ✔ Release ALS Phase 2b clinical study top-line results
- ✔ Initiated Alzheimer's Phase 2 study

2024

- ***Neurofilament Results***
- ***Biomarker Results***
- ***ALS End of Phase 2 Meeting with the FDA and EMA***
- ***Initiate ALS Phase 3 clinical study as needed***

NeuroSense Therapeutics

Nasdaq: **NRSN**

For more information:

info@neurosense-tx.com