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Prilenia Announces Clinical Data in Support of its Plans to Initiate Global Phase 3 Study in ALS

Prilenia Therapeutics B.V., a clinical stage biotechnology company focused on the urgent mission to develop novel therapeutics to slow the progression of neurodegenerative diseases and neurodevelopmental disorders, will present clinical data supporting a future Phase 3 study in amyotrophic lateral sclerosis (ALS) during the 14th Annual California ALS Research Summit in Los Angeles. The Company has completed discussions with global regulatory agencies regarding the next stage of development of pridopidine for ALS and is planning for a single pivotal Phase 3 study to start in H2 2024.

Pridopidine is an investigational oral, small molecule, highly selective and potent Sigma-1 Receptor (S1R) agonist being studied as a potential treatment for ALS and Huntington's disease (HD). The S1R is highly expressed in the brainstem and spinal cord, areas implicated in ALS and important for bulbar function and speech.

"Based on the clinical data generated to date, pridopidine has the potential to become a meaningful treatment for ALS, slowing key measures of disease progression, including function, respiration, quality of life and impact on speech, which is very meaningful for patients and caregivers, as well as prolonging overall survival," said Dr. Michael R. Hayden, CEO and Founder of Prilenia. "We believe it is important for Prilenia to advance our clinical program in ALS, and we are actively planning a single, global, pivotal Phase 3 clinical trial. Our sincere appreciation to the many ALS patients, caregivers and healthcare providers who have contributed so much to our clinical studies as well as to those who will participate in future trials. We also are grateful to Dr. Merit Cudkowicz and the entire team at the Sean M. Healey & AMG Center for ALS for their innovative and passionate approach to evaluating pridopidine as we continue our close working relationship."

"In the Phase 2 clinical trial, pridopidine showed encouraging results for the potential treatment of ALS across multiple secondary and exploratory measures with an excellent safety profile, and we are pleased to work closely with Prilenia on the advancement of this program into Phase 3," said Merit Cudkowicz, M.D., MSc, principal investigator and sponsor

of the HEALEY ALS Platform Trial, Director of the Sean M. Healey & AMG Center for ALS, Chair of the Department of Neurology at Massachusetts General Hospital and the Julieanne Dorn Professor of Neurology at Harvard Medical School.

While pridopidine did not meet the primary outcome measure, data from the Phase 2 HEALEY ALS Platform Trial evaluating the safety and efficacy of pridopidine as a potential treatment for ALS show in the pre-specified subgroup of participants with definite ALS who were also early in the course of the disease (less than 18 months from symptom onset) that pridopidine was associated with slower disease progression relative to placebo in ALSFRS-R (Δ2.4, p=0.19), respiratory domain (Δ1.04, p=0.18), and dyspnea (Δ1.35, p=0.014). Less worsening was observed on the ALSAQ-40 quality of life scale (Δ-10.83, p=0.018) and its eating and drinking (Δ-19.18, p=0.015) and communication (Δ-13.04, p=0.12) domains.

Pridopidine was also observed to have beneficial effects compared to placebo in speech in the full analysis set (speaking rate, p=0.027, articulation rate p=0.0129, phonation time p=0.076, and articulation precision p=0.1138). Speech is a highly clinically relevant endpoint in ALS, and measures of speech are associated with overall ALS and bulbar disease severity. As ALS progresses, it is common for patients to have difficulty speaking due to weakening muscles (dysarthria). This poses significant communications challenges with family, friends and healthcare providers.

Additional analyses from the same Phase 2 study of participants with definite or probable ALS who were also early and fast progressors were conducted. In this subgroup, there was a significant and meaningful (41 percent) slowing of disease progression compared to placebo at 24 weeks in ALSFRS-R (Δ5.2, p=0.04). This slowing of disease progression was already observed at 8 weeks (44.5 percent, p=0.02) and 16 weeks (52 percent, p=0.014). This group also showed greatest improvements vs placebo in ALSFRS-R respiratory domain (Δ1.81, p=0.08), dyspnea (Δ1.41, p=0.019), speaking rate (Δ1.08, p=0.00004) and articulation rate (Δ1.03, p=0.00002).

Furthermore, survival benefits from post-hoc analyses of the placebo-controlled and open-label extension portions of the study show that pridopidine provided an increase in survival time for the specific subgroup consisting of participants with definite or probable ALS who were also early in the course of the disease. A Kaplan-Meier survival analysis showed a prolongation of median survival time from ~300 to 600 days in these participants compared to the delayed-start placebo participants (log rank test: p=0.069). The Cox Proportional Hazard Ratio (HR), adjusted for baseline characteristics, was 0.429 (p=0.052), representing a 57 percent improvement in survival benefit.

Altogether, these results are encouraging and further inform the ongoing planning of a Phase 3 study.

Preliminary topline results in the full analysis set of this Phase 2 study were previously announced. Pridopidine was well-tolerated with no serious treatment-related adverse events, with a safety and tolerability profile similar to placebo and consistent with previous clinical studies.

About Pridopidine and the Sigma-1 Receptor (S1R)

Pridopidine (45 mg twice daily) is an oral, highly selective, and potent investigational S1R agonist that has exhibited a safety and tolerability profile similar to placebo in clinical studies to date. The S1R protein is highly expressed in the brain and spinal cord, where it regulates several key processes that are commonly impaired in various neurodegenerative diseases. Activation of the S1R by pridopidine stimulates multiple cellular protective pathways, including autophagy, axonal transport, mitochondrial energy production and calcium homeostasis, which are essential to neuronal function and survival, and may lead to neuroprotective effects.

Source: **Prilenia Therapeutics B.V.**