NEWS RELEASE

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

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NAARDEN, Netherlands & WALTHAM, Mass.--(BUSINESS WIRE)-- **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.

In collaboration with Massachusetts General Hospital and the Healey Center and through the ACT for ALS (Accelerating Access to Critical Therapies for ALS Act), **the National Institutes of Health (NIH) has provided a grant** to support expanded access to pridopidine for 200 persons with ALS in the U.S. who are not eligible for active clinical trials.

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.

Mutations in the S1R gene cause ALS with the time of onset related to the expression of the S1R gene. For example, patients with no S1R protein have juvenile-onset ALS, while patients with diminished S1R expression have adult-onset ALS. The S1R positively regulates key cellular pathways that are commonly impaired in ALS and other neurodegenerative diseases. In ALS cell culture and mouse models, pridopidine has been shown to be neuroprotective, specifically mediated via the activation of S1R.

Prilenia holds Orphan Drug designation for pridopidine in ALS and Huntington's Disease (HD) in the U.S. and EU. In addition, pridopidine has received Fast Track designation by the U.S. Food and Drug Administration (FDA) for the treatment of HD. Pridopidine is not yet approved in the U.S. or EU.

About the HEALEY ALS Platform Study – Pridopidine Regimen

The Phase 2 clinical study, led by the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital, was designed to evaluate the potential safety and efficacy of pridopidine, along with multiple other investigational products simultaneously, for the treatment of ALS.

Eligible participants had El Escorial possible, probable, or definite ALS, symptom onset <36mo and vital capacity >50%-predicted. Pridopidine 45 mg bid (n=121) was compared to a shared placebo (n=164). The primary endpoint

was change from baseline through 24 weeks in ALSFRS-R total (Full Analysis Set, FAS). Secondary and exploratory endpoints included speech, respiration, and quality of life measurements. Prespecified and post-hoc subgroups included definite or probable ALS, early (<18mo symptom onset) and fast progressors (pre-baseline slope>=-1). Nominal p-values are reported.

About Expanded Access for Pridopidine

The Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital has been **awarded a grant from the National Institutes of Health (NIH)** - Neurological Disorders and Stroke (NINDS) to conduct an intermediate size Expanded Access Protocol (EAP) in ALS in collaboration with Prilenia Therapeutics. The EAP made possible by this award will allow ALS individuals who are otherwise not eligible for participation in clinical trials of pridopidine to access this investigational drug.

Additionally, this EAP will provide real world safety, biomarker, and clinical data in up to two hundred (200) ALS individuals treated with pridopidine for up to two (2) years, thus contributing to our understanding of the effects of pridopidine in a broad population. The pridopidine EAP will be conducted at up to 45 enrolling centers across the U.S. The enrollment phase is anticipated to start in the Spring of 2024.

Additional information about Prilenia's EAP policy is available on our website.

About Prilenia

Prilenia is a clinical stage biotechnology company founded in 2018 focused on the urgent mission to develop novel therapeutics to slow the progression of neurodegenerative diseases and neurodevelopmental disorders. The initial focus of the company has been on HD and ALS.

Prilenia is backed by a group of well-respected investors including: Forbion, Morningside, Sands Capital, SV Health Investors, Sectoral Asset Management, Talisman, Amplitude Ventures and the ALS Investment Fund. The Company is based in Naarden, the Netherlands, Herzliya, Israel and Waltham, Massachusetts in the U.S.

For more information, visit **www.prilenia.com** and follow us on **LinkedIn** and **Twitter**.

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