NeuroSense Investor Relations

NeuroSense Achieves Primary Endpoint in Phase 2b ALS Study with Statistically Significant Reduction of TDP-43, the Defining Pathological Hallmark of ALS

- *First randomized, double-blind, placebo-controlled trial to demonstrate treatment-associated reduction of TDP-43 in people living with ALS*
- *TDP-43 pathology is present in more than**97%** of ALS cases and is widely recognized as a central driver of disease progression*
- *PrimeC demonstrates target engagement with consistent effects across clinical outcomes, survival, and biomarkers, supporting its potential as a disease-modifying therapy*

CAMBRIDGE, Mass., June 29, 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 its Phase 2b PARADIGM study of PrimeC in amyotrophic lateral sclerosis (ALS) has successfully met its primary efficacy endpoint, demonstrating a statistically significant reduction in TDP-43 levels compared to placebo. This is the first randomized, double-blind, placebo-controlled clinical study to demonstrate a treatment-associated reduction in TDP-43 in people living with ALS. The analysis was performed using the NeuroDex ExoSORT procedure, an immunoaffinity-based methodology that selectively isolates neuron-derived extracellular vesicles (NDEs). This approach enables measurement of neuron-derived TDP-43, providing a CNS-relevant signal that can be distinguished from TDP-43 released by non-neuronal cells and peripheral tissues.

TDP-43 is the defining pathological hallmark of ALS, present in more than 97% of cases, and is widely recognized as a central driver of disease progression. The observed reduction in TDP-43 provides biological evidence that PrimeC is engaging a core disease mechanism.

Primary Efficacy Endpoint Achieved with Statistical Significance

The randomized, double-blind, placebo-controlled Phase 2b PARADIGM study evaluated the safety, tolerability, biomarkers and efficacy of PrimeC in people with ALS. At Day 180, the pre-specified primary endpoint timepoint, PrimeC produced a statistically significant reduction in TDP-43 versus placebo ($p=0.0421$). The effect was sustained and deepened over the full 18 months of the study, with continuously treated PrimeC participants maintaining lower TDP-43 levels than the placebo arm at Day 540 ($p<0.001$).

These findings build upon previously reported clinical outcomes from the PARADIGM study, including:

- Statistically significant slowing of ALSFRS-R decline at 12 and 18 months (36.5%, $p=0.008$; 32.8%, $p=0.007$)
- Statistically significant ~15-month median survival benefit (HR 0.35, $p=0.004$)
- Consistent modulation of TDP-43, iron-regulatory and ALS-associated microRNA, supporting multi-target engagement
- Favorable safety and tolerability profile with no new safety signals observed over up to 18 months of treatment

"Achieving the primary endpoint of PARADIGM with a statistically significant reduction in TDP-43 marks a defining moment for NeuroSense and for ALS research," said Alon Ben-Noon, Chief Executive Officer of NeuroSense. "For decades, TDP-43 has been recognized as the pathological signature of ALS, yet demonstrating a treatment-associated reduction in people with ALS has remained elusive. Combined with the clinically meaningful slowing of disease progression, significant survival benefit, and consistent biomarker findings previously reported from PARADIGM, these results provide a compelling and highly differentiated body of evidence supporting PrimeC's potential as a disease-modifying therapy. We believe this growing dataset further validates our scientific approach and positions PrimeC as one of the most comprehensively supported therapeutic candidates in ALS today."

"One of the central questions in ALS drug development is whether a therapy is truly affecting the underlying biology of the disease," said Prof. Merit Cudkowicz, MD, MSc, Director of the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital, and Professor of Neurology at Harvard Medical School. "The TDP-43 findings reported in PARADIGM are particularly important because they suggest target engagement of a pathological process present in the majority of people with ALS. When viewed together with the previously reported safety, biomarker and clinical outcome data, and the high unmet need, these results provide compelling data supporting advancement into a confirmatory Phase 3 clinical trial."

"It is remarkable to see that the increase in NDE-associated TDP-43 observed in the placebo group follows the same trajectory as that identified in our longitudinal studies. This effect, together with the positive outcome of PARADIGM, highlights the promise of TDP-43 as a biomarker for monitoring treatment response," said Dr. Erez Eitan, CEO of NeuroDex.

Having secured FDA clearance to initiate its global Phase 3 (PARAGON) study, NeuroSense is advancing trial preparations while progressing regulatory interactions across multiple jurisdictions, including Canada.

About NeuroSense

NeuroSense Therapeutics is a late-clinical stage biotechnology company developing novel treatments for severe neurodegenerative diseases, including amyotrophic lateral sclerosis (ALS) and Alzheimer's disease. The Company's lead product candidate, PrimeC, is a novel oral therapy designed to target multiple key biological pathways underlying disease progression, including neuroinflammation, oxidative stress and dysregulated iron metabolism.

NeuroSense has generated compelling clinical data from its Phase 2b PARADIGM study in ALS, demonstrating meaningful slowing of disease progression. The Company also reported significant biological activity across multiple biomarkers associated with ALS, including microRNAs, supporting PrimeC's multi-target mechanism of action. Notably, long-term follow-up data indicated a meaningful survival benefit, representing a potentially important advancement in the treatment of ALS.

NeuroSense has received clearance from the U.S. Food and Drug Administration (FDA) to initiate a pivotal Phase 3 clinical trial (PARAGON) in ALS, which is expected to enroll approximately 300 participants, primarily in the United States.

For additional information, we invite you to visit ourwebsite and follow us on LinkedIn, YouTube and X. Information that may be important to investors may be routinely posted on our website and these social media channels.

About PrimeC

PrimeC, NeuroSense's lead drug candidate, is a novel extended-release oral formulation composed of a unique fixed-dose combination of two FDA-approved drugs: ciprofloxacin and celecoxib. PrimeC is designed to synergistically target several key mechanisms of ALS and AD, that contribute to neuron degeneration, inflammation, iron accumulation and impaired ribonucleic acid ("RNA") regulation to potentially inhibit the progression of ALS and AD.

About ALS

Amyotrophic lateral sclerosis ("ALS") is an incurable neurodegenerative disease that causes complete paralysis and death within 2-5 years from diagnosis. Every year, more than 5,000 people are diagnosed with ALS in the U.S. alone, with an annual disease burden of $1 billion. The number of people living with ALS is expected to grow by 24% by 2040 in the U.S. and EU.

About ExoSORT and Neuron-derived EV

ExoSORT™ is NeuroDex's proprietary automated platform for the enrichment of neuron-derived extracellular vesicles (NDEs) from blood samples. Utilizing a combination of highly specific neuronal antibodies and a scalable 96-well workflow, ExoSORT™ selectively isolates extracellular vesicles originating from the brain, increasing the neuronal signal by more than 50-fold compared to conventional plasma analyses.

By enriching for brain-derived vesicles, ExoSORT™ enables detection of disease-associated proteins present in multiple tissues, like TDP-43.

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 potential of PrimeC. 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 that 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 March 31, 2026 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.

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