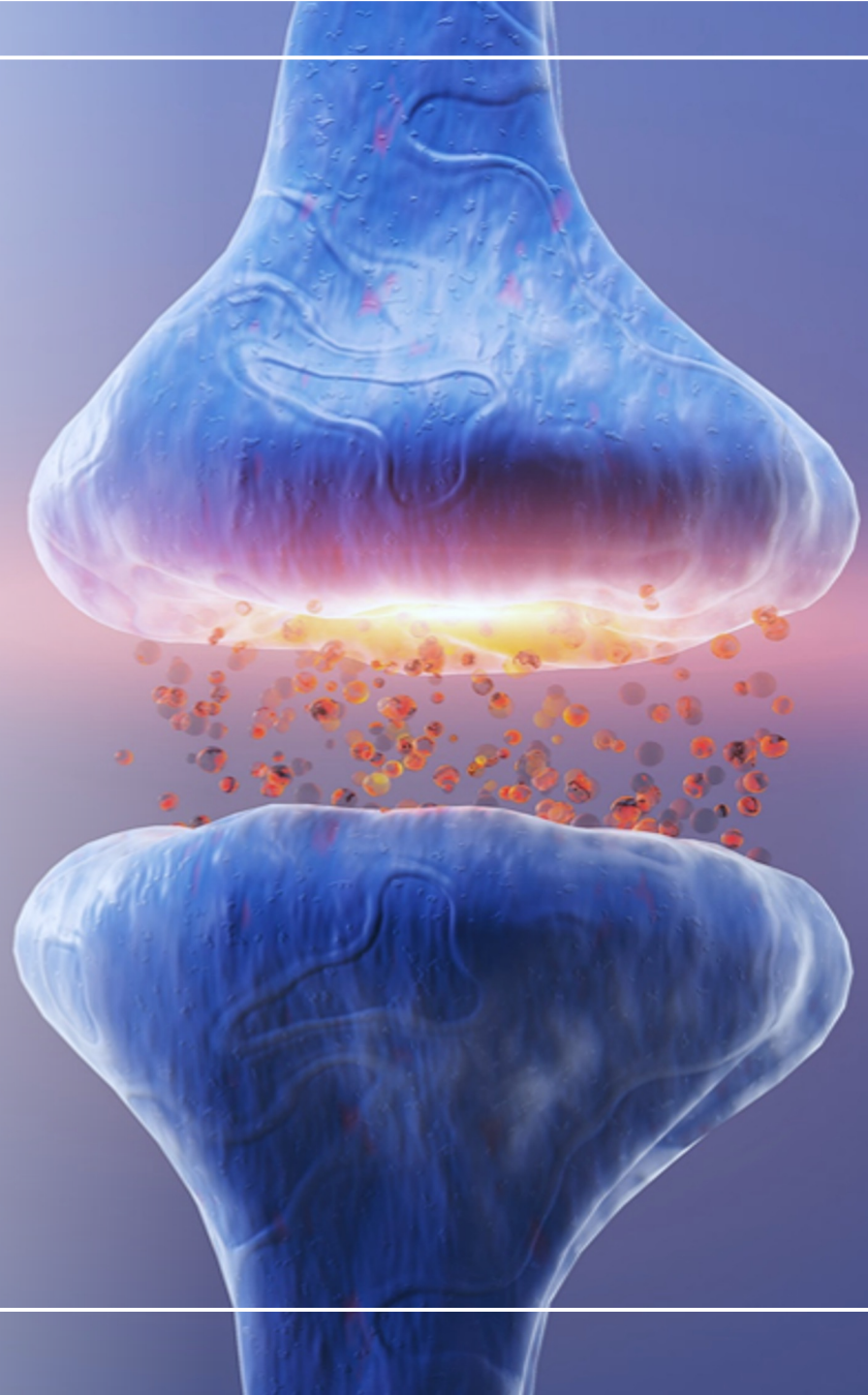
NeuroSense Therapeutics



January 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:
Neurofilament results (Jan 2024)
Biomarker results (H1 2024)

Existing partnership with big pharma, and **fully funded through Q2 2024**

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

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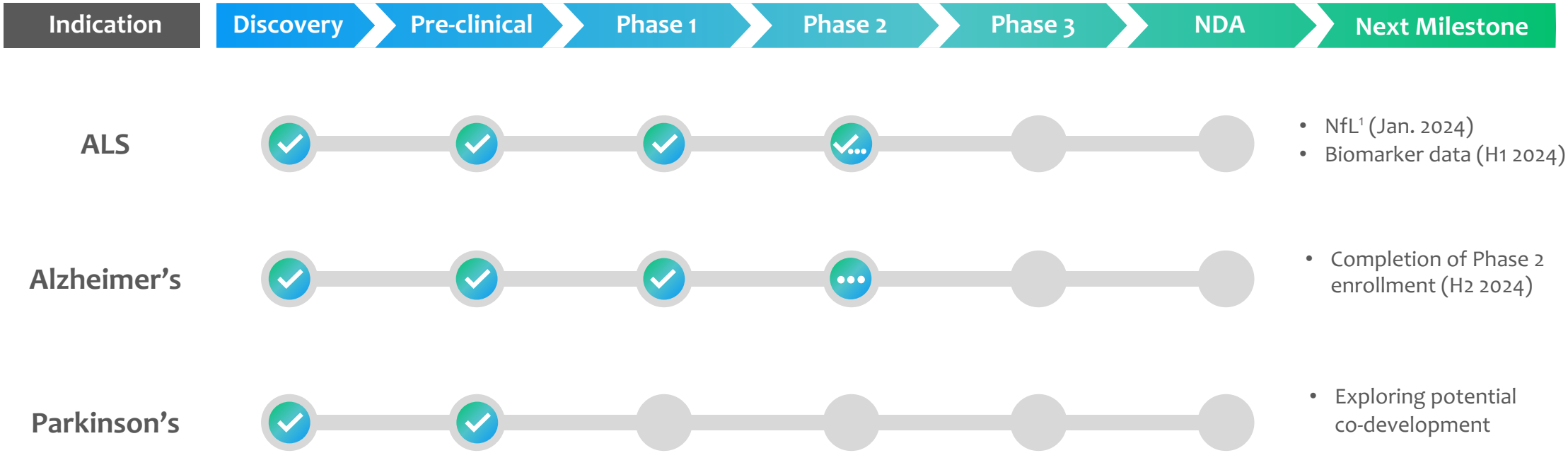
Focused Pipeline

Diseases with Limited Treatment Options and High Commercial Opportunity



[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

A Unique Synergistic Formulation With A Powerful Outcome

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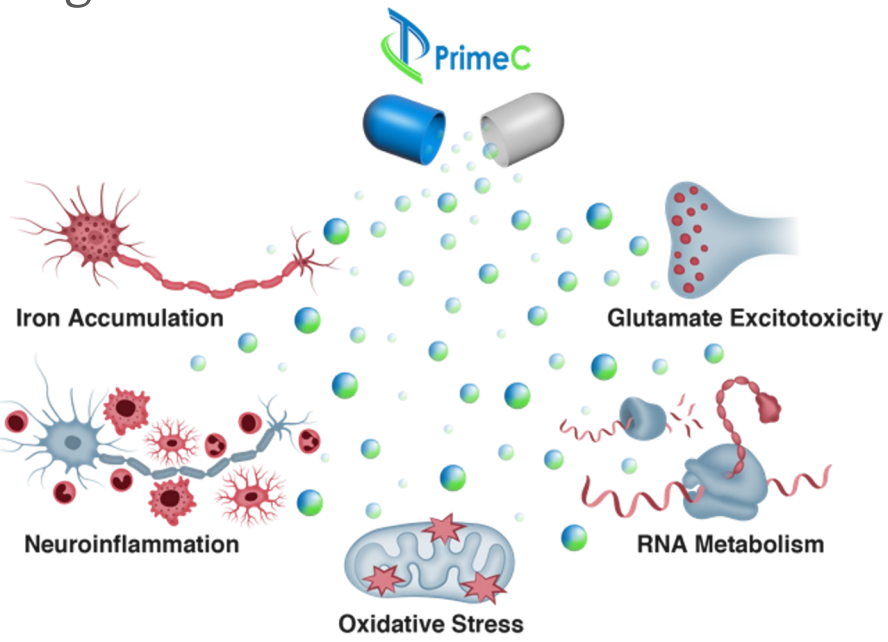
PrimeC is a novel formulation, consisting of **specific doses** of two FDA-approved drugs, designed to work **synergistically** on more than one target in ALS

Celecoxib - an 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 neuron death in ALS

