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NeuroSense's Phase 2b ALS Trial Achieves Primary Safety and Tolerability & Secondary Clinical Efficacy Endpoints

Top-Line Results from 6-month double-blind Phase 2b PARADIGM trial with NeuroSense's lead drug candidate for ALS, PrimeC, include:

- PrimeC achieved primary safety and tolerability endpoints with a safety and tolerability profile comparable to placebo
- Meaningful slowing of disease progression: 29% difference (P=0.12) in favor of ALSFRS-R outcome for patients treated with PrimeC vs placebo
- Slow Vital Capacity: observed a positive trend in favor of patients treated with PrimeC compared to placebo
- Neurofilament biomarker results from Biogen collaboration expected in January 2024
- Primary biomarker endpoints and exploratory biomarkers from this trial, expected in H1 2024

NeuroSense Therapeutics, a company developing treatments for severe neurodegenerative diseases, reported that it met its primary safety and tolerability endpoints and achieved secondary clinical efficacy endpoints in the top-line results of its randomized, placebo-controlled, double-blind segment the Company's Phase 2b amyotrophic lateral sclerosis ("ALS") trial of PrimeC ("PARADIGM"). The trial's secondary clinical efficacy outcome measure endpoints included Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised ("ALSFRS-R") and Slow Vital Capacity ("SVC"), a measure of respiratory function. NeuroSense expects to report an additional primary biomarker endpoint of the assessment of ALS hallmarks, TDP-43 and Prostagladin2, to evaluate PrimeC's biological activity, in the first half of 2024 following the completion of the analysis of participants' plasma.

The PARADIGM (NCT05357950) trial is a prospective, multinational, randomized, double-blind, placebo-controlled Phase 2b clinical trial of PrimeC in ALS. Participants living with ALS in Canada, Italy, and Israel were enrolled and dosed for 6 months after being randomized 2:1 to receive PrimeC or placebo, respectively. After completion of the 6-month double-blind segment, the participants had the option to enroll in a 12-month open label extension (OLE), during which they all receive treatment with PrimeC.

Over the course of 6 months, patients treated with PrimeC experienced a slowing of disease progression, including preserved daily function. The clinical efficacy results showed a 29%

difference in favor of PrimeC in ALSFRS-R (p=0.12) and a 13% difference in favor of PrimeC in SVC (p=0.5) based on data from 68 out of 69 patients, due to 1 misdiagnosed participant. These data include 45 patients randomized to the PrimeC arm and 23 patients randomized to the placebo arm, from the 6-month double-blind segment. The safety and tolerability profile of PrimeC was comparable to the placebo. Nearly all participants, 96%, who completed the 6-month double-blind portion of the trial chose to receive treatment with PrimeC through the 12-month open label extension. To date, all the participants who already completed the 18-month trial have opted to continue treatment of PrimeC by joining a subsequent investigator-initiated trial.

NeuroSense expects to report results from a strategic collaboration with Biogen in January 2024, evaluating the impact of PrimeC on neurofilament levels in participants enrolled in PARADIGM. Upon receipt of results, Biogen has the right of first refusal to co-develop/commercialize PrimeC for the treatment of ALS for a limited time following the results.

"The clinical advancement of a new therapy that helps slow down the progression of ALS, with the potential to preserve quality of life, has the capacity to significantly positively impact people living with ALS and their families. While the ALSFRS-R and SVC results are Phase 2 data and were not powered for statistical significance, the positive results support moving forward to a Phase 3 pivotal trial. The biomarker data will also be very informative, and I look forward to seeing those results in early 2024," stated Merit Cudkowicz, M.D., Chair of Neurology at Massachusetts General Hospital, the Director of the Healey & AMG Center for ALS, Julieanne Dorn Professor of Neurology at Harvard Medical School, and member of NeuroSense's Scientific Advisory Board. "I am excited by the top-line clinical data from PARADIGM, as this is an important milestone for the patients I care for and for the entire ALS community."

"The release of this portion of the top-line results of the PARADIGM trial marks an exciting milestone for NeuroSense as we take another step toward helping people suffering from this dire disease. We look forward to meeting with the FDA to determine the best path forward and to advancing discussions with strategic partners who share our vision for PrimeC to benefit people living with ALS," stated Alon Ben Noon, CEO of NeuroSense. "I would like to thank my devoted team and everyone who made this possible, the trial participants, their caregivers and families, as well as the sites' principal investigators and trial coordinators for their tremendous contribution to PARADIGM."

"In addition to the safety and tolerability profile observed, we believe the 29% difference observed in ALSFRS-R in favor of PrimeC as well as the 13% decline in SVC compared to the placebo arm, illustrate PrimeC's potential to render a meaningful clinical benefit to people living with ALS," stated Dr. Ferenc Tracik, NeuroSense's Chief Medical Officer. "With the trial powered to determine statistically significant changes in ALS biomarkers, we look forward to the additional primary endpoint data in the first half of 2024."

Source: **NeuroSense Therapeutics press release**