NeuroSense Investor Relations

NeuroSense Reports Additional Positive Results from its ALS Phase 2b PARADIGM Trial

- ***PrimeC demonstrated a clinically meaningful effect on quality of life and on complication free-survival for patients with ALS***
- ***Standard ALS Measure ALSFRS-R already demonstrated a statistically significant effect of PrimeC on slowing down disease progression***
- ***Further analysis of PARADIGM is on track with neurofilament results expected in Q1 and TDP-43 and ProstaglandinJ2 biomarkers expected in the first half of 2024***

CAMBRIDGE, Mass., Feb. 21, 2024 /PRNewswire/ -- NeuroSense Therapeutics Ltd. (Nasdaq: NRSN) ("NeuroSense"), a company developing treatments for severe neurodegenerative diseases, today reports additional positive data from its six-month double-blind Phase 2b PARADIGM trial of NeuroSense's lead drug candidate PrimeC for the treatment of amyotrophic lateral sclerosis ("ALS").

The PARADIGM trial's secondary clinical efficacy outcome measure endpoints included Quality of Life and Survival. Consistent with the previously reported results, PrimeC displayed a clinically meaningful effect on various aspects of patients' quality of life, including mental and physical health. Moreover, analyses pertaining to survival outcomes emphasized the implications of PrimeC intervention in mitigating disease progression and burden. PrimeC achieved an improvement in complication-free survival compared to placebo (in several methodologies, including MiToS and King's Advanced Stage-free Survival), reducing the risk of ALS disease complications or death by up to 53%. These survival analyses observe time from participant randomization to death from any cause or respiratory insufficiency (defined as tracheostomy or the use of non-invasive mechanical ventilation for over 22 hours per day for 10 or more consecutive days), or time to hospitalization due to ALS-related complications or advancements in MiToS or King's stages.

"PrimeC's demonstrated positive effect on quality of life and survival, aligned with the already positive clinical outcome measures, in a relatively small Phase 2b clinical trial truly demonstrates its potential to deliver a meaningful benefit," stated Ferenc Tracik, M.D., NeuroSense's Chief Medical Officer. "From a clinical perspective, these parameters are crucial to neurologists, but more importantly to people living with ALS."

This news comes on the heels of the recent positive top-line results reported in December 2023 from the PARADIGM trial in 68 participants, which met its primary endpoint of safety and tolerability, establishing a robust safety profile of PrimeC. In addition, PrimeC demonstrated a statistically significant slowing of disease progression with a 37.4% (p=0.03) difference in the gold standard ALS tracking measure, the ALS Functional Rating Scale-Revised ("ALSFRS-R"), in favor of PrimeC vs placebo, and 17.2% (p=0.39) difference in Slow Vital Capacity ("SVC") in favor of PrimeC vs placebo, based on the pre-specified Per Protocol (PP) population analysis. The PP analysis population includes all participants who adhered to the trial protocol and treatment plan without any major protocol deviations and includes 62 patients (43 active and 19 placebo).

"The positive impact of PrimeC on quality of life and complication-free survival, together with its demonstrated ability to meaningfully slow down disease progression, is of great value, as we see that we have the potential to profoundly affect patients' lives across the board. We are in great anticipation to soon report on the status of our collaboration on neurofilaments and how this may contribute to expediting the development of PrimeC," stated Alon Ben-Noon, NeuroSense's CEO.

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 patients are diagnosed with ALS in the U.S. alone, with an annual disease burden of $1 billion. The number of patients with ALS is expected to grow by 24% by 2040 in the U.S. and EU.

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 PARADIGM

PARADIGM is a prospective, multinational, randomized, double-blind, placebo-controlled Phase 2b (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 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.

An analysis of the ITT top-line data from the 6-month double-blind segment of the trial showed clinically meaningful signs of efficacy with a 29% difference in ALSFRS-R (p=0.12) and a 13% difference in SVC (p=0.5), both in favor of PrimeC vs placebo. These data include all 68 people living with ALS enrolled in Canada, Italy, and Israel, with the exclusion of one patient who was misdiagnosed. Most patients enrolled in both the active and placebo arms of 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 ALS Complication-free and MiTos/King's Advanced Stage-free Survival Analyses

ALS Complication-free Survival is defined as time from randomization to death from any cause, or respiratory insufficiency (defined as tracheostomy or the use of non-invasive mechanical ventilation for over 22 hours per day for 10 or more consecutive days), or time to hospitalization due to ALS-related complications. MiToS Advanced Stage-free Survival or King's Advanced Stage-free Survival is defined as time from randomization to death from any cause or respiratory insufficiency similarly, however, also utilizes time to increase in MiToS stage or King's stage. MiToS Advanced Stage is based on functional ability (ALSFRS-R) stages from normal functionality to death, while King's stage is based on advancements in disease burden (clinical involvement, feeding, or respiratory failure).

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 our website and follow us on LinkedIn and X.

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 PrimeC as a potential treatment for people with ALS and the timing for release of neurofilament results and TDP-43 and ProstaglandinJ2 biomarker results. 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 a delay in the reporting of additional results from PARADIGM clinical trial, unexpected R&D costs or operating expenses, the timing of expected regulatory and business milestones, risks associated with meeting with the FDA to determine the best path forward following the results from PARADIGM clinical trial, including a delay in any such meeting, a delay in patient enrollment for a Phase 2 trial for Alzheimer's disease or its planned Phase 3 pivotal ALS trial of PrimeC; 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 the company; 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 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. Forward-looking statements contained in this announcement are made as of this date, and NeuroSense Therapeutics Ltd. undertakes no duty to update such information except as required under applicable law.

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