Synergistic Benefit: *In-Vitro* & *In-Vivo*

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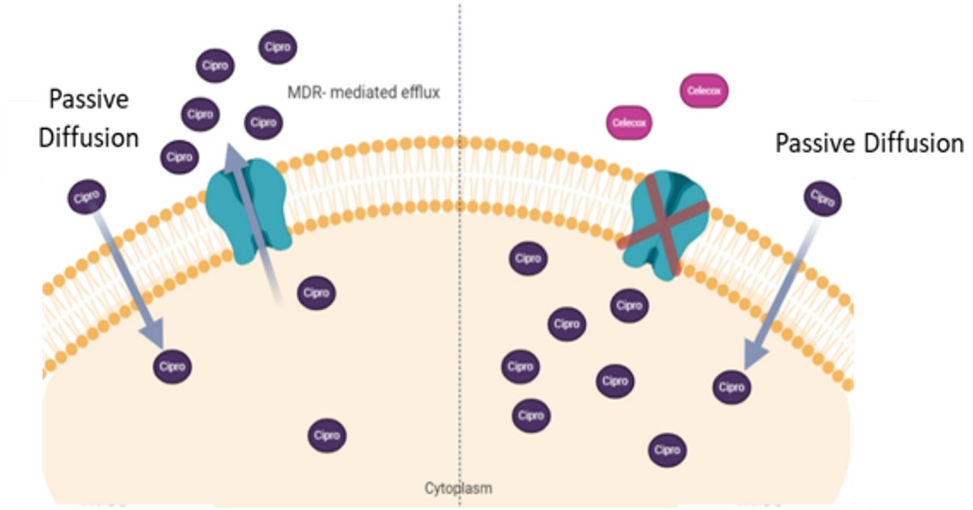
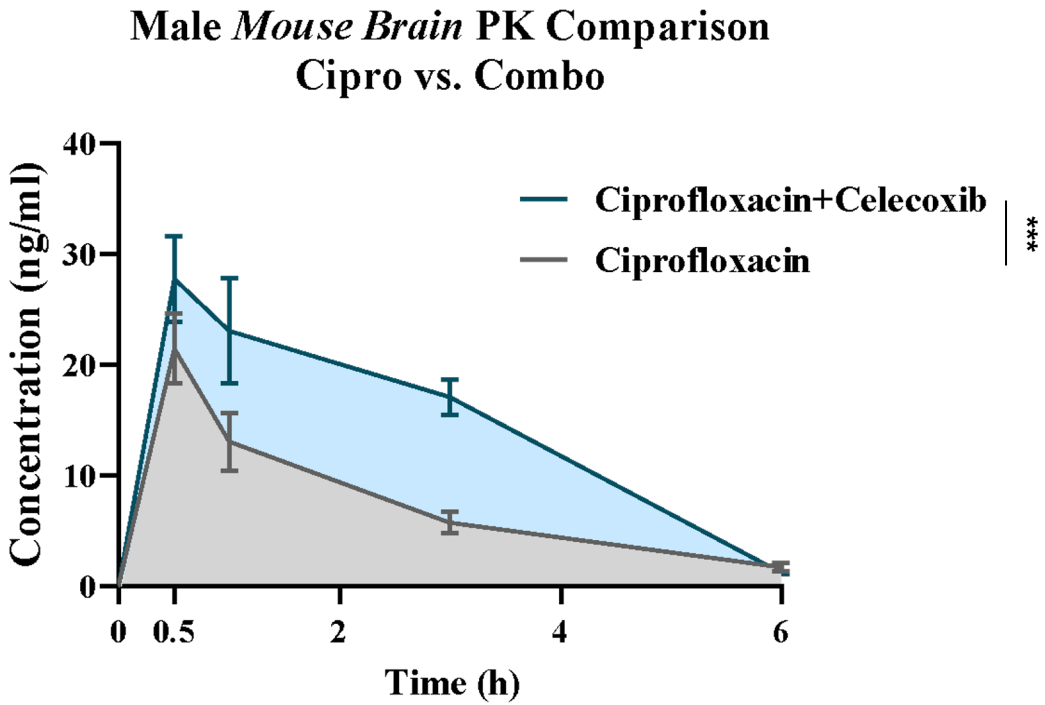
Synergistic Mode of Action



This finding is attributed to **Celecoxib** blocking exit of **Ciprofloxacin** in the neuron

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**

PrimeC Demonstrated Statistically Significant Efficacy in Key Pre-Clinical Study

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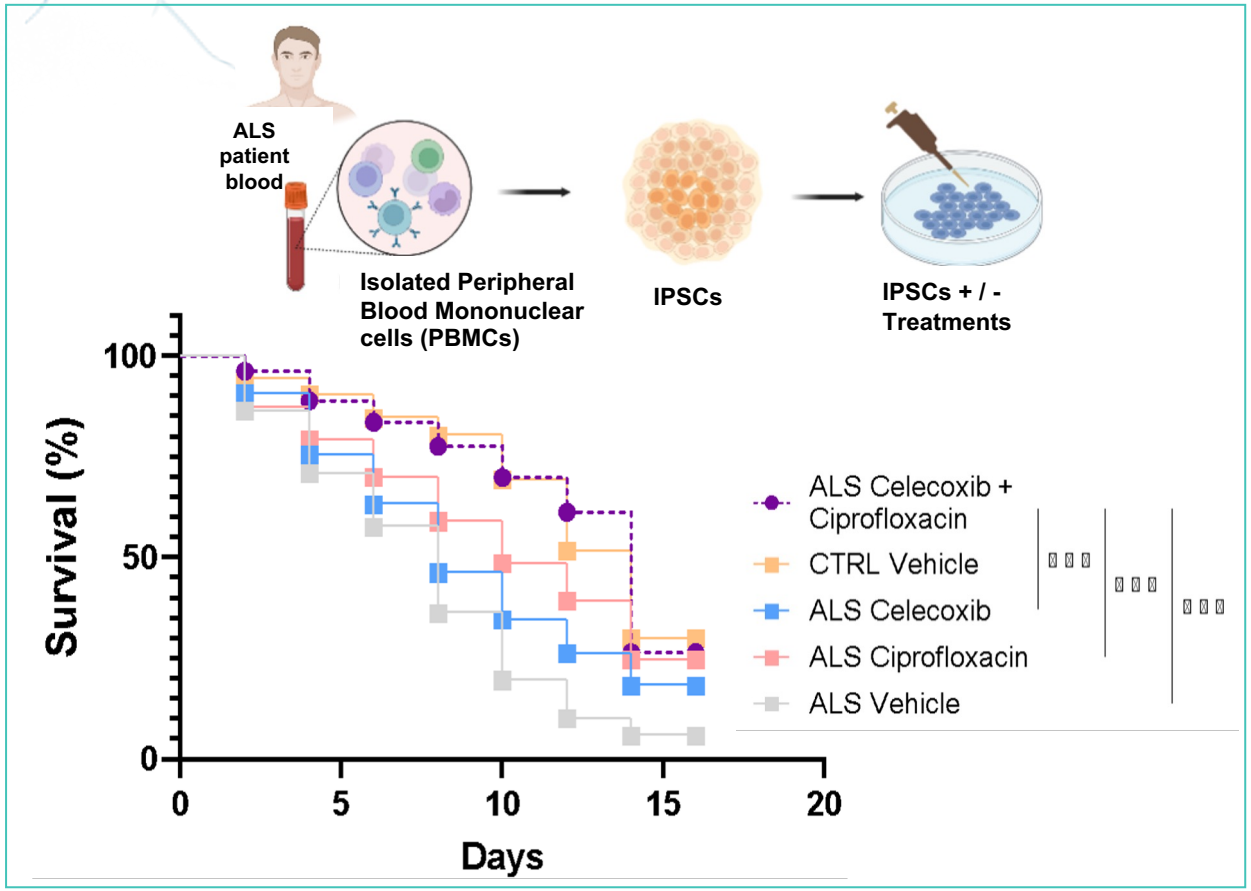
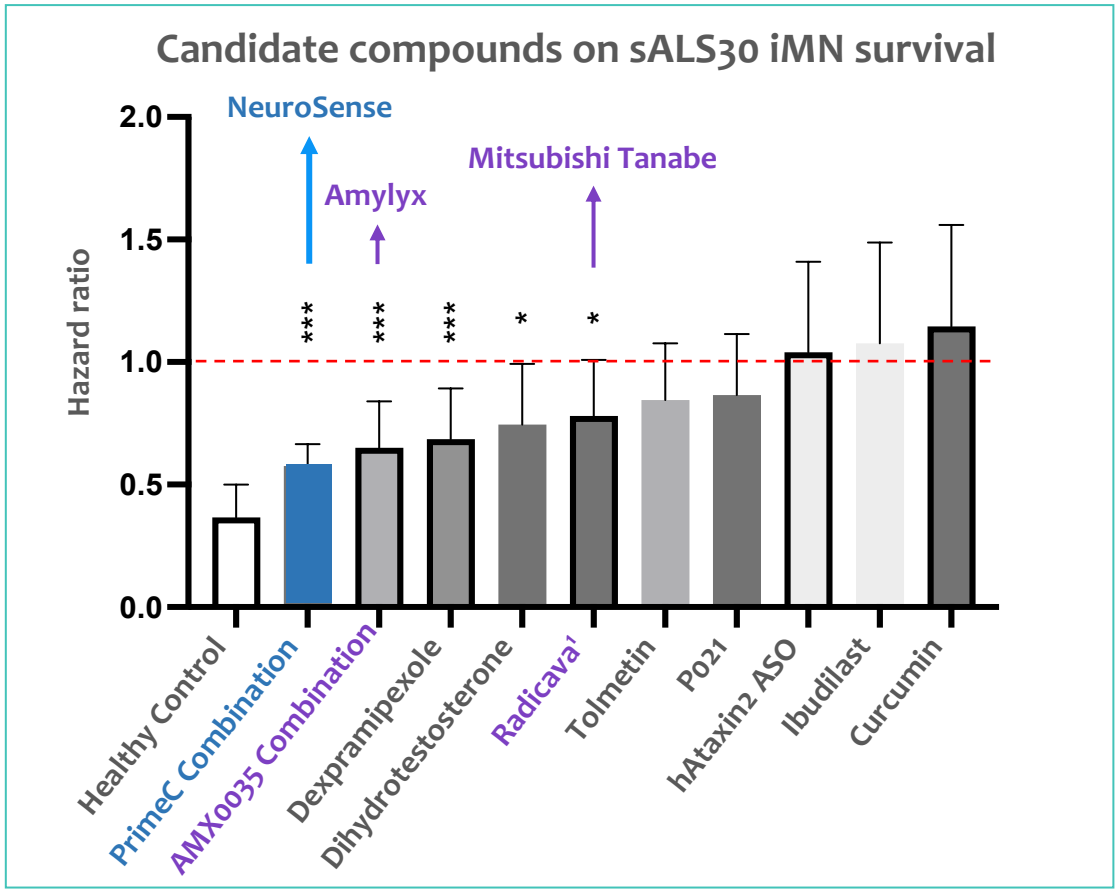
Studies were conducted in the laboratory of Dr. Justin Ichida, University of Southern California, using an induced Pluripotent Stem Cell (iPSC) Model Generated from People Living with ALS



