

JAMA Neurology Publishes Results from PARADIGM Phase 2b Trial of PrimeC in ALS Demonstrating Meaningful Clinical Outcomes and Biological Activity

The Journal of the American Medical Association (JAMA Neurology) publication highlights consistent clinical and biomarker findings from NeuroSense PARADIGM Phase 2b trial in ALS, including slower functional decline, reduced risk of ALS-related complications, and modulation of disease-relevant biomarkers

CAMBRIDGE, Mass., March 16, 2026 /PRNewswire/ -- NeuroSense Therapeutics Ltd. (NASDAQ: NRSN) ("NeuroSense"), a late-stage clinical biotechnology company focused on developing disease-modifying treatments for neurodegenerative diseases, today announced that results from the Phase 2b clinical trial (PARADIGM) evaluating PrimeC in people living with amyotrophic lateral sclerosis (ALS) have been published in [JAMA Neurology](#).

Earlier today, *Mass General Brigham (MGB) and Barrow Neurological Institute (BNI)* issued a [joint announcement](#) highlighting the publication and the contributions of the investigators involved in the PARADIGM trial. NeuroSense is honored to collaborate with these leading ALS research centers of excellence and their distinguished clinical teams in advancing research for people living with ALS.

PARADIGM was a randomized, double-blind, placebo-controlled trial that evaluated the safety, biological activity, and potential clinical effects of PrimeC during a 6-month blinded treatment period followed by a 12-month open-label extension.

PrimeC is a novel fixed-dose oral combination formulated in a synchronized extended-release composition designed to concurrently address three key mechanisms implicated in ALS progression: neuroinflammation, iron dysregulation, and microRNA-mediated regulatory pathways.

The publication was authored by a distinguished international group of ALS investigators, including **Merit Cudkowicz, MD, MSc (Mass General Brigham and Harvard Medical School)**, **Vivian Drory, MD (Tel-Aviv Sourasky Medical Centre)**, **Adriano Chiò, MD, PhD (University of Torino)**, **Christian Lunetta, MD (IRCCS Maugeri)**, **Christen Shoemith, MD (London Health Sciences Centre)**, **Ruben van Eijk, MD, PhD (UMC Utrecht)**, **Jeffrey Rosenfeld, MD, PhD (Loma Linda University)**, and **Jeremy Shefner, MD, PhD (Barrow Neurological Institute)**, together with additional collaborators across North America, Europe, and Israel.

Key highlights from the PARADIGM phase 2b study published

- **Strong safety and tolerability profile:** PrimeC demonstrated a safety profile comparable to placebo over 18 months, with most treatment-related adverse events mild to moderate and transient.
- **Clinically meaningful functional outcomes:** Continuous treatment with PrimeC was associated with slower functional decline and improved long-term outcomes, including a **7.92-point advantage in ALSFRS-R at 18 months, which represents over 36% benefit of slowing disease progression** ($p=0.007$) and significant improvement in bulbar function ($P=0.001$).
- **Reduction in risk of major ALS complications:** Early initiation of PrimeC was associated with a **64% relative reduction in risk of ALS-related complications** ($p=0.02$), including respiratory failure, hospitalization, or death.
- **Biological evidence supporting disease modification:** PrimeC treatment was associated with significant modulation of ALS-related microRNAs and iron-regulatory biomarkers, supporting its biological activity and reinforcing the potential for **disease-modifying effects**.
- **Supports advancement to Phase 3:** These findings support the continued clinical development of PrimeC and its advancement to a **confirmatory Phase 3 clinical trial in ALS**.

*"ALS is one of the most serious neurological diseases, and there is an urgent need for therapies that can meaningfully alter its course," said **Merit Cudkowicz, MD, MSc**, Director of the Healey & AMG Center for ALS at Mass General Brigham and Julieanne Dorn Professor of Neurology at Harvard Medical School. "What is particularly noteworthy about the PARADIGM results is the consistency of the findings across clinical outcomes and disease-relevant biomarkers, in addition to good safety. These results provide a strong scientific rationale for continuing the clinical development of PrimeC and support its evaluation in a larger confirmatory Phase 3 trial."*

*"What stands out about the PARADIGM study is the multiple clinical endpoints suggest the same level of clinical benefit and that multiple biomarkers are consistent with clinical endpoints," said **Jeremy M. Shefner, MD, PhD**, Professor of Neurology at the Barrow Neurological Institute and corresponding author of the publication. "Together, these findings provide a strong scientific foundation for advancing PrimeC into a Phase 3 trial designed to validate its impact for patients."*

*"The publication of the PARADIGM results in the prestigious JAMA Neurology represents an important milestone for NeuroSense and for people living with ALS," said **Ferenc Tracik, MD**, Chief Medical Officer of NeuroSense Therapeutics. "This*

article integrates PrimeC's safety, clinical, and biomarker data over 18 months. The consistent findings of slower functional decline, reduced risk of ALS-related complications, and modulation of iron-regulatory and microRNA biomarkers strengthen confidence in PrimeC's potential as a disease-modifying therapy. These findings directly informed the design of our Phase 3 trial, which has received FDA clearance to proceed."

