NeuroSense Investor Relations

New Analysis Shows PrimeC Significantly Improves Key miRNAs in ALS Patients

Groundbreaking PARADIGM Trial Offers New Hope for ALS Treatment

CAMBRIDGE, Mass., Oct. 24, 2024 /PRNewswire/ -- NeuroSense Therapeutics Ltd. (Nasdaq: NRSN) ("NeuroSense"), a late-clinical stage biotechnology company developing novel treatments for severe neurodegenerative diseases, today announced transformative findings from its PARADIGM clinical trial of PrimeC. These results illuminate a new frontier in the treatment of ALS (Amyotrophic Lateral Sclerosis), a disease long considered untreatable at its core. The trial demonstrating the significant impact of PrimeC on the regulation of microRNAs (miRNAs), which play a key role in ALS progression, providing compelling evidence of the drug's potential to alter the underlying mechanisms of the disease.

ALS is a fatal disease, known for its relentless destruction of motor neurons, leading to loss of muscle function, speech, and eventually, the ability to breathe. Understanding the molecular drivers of ALS is key to finding a way to slow or stop its progression. These findings represent a breakthrough in that understanding.

Key Findings:

- **Regulation ofCritical miRNAs**: The PARADIGM trial revealed that PrimeC regulates specific miRNAs - key genetic markers that control gene expression involved in ALS progression. These miRNAs were unchanged in the placebo group, underscoring the profound impact of PrimeC on ALS's pathological pathways. MicroRNAs play a crucial role in regulating how genes express themselves, and their dysregulation has long been linked to ALS. By restoring balance to these genetic regulators, PrimeC offers a new method of combating this devastating disease.
- **Restoring miRNA Balance in ALS Treatment:** PrimeC enhances microRNA (miRNA) maturation, addressing the underlying mechanisms of ALS. By influencing Dicer, the endonuclease that processes precursor miRNA into active forms, PrimeC may restore the balance of dysregulated miRNAs in ALS patients. This modulation is thought to facilitate the production of functional miRNAs that regulate gene expression, allowing PrimeC to target disrupted genetic pathways in ALS and potentially slow disease progression and improve patient outcomes. **Clear Differentiation from Placebo**: Patients treated with PrimeC demonstrated consistent effect in miRNA manifestation, with no similar changes seen in the placebo group. This clear distinction offers compelling evidence of PrimeC's potential as a disease modifying treatment, rather than a symptomatic one.

Conclusion:

In conclusion, PrimeC demonstrated beneficial regulation of key miRNAs, supporting its potential to engage critical genetic targets involved in ALS progression. The 2-fold reduction of several miRNAs following PrimeC treatment is particularly striking, offering both a powerful biomarker for tracking ALS and a potential pathway for new therapeutic strategies. This regulation of miRNAs underscores PrimeC's capability to influence ALS at the regulatory level, where previous treatments have struggled.

This work was done in collaboration with ProfessorNoam Shomron who is a world-leading scientist in the field of genetics.

The results from the PARADIGM trial reflect NeuroSense Therapeutics' dedication to developing treatments that go beyond surface-level symptom management, aiming instead to address the root causes of neurodegenerative diseases. PrimeC's ability to regulate miRNAs represents an important step toward a future where ALS patients have more therapeutic options.

For more information about NeuroSense Therapeutics and its ongoing research, visitwww.neurosense-tx.com.

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 PARADIGM

PARADIGM is a prospective, multinational, randomized, double-blind, placebo-controlled Phase2b (NCT05357950) clinical trial of PrimeC in ALS. The trial included 68 participants living with ALS in Canada, Italy, and Israel. 96% of the trial participants who completed the 6-month double-blind portion of the trial chose to receive treatment with PrimeC through a 12-month open label extension. Furthermore, to date (June 2024) all participants that completed the 18-month trial treatment duration, requested to continue PrimeC, which is provided to them in an Investigator Initiated Trial, not limited with time.

As previously reported, in the 6-month double-blind segment of the trial, the data showed clinically meaningful signs of efficacy with a 29% difference in favor of PrimeC vs placebo in analysis of the intent to treat (ITT) population. In the PP top-line analysis from PARADIGM, a statistically significant slowing of disease progression was observed with a 37.4% (p=0.03)

difference in ALSFRS-R in favor of PrimeC vs placebo. Most patients enrolled in both the active and placebo arms of the trial were concurrently treated with Riluzole, the ALS standard of care medication, indicating PrimeC slowed disease progression well beyond the level afforded by the FDA approved ALS drug.

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 that contribute to motor neuron degeneration, inflammation, iron accumulation and impaired ribonucleic acid ("RNA") regulation to potentially inhibit the progression of ALS. NeuroSense completed a Phase 2a clinical trial which met its safety and efficacy endpoints including reducing functional and respiratory deterioration and statistically significant changes in ALS-related biological markers indicating PrimeC's biological activity. PrimeC was granted Orphan Drug Designation by the U.S. Food and Drug Administration and the European Medicines Agency.

About NeuroSense

NeuroSense Therapeutics, Ltd. is a clinical-stage biotechnology company focused on discovering and developing treatments for patients suffering from debilitating neurodegenerative diseases. NeuroSense believes that these diseases, which include amyotrophic lateral sclerosis (ALS), Alzheimer's disease and Parkinson's disease, among others, represent one of the most significant unmet medical needs of our time, with limited effective therapeutic options available for patients to date. Due to the complexity of neurodegenerative diseases and based on strong scientific research on a large panel of related biomarkers, NeuroSense's strategy is to develop combined therapies targeting multiple pathways associated with these diseases.

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.

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 Prime C's potential to treat ALS. Further, certain forward-looking statements 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 risk of a delay in submission by the Company of its regulatory dossier, that regulatory approvals for PrimeC will be delayed or not obtained in Canada or elsewhere; that the market opportunity in Canada will not be as currently estimated; unexpected R&D costs or operating expenses, insufficient capital to complete development of PrimeC, a delay in the reporting of additional results from PARADIGM clinical trial, the timing of expected regulatory and business milestones, risks associated with meeting with the FDA and Health Canada to determine the best path forward following the results from PARADIGM clinical trial, including a delay in any such meeting; the potential for PrimeC to safely and effectively target ALS; preclinical and clinical data for PrimeC; the uncertainty regarding outcomes and the timing of current and future clinical trials; timing for reporting data; the development and commercial potential of any product candidates of Neurosense; 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 4, 2024 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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For further information: For further information: Email: info@neurosense-tx.com, Tel: +972 (0)9 799 6183