Collaboration with Dr. Ichida

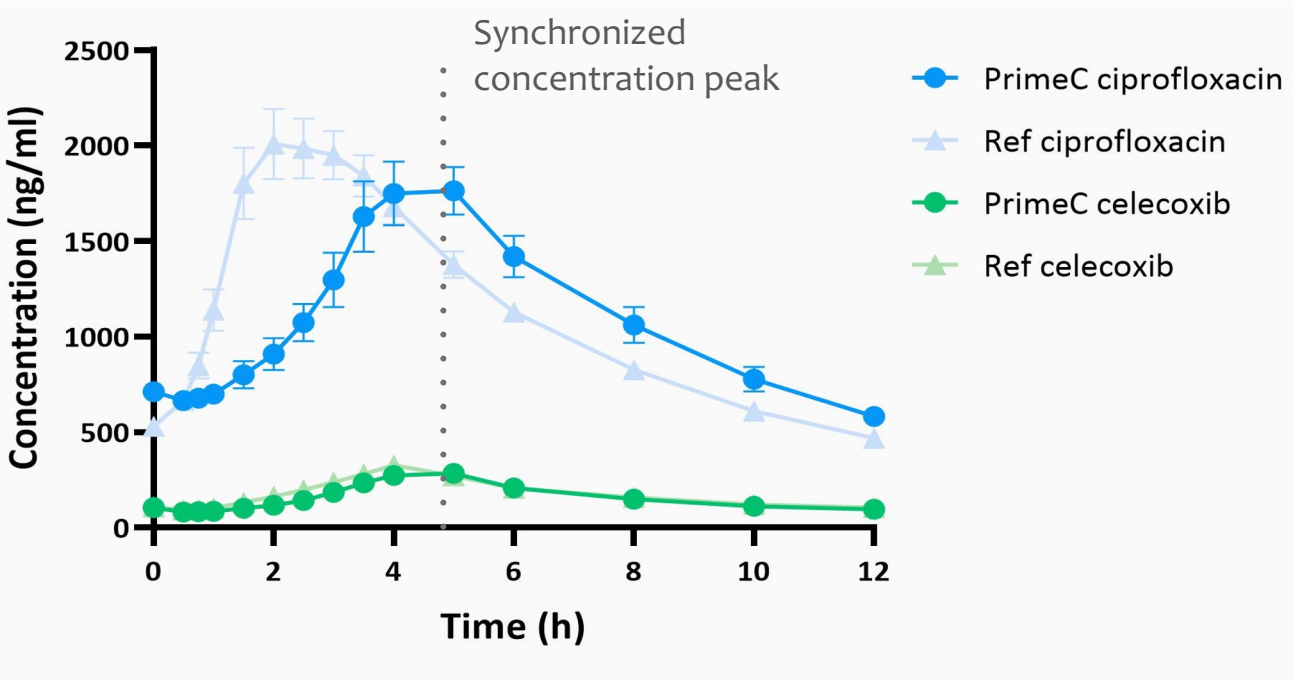


Independent, non-sponsored research

[1] Radicava is a registered trademark of Mitsubishi Tanabe Pharma Corporation

PrimeC Unique Formulation Induces a Synchronized PK Profile

PK **profile** studies
in **humans**



A synchronized PK profile of the two compounds, potentially **maximizes the synergy between them**