PARADIGM Study Overview

PARADIGM was a multinational Phase 2b randomized, double-blind, placebo-controlled clinical trial conducted at leading ALS referral centers in Italy, Canada, and Israel.

The study enrolled 68 participants with definite or probable ALS, randomized in a 2:1 ratio to receive PrimeC or placebo for six months. The double-blind phase was followed by a 12-month open-label extension, during which all participants received PrimeC while maintaining blinding to original treatment assignment.

Even though the trial was not powered to demonstrate definitive efficacy, participants who received PrimeC from the outset maintained a clinically meaningful 7.92-point functional advantage in ALSFRS-R at 18 months, which represents over 36% benefit of slowing disease progression ($p=0.007$), with the largest improvement observed in the bulbar domain ($p=0.001$), a key determinant of speech, swallowing, and quality of life in ALS.

In addition, ALS complication-free survival demonstrated a 64% relative risk reduction favoring early treatment ($p=0.02$), suggesting potential long-term clinical benefit.

Biomarker Findings

The trial also demonstrated biological activity consistent with PrimeC's proposed multi-pathway mechanism.

Markers of iron metabolism, which are frequently dysregulated in ALS, showed favorable significant changes, including preservation of transferrin levels and stabilization of ferritin.

In parallel, plasma microRNA analysis revealed statistically significant downregulation of ALS-associated microRNAs miR-199a-3p, miR-199a-5p, miR-181a-5p, and miR-181b-5p, which have been linked to disease severity and prognosis.

Together, these findings provide biological evidence that PrimeC engages disease-relevant pathways and support its continued development as a potential disease-modifying therapy.

About PrimeC

PrimeC is an investigational fixed-dose oral combination therapy composed of celecoxib and ciprofloxacin in a synchronized extended-release formulation. The therapy is designed to simultaneously target multiple biological mechanisms implicated in ALS progression, including neuroinflammation, iron dysregulation, and microRNA dysregulation.

The therapeutic rationale for PrimeC is supported by preclinical evidence across ALS disease models and human induced pluripotent stem cell-derived motor neuron systems and has now been evaluated in a randomized Phase 2b clinical trial.

About NeuroSense Therapeutics

NeuroSense Therapeutics is a clinical-stage biopharmaceutical company focused on developing disease-modifying therapies for people living with ALS and other neurodegenerative diseases. The company's lead program, PrimeC, is designed to simultaneously target multiple biological pathways implicated in ALS progression.

Forward-Looking Statements

This press release contains "forward-looking statements" that are subject to substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this press release are forward-looking statements. Forward-looking statements contained in this press release may be identified by the use of words such as "anticipate," "believe," "contemplate," "could," "estimate," "expect," "intend," "seek," "may," "might," "plan," "potential," "predict," "project," "target," "aim," "should," "will" "would," or the negative of these words or other similar expressions, although not all forward-looking statements contain these words. Forward-looking statements are based on NeuroSense Therapeutics' current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict and include statements regarding the timing of regulatory filings, meetings and regulatory decisions. Further, certain forward-looking statements, including statements regarding future development of PrimeC, are based on assumptions as to future events that may not prove to be accurate. The future events and trends may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward looking statements. These risks include the uncertainty regarding outcomes and the timing of current and future clinical trials; the risk the PrimeC will not advance towards later-stage development, timing for reporting data, including from the study of PrimeC in Alzheimer's disease; that the study will not be successful; the ability of NeuroSense to remain listed on Nasdaq; and other risks and uncertainties set forth in NeuroSense's filings with the Securities and Exchange Commission

(SEC). You should not rely on these statements as representing our views in the future. More information about the risks and uncertainties affecting NeuroSense is contained under the heading "Risk Factors" in the Annual Report on Form 20-F filed with the Securities and Exchange Commission on April 7, 2025 and NeuroSense's subsequent filings with the SEC. Forward-looking statements contained in this announcement are made as of this date, and NeuroSense undertakes no duty to update such information except as required under applicable law.

Logo: https://mma.prnewswire.com/media/1707291/NeuroSense_Therapeutics_Logo.jpg

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Additional assets available online: [Photos \(1\)](#)

<https://neurosense.investorroom.com/2026-03-16-JAMA-Neurology-Publishes-Results-from-PARADIGM-Phase-2b-Trial-of-PrimeC-in-ALS-Demonstrating-Meaningful-Clinical-Outcomes-and-Biological-Activity>