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

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NST002

15 patients

Open-Label

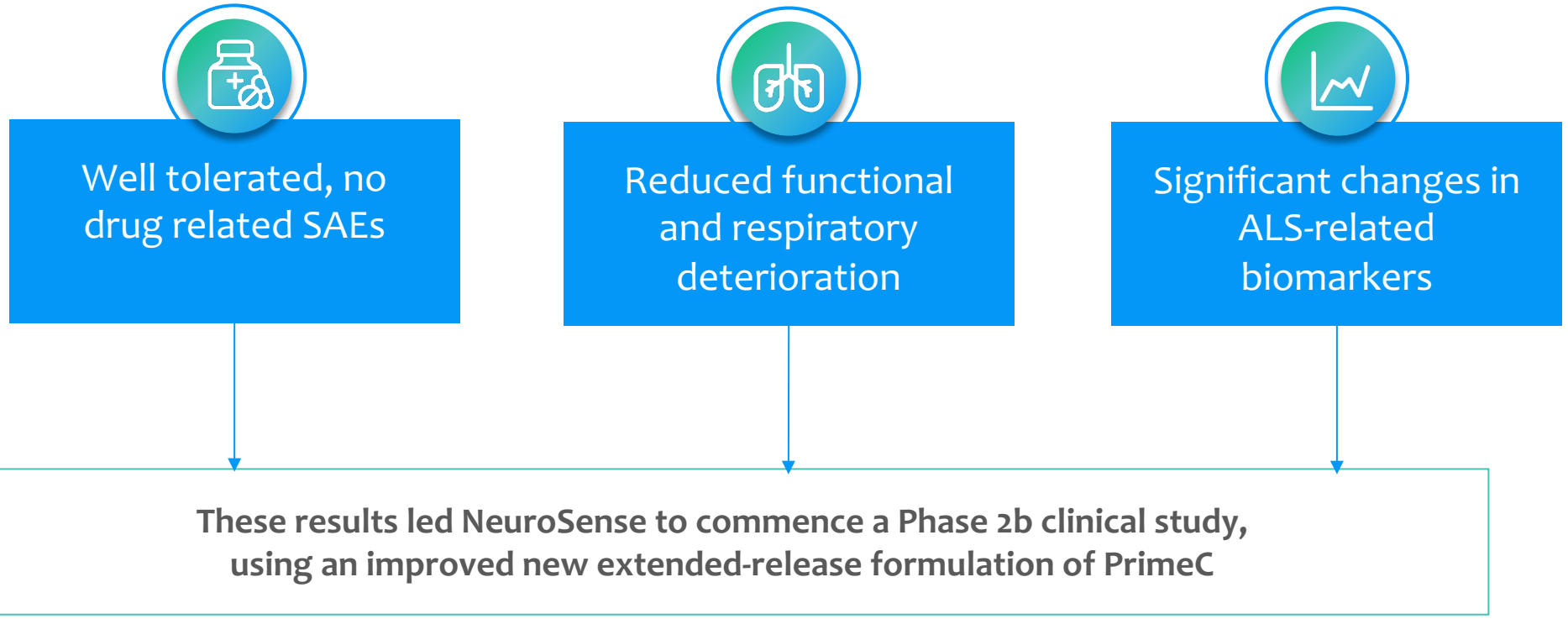
Intermediate formulation of PrimeC

12-month dosing

Clinic visit every **3** months

Phone visit every **1.5** months

Location: Tel Aviv Sourasky Medical Center



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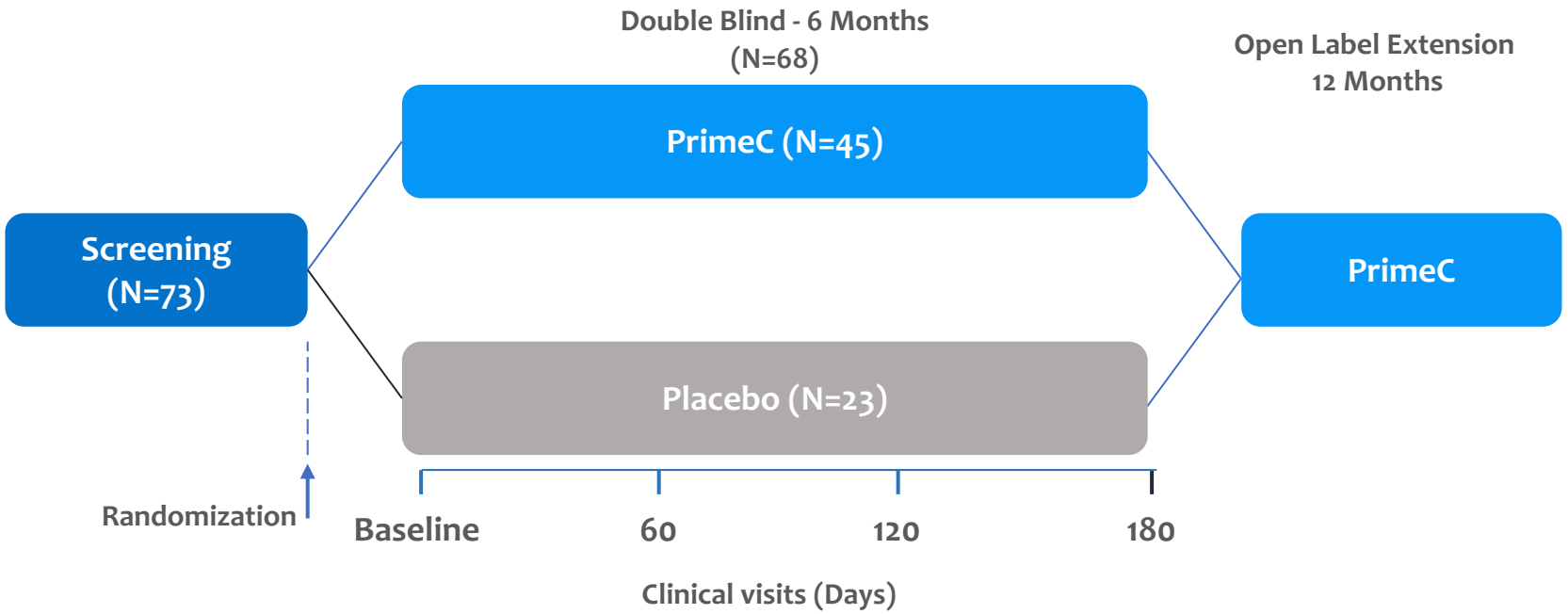
PrimeC Phase 2b Trial Design

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

PARADIGM
SHIFTING THE PARADIGM



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

PARADIGM used PrimeC's novel extended-release formulation

- *4 Screen Failures*
- *One participant misdiagnosed for ALS*

PrimeC Phase 2b Trial Endpoints

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PARADIGM
SHIFTING THE PARADIGM

1 Primary Endpoints

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

2 Secondary Efficacy Endpoints

- ALSFRS-R (ALS Functional Rating Scale)
- SVC (Slow Vital Capacity)
- Survival

Exploratory Endpoint

- Neurofilaments (results expected Jan 2024)

PrimeC Phase 2b Study

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[1]

Analysis
Pre-defined populations

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

[1]Tripepi G, Chesnaye NC, Dekker FW, Zoccali C, Jager KJ. Intention to treat and per protocol analysis in clinical trials. Nephrology. 2020;25:513–517.

PrimeC Phase 2b Study
Inclusions / Exclusions

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PARADIGM
SHIFTING THE PARADIGM

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

PrimeC Phase 2b Study:
Well Balanced Enrollment

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PARADIGM
SHIFTING THE PARADIGM

	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

PrimeC Phase 2b Study Results
Achieved Primary Endpoints with a Safety and Tolerability Profile Comparable to Placebo

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PARADIGM
SHIFTING THE PARADIGM

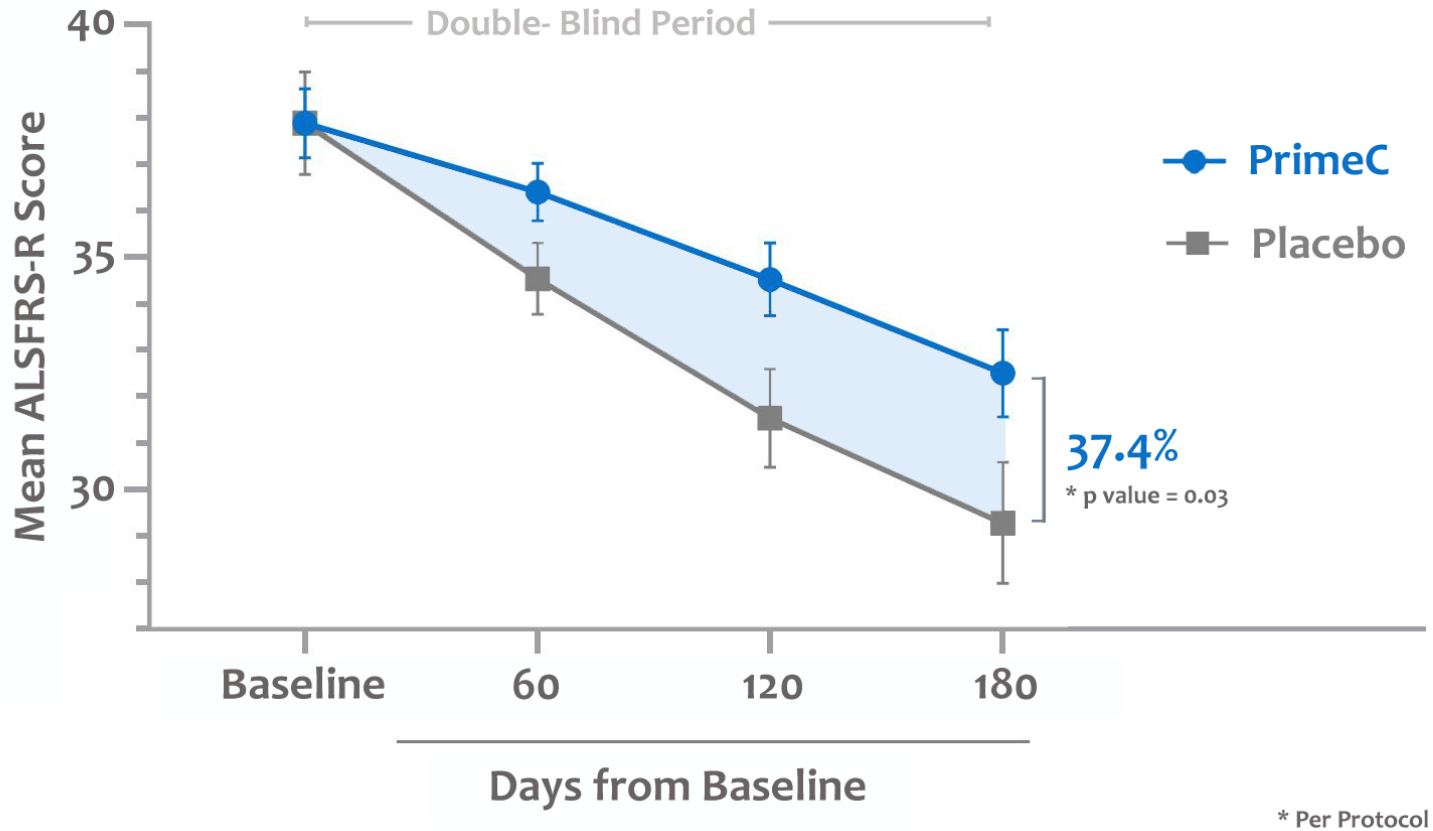
Summary of All Adverse Events	PrimeC (N=45)	Placebo (N=23)
Adverse Events (AE)	68.9%	65.2%
Treatment-Emergent AEs (TEAE)	68.9%	65.2%
Study Drug Related Treatment-Emergent AEs (TEAE)	20.0%	4.3%
Serious Treatment-Emergent AEs (TEAE)	8.9%	8.6%
Subject death	4.4%	4.3%
TEAE leading to Study Drug Discontinuation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

No Drop-outs Due To Adverse Events

Phase 2b Study Results – Per Protocol Population Analysis

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



* Per Protocol Population

Note: A 29% reduction (p-0.12) in ALSFRS-R was observed in the ITT analysis

Losing or Keeping a Single Point On the ALSFRS-R May Have a Significant Impact

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PARADIGM
SHIFTING THE PARADIGM

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.

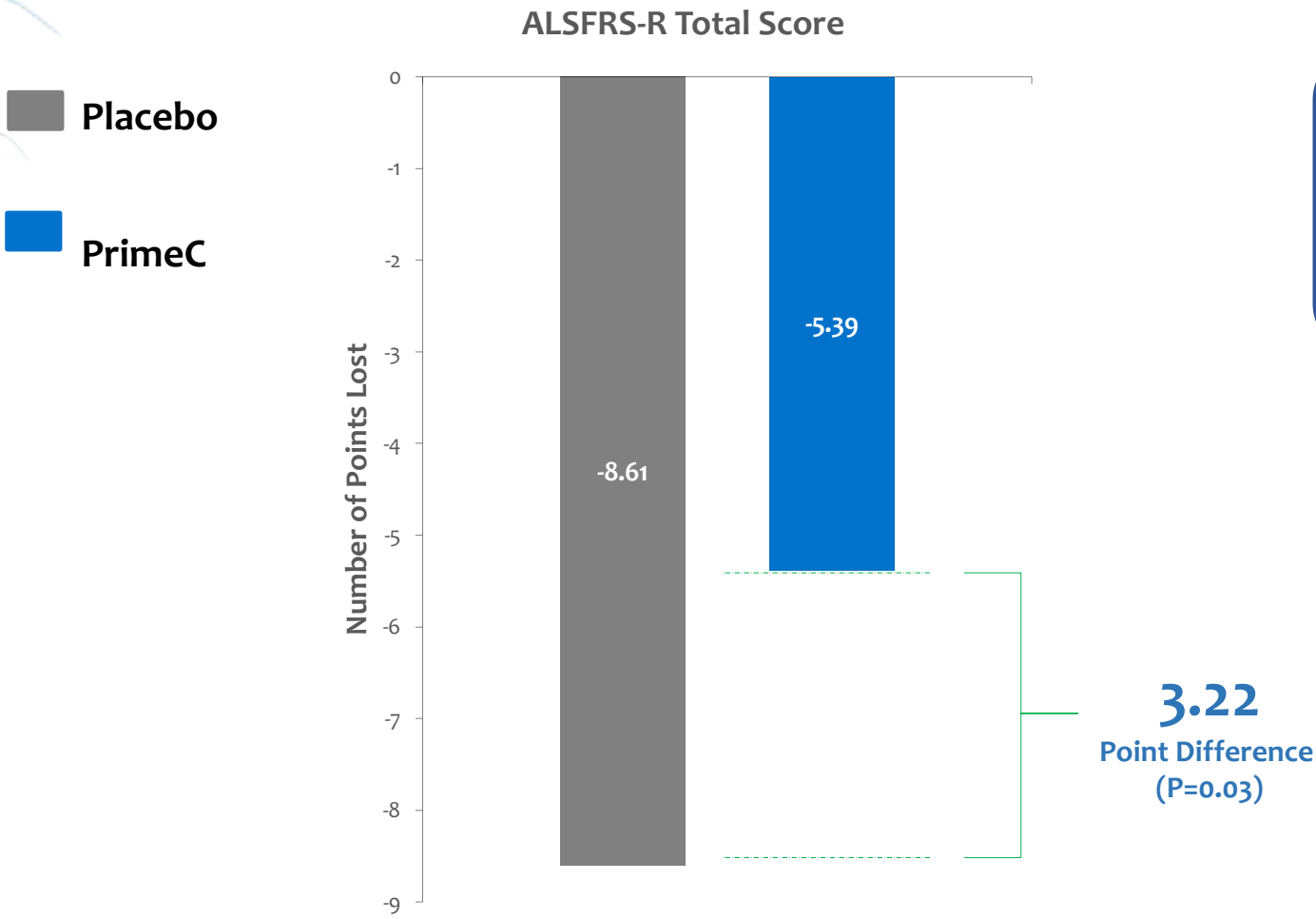
A 1-point drop on the swallowing assessment scale can mark the critical threshold between self-sufficiency and the necessity of supplemental tube feeding.

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

Phase 2b Study Results – Per Protocol Population Analysis

PrimeC Slowed the Loss of Physical Functions vs Placebo



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

Source: https://www.alspathways.ca/category/assessing-function/

Phase 2b Study Results – Per Protocol Population Analysis

PrimeC Slowed the Loss of Physical Functions vs Placebo

NeuroSense Therapeutics
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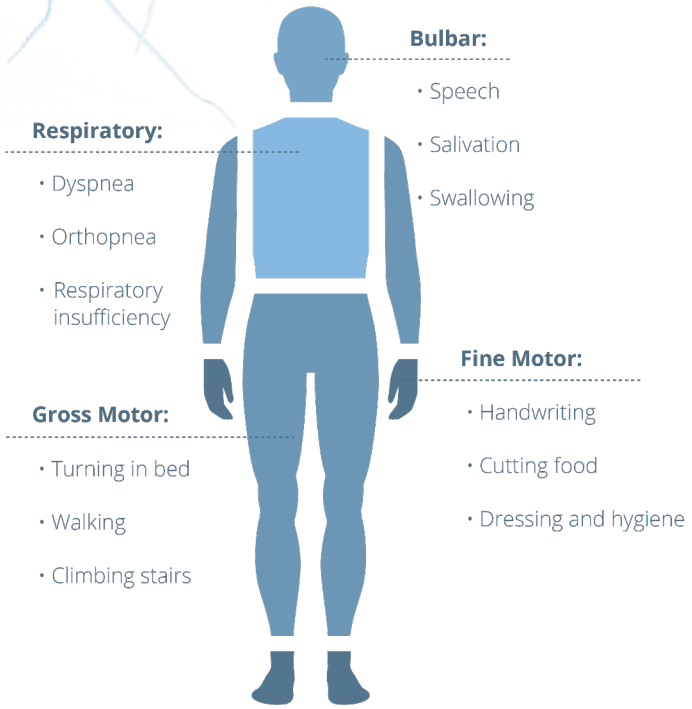
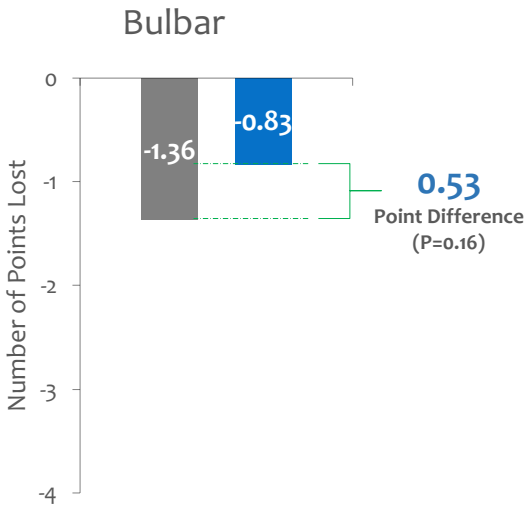
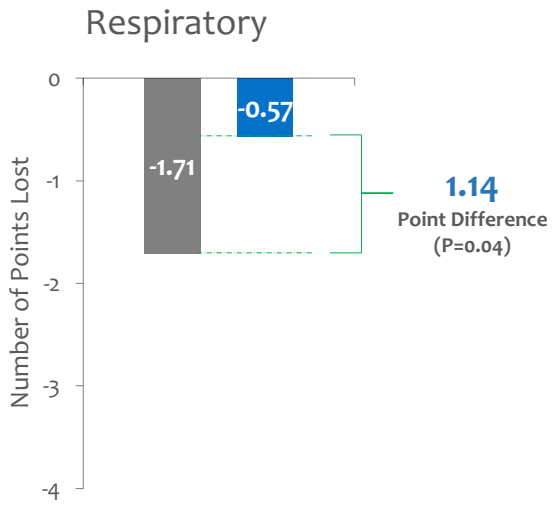
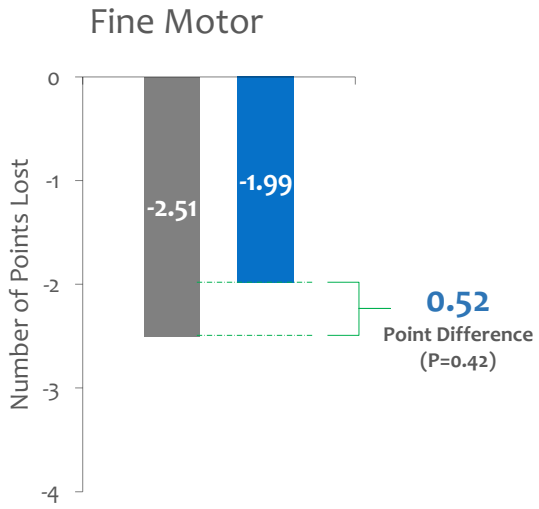
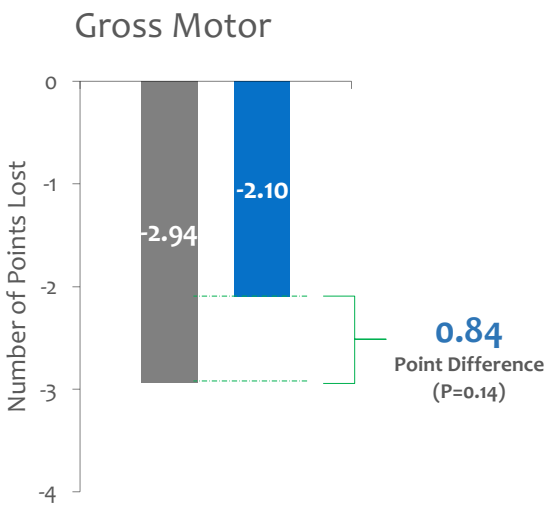
PARADIGM SHIFTING THE PARADIGM









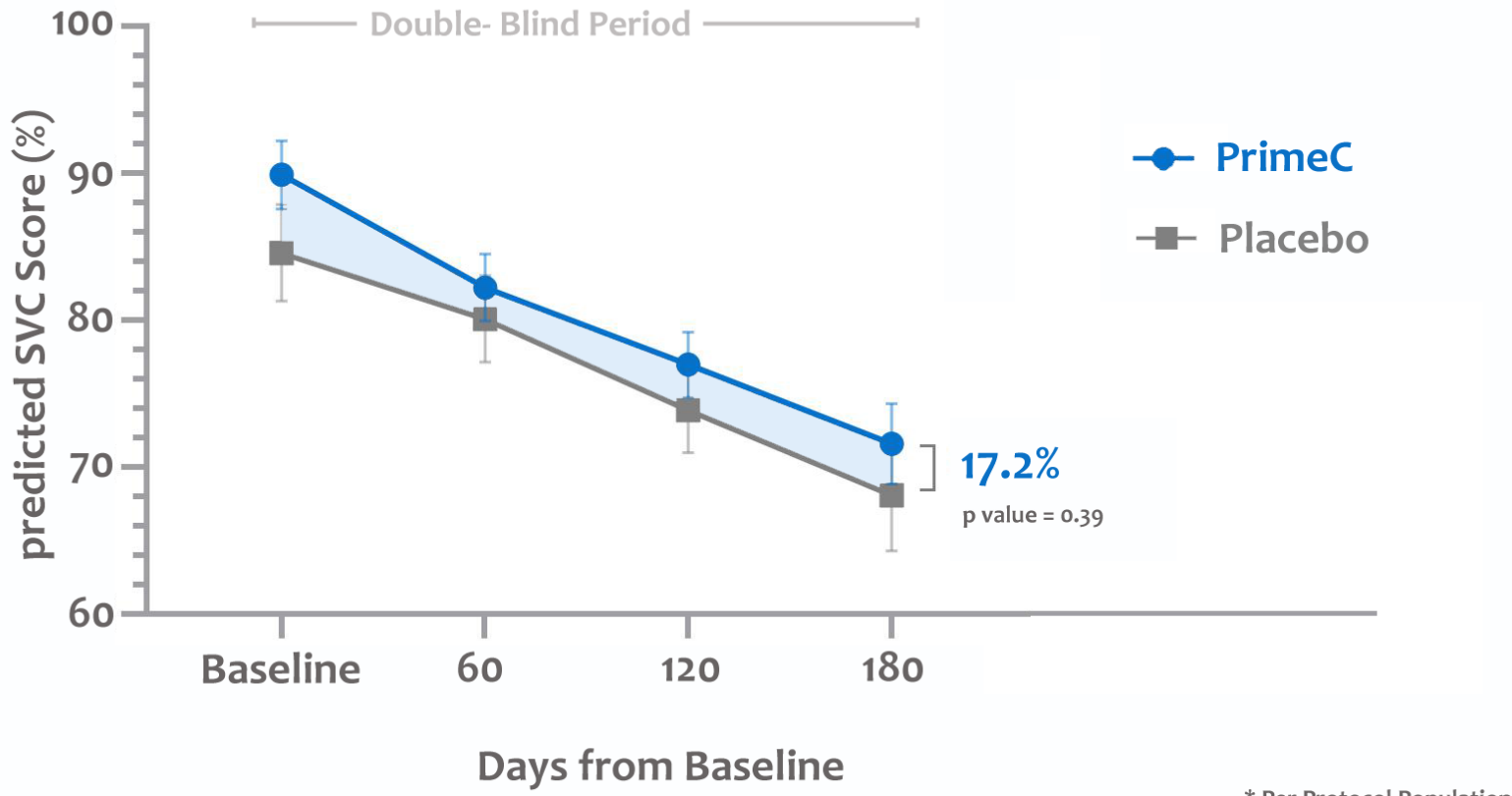


Background
Respiratory failure is the most common cause of death from ALS

Source: https://www.alspathways.ca/category/assessing-function/

Phase 2b Study Results – Per Protocol Population Analysis

PrimeC Attenuated Slow Vital Capacity (SVC) by 17.2%



Note: A 13.3% reduction (p=0.5) in SVC was observed in the ITT analysis

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Pioneering Approach to ALS Biomarker Research To Maximize Clinical Efforts

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 — indiviv
- microRNA Profiling — macrogen; TEL AVIV UNIVERSITY
- Neuronal Derived Exosomes
- Neurofilaments — Biogen
- Identification of Novel Biomarkers — MASSACHUSETTS GENERAL HOSPITAL; HARVARD

Proven Success of Combined Therapy

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Case Study: Amylyx (NASDAQ: AMLX)

Market Cap: ~ $1 B (Jan 2024)

Drug: ALS Combination Therapy of generic + supplement

Price: $158,000/ year

Estimated 2026 Sales: $1.1B/ year[1]

The FDA approved Amylyx's drug, AMX0035 (Relyvrio[2]), in September 2022 after Phase 2 clinical trial attenuated diseases progression ***(ALSFRS-R) by 25%*** *when compared to placebo[3]*

Successful combination strategies in neurology:

Alzheimer's
Donepezil + Memantine

Parkinson's
Entacapone + levodopa/carbidopa

ALS
Sodium Phenybuterate + Taurursodiol

SMA
Onasemnogene + Nusinersen

Epilepsy
Lamotrigine + Valproate/Carbamazepine

[1] SVB Securities analyst Marc Goodman
[2] Relyvrio is a registered trademark of Amylyx
[3] Study results are not for comparison

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PrimeC: Strong Clinical and Commercial Potential

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

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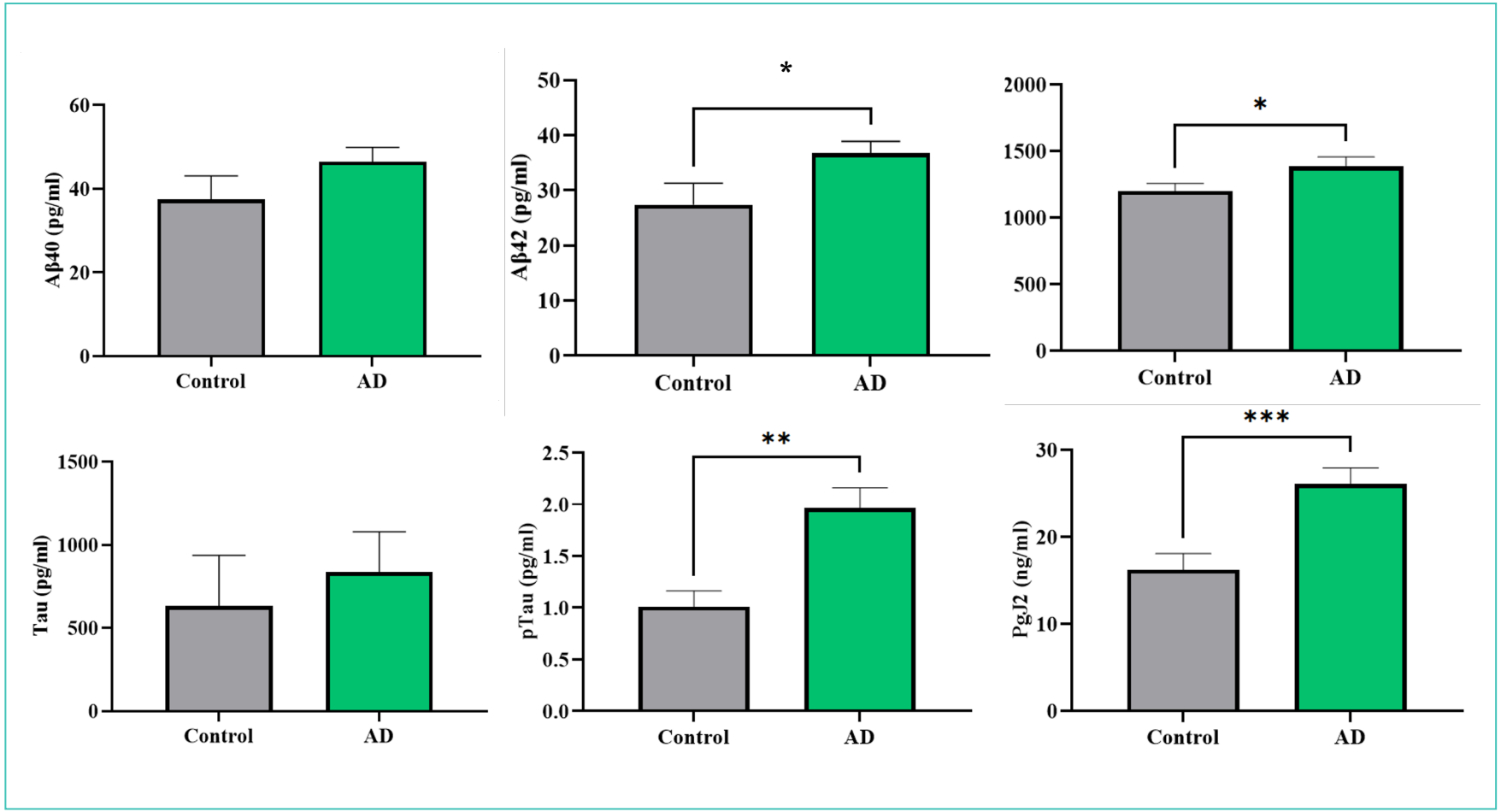

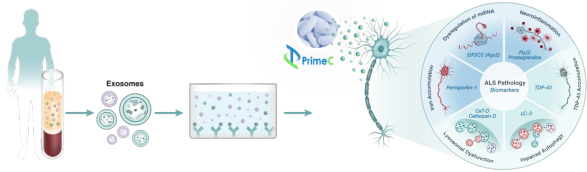

Biomarkers tested in Neuronal Derived Exosomes comparing non-treated Healthy vs. AD patients, **to elucidate the potential target engagement of CogniC.**

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

AD Phase 2 Study Design

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

NeuroSense Therapeutics
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RoΛD

20 patients with mild to moderate AD

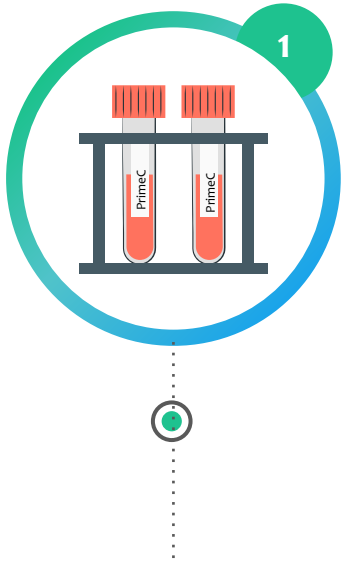
1:1 PrimeC to Placebo

CogniC- intermediate formulation (=PrimeC - ER)

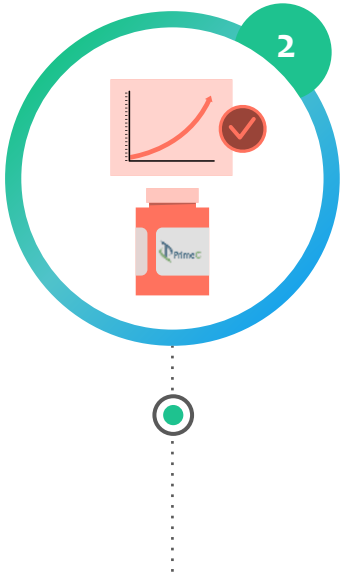
12-month dosing

Clinic visit every **3** months

Single-center



Primary Endpoint Safety & Tolerability



Secondary Efficacy Clinical Outcomes

Target Engagement Biomarkers

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Exceptional Scientific Advisory Board

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

Key Collaborations

HARVARD MEDICAL SCHOOL

MASSACHUSETTS GENERAL HOSPITAL

Tel-Aviv Sourasky Medical Center

Biogen

NeuraLight

Quantalx Neuroscience

inoviv

TEL AVIV UNIVERSITY

UMC Utrecht

USC

EUPALS European Organisation for Professionals and Patients with ALS

ALS ASSOCIATION

IsrA.L.S

EVERYTHINGALS CARE TO CURE

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

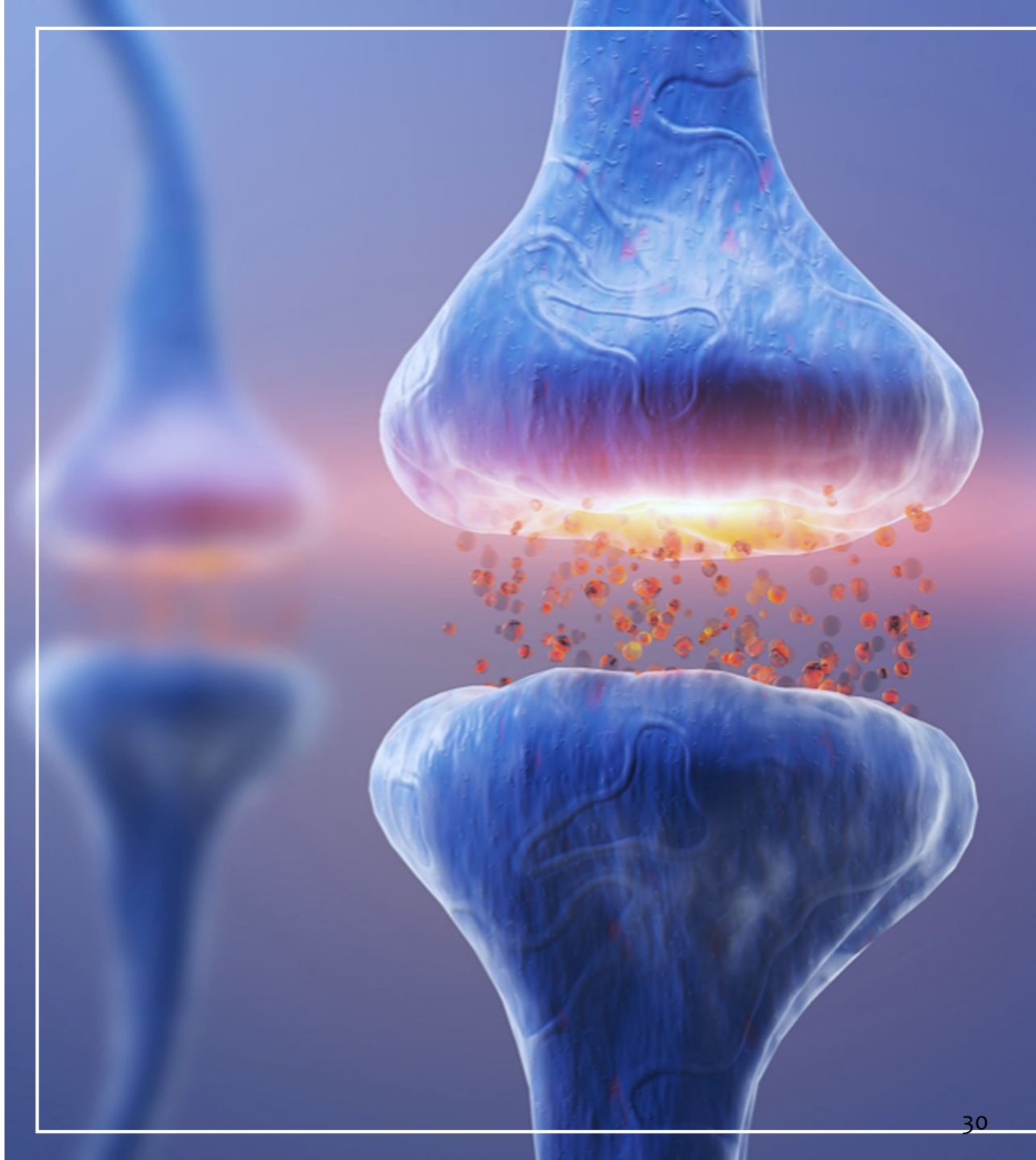
- ***Neurofilament Results***
- ***Biomarker Results***
- ***ALS End of Phase 2 Meeting with the FDA and EMA***
- ***Initiate ALS Phase 3 clinical study as needed***

NeuroSense Therapeutics

Nasdaq: **NRSN**

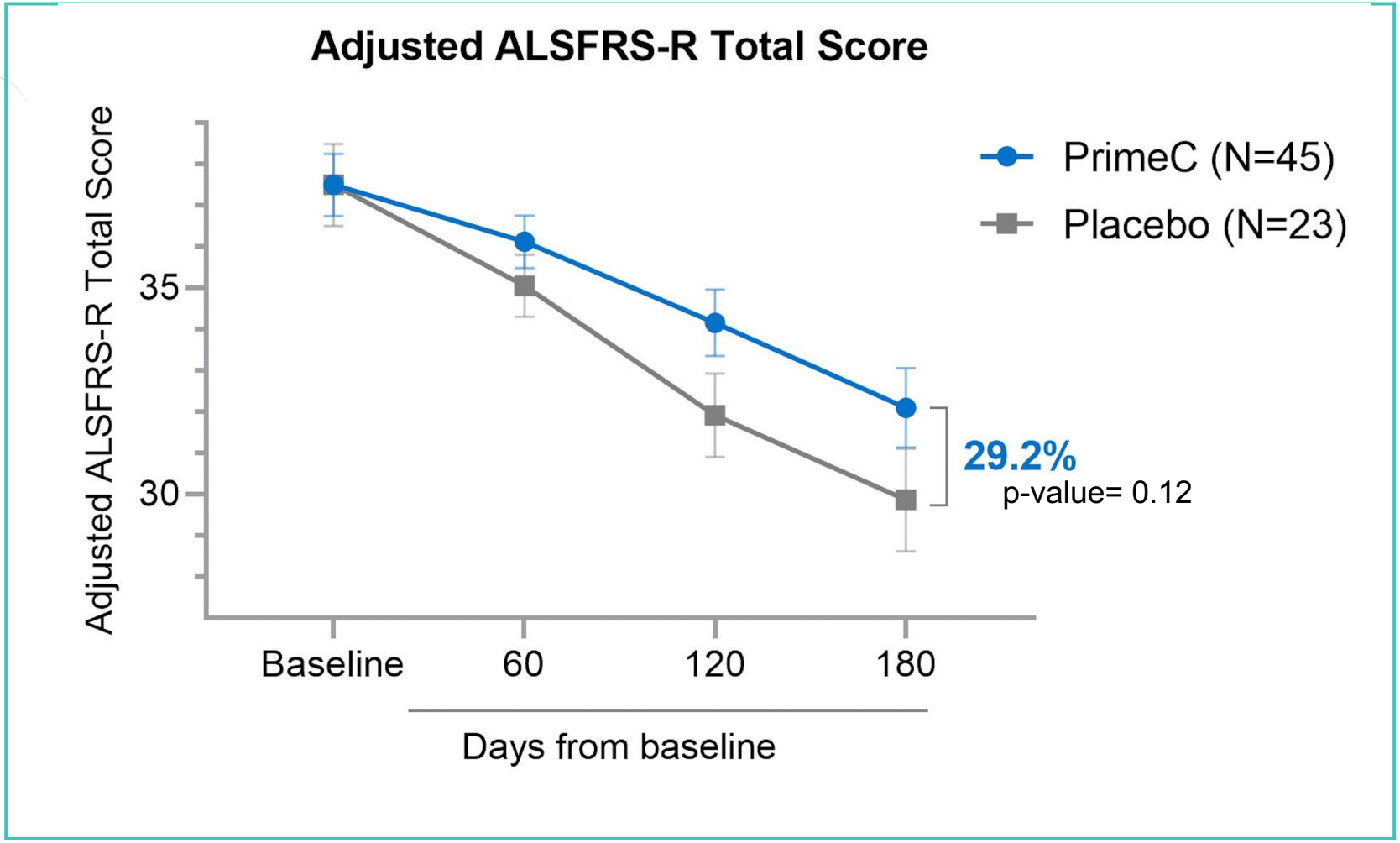
For more information:

info@neurosense-tx.com



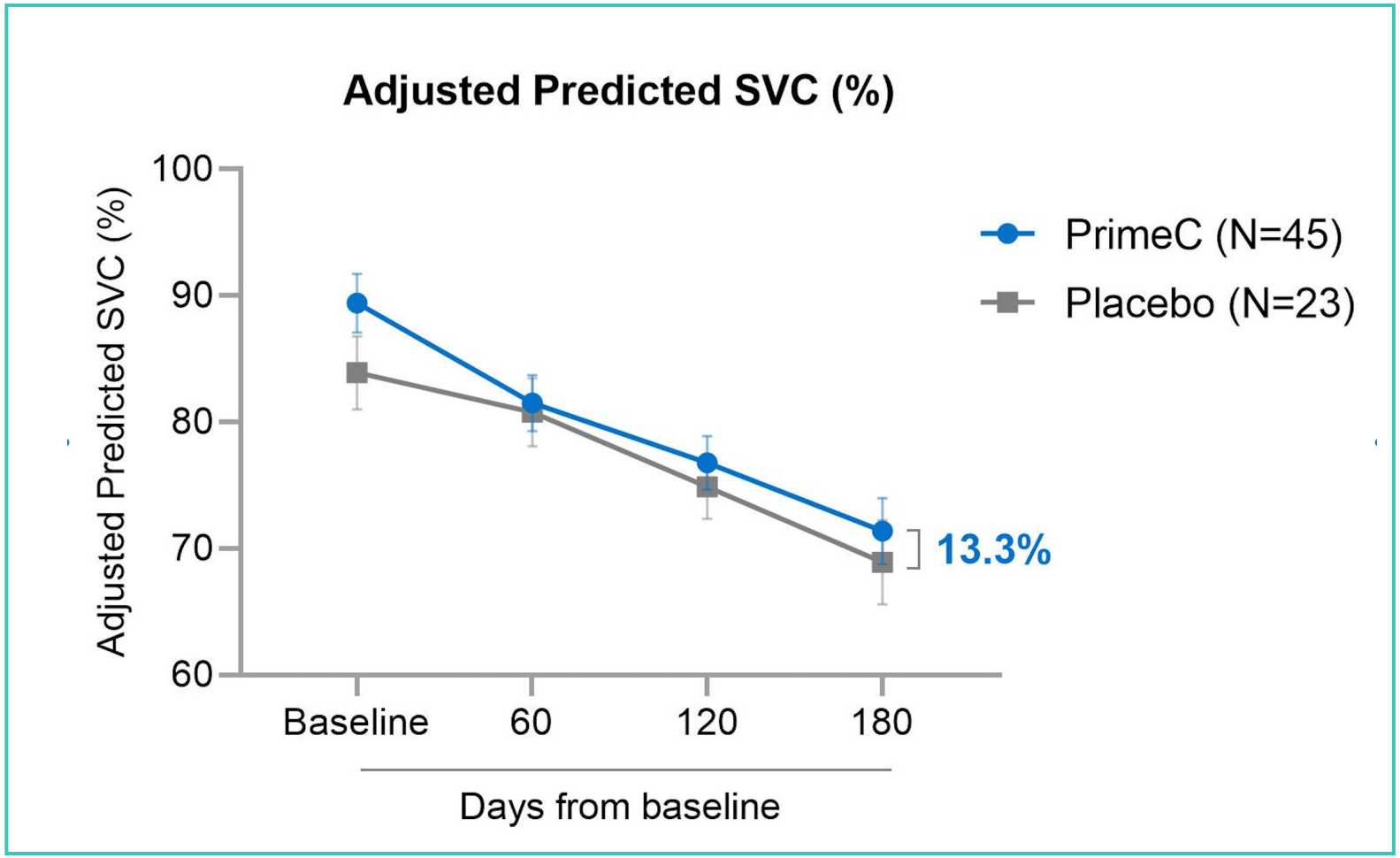
Phase 2b Study Results – Intent to Treat Analysis

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



Phase 2b Study Results – Intent to Treat Analysis

Slow Vital Capacity (SVC): Observed a 13.3% Decrease in Patients treated with PrimeC vs Placebo



PrimeC Slowed the Loss of Physical Function vs. Placebo at 6-months

NeuroSense Therapeutics
Nasdaq: NRSN

PARADIGM
SHIFTING THE PARADIGM

	Intention To Treat (ITT)						Per Protocol (PP)					
Sensitivity Analysis: Mixed Model of Repeated Measures - Double-blind Period; Day 180	n	PrimeC (N=45) Adjusted Mean [95% CI]	n	Placebo (N=23) Adjusted Mean [95% CI]	Mean Difference (95% CI)	P-value	% Difference PrimeC vs Placebo	n	PrimeC (N=43) Adjusted Mean [95% CI]	n	Placebo (N=19) Adjusted Mean [95% CI]	Mean Difference (95% CI)	P-value	% Difference PrimeC vs Placebo
ALSFRS-R Total Score	40	32.09 [30.206, 33.981]	#	29.862 [27.424, 32.301]	2.232 [-0.606, 5.069]	0.12	29.22	40	32.515 [30.686, 34.343]	17	29.295 [26.742, 31.848]	3.220 [0.337, 6.103]	0.03	37.42
Bulbar Domain Score	40	10.263 [9.808, 10.718]	#	9.849 [9.255, 10.443]	0.414 [-0.285, 1.113]	0.24	33.09	40	10.272 [9.824, 10.720]	17	9.740 [9.094, 10.385]	0.532 [-0.215, 1.280]	0.16	39.12
Fine Motor Domain Score	40	5.887 [5.076, 6.698]	#	5.495 [4.464, 6.527]	0.392 [-0.779, 1.563]	0.51	16.30	40	6.111 [5.274, 6.948]	17	5.595 [4.444, 6.747]	0.516 [-0.759, 1.791]	0.42	20.60
Gross Motor Domain Score	40	4.689 [3.931, 5.447]	#	4.185 [3.244, 5.126]	0.504 [-0.544, 1.553]	0.34	19.27	40	4.804 [4.040, 5.568]	17	3.965 [2.940, 4.989]	0.840 [-0.274, 1.953]	0.14	28.59
Respiratory Domain Score	40	11.064 [10.422, 11.707]	#	10.255 [9.385, 11.125]	0.809 [-0.256, 1.874]	0.13	52.36	40	11.132 [10.516, 11.747]	17	9.992 [9.086, 10.898]	1.140 [0.067, 2.213]	0.04	66.74
Percent Predicted Slow Vital Capacity (%)	40	71.378 [66.290, 76.467]	#	68.909 [62.368, 75.449]	2.469 [-4.873, 9.811]	0.5	13.28	40	71.588 [66.224, 76.951]	16	68.096 [60.609, 75.583]	3.492 [-4.640, 11.624]	0.39	17.28