NEWS RELEASE

Prilenia Shares Preliminary Topline Results from Phase 3 PROOF-HD Clinical Trial in Huntington's Disease and Data from Phase 2 HEALEY ALS Platform Trial of Pridopidine at the 75th American Academy of Neurology (AAN) Annual Meeting

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- PROOF-HD primary endpoint (Unified Huntington Disease Rating Scale-Total Functional Capacity) and the key secondary endpoint (Composite Unified Huntington's Disease Rating Scale) did not reach statistical significance
- PROOF-HD marks the first time that any trial in Huntington's disease (HD) suggests benefit on multiple important clinical measures
- Pre-specified analyses in PROOF-HD, excluding patients on neuroleptics and chorea medications, showed clinically meaningful and nominally significant benefits and improvements from baseline of pridopidine as compared to placebo on disease progression, motor and cognitive outcome measures
- Q-Motor, an objective measure of motor function, showed robust beneficial effects for participants treated with pridopidine in PROOF-HD at various timepoints
- In both PROOF-HD and the HEALEY ALS Platform Trial, pridopidine was well-tolerated with no serious treatment related adverse events
- The Company is committed to advancing pridopidine in HD and amyotrophic lateral sclerosis (ALS)

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, today announced preliminary topline results of its Phase 3 PROOF-HD clinical study evaluating the safety and efficacy of pridopidine in individuals with Huntington's disease (HD). These initial results, along with recently announced findings from the pridopidine arm of the HEALEY ALS Platform Trial, were presented today at the 75th American Academy of Neurology (AAN) Annual Meeting taking place in Boston, MA.

Pridopidine is an investigational oral, small molecule, highly selective and potent Sigma-1 Receptor (S1R) agonist, and its safety and efficacy have not been determined by the FDA.

Preliminary analysis of PROOF-HD indicated that the Phase 3 study did not meet its primary endpoint, change from baseline compared to placebo at 65 weeks, as measured by the Unified Huntington Disease Rating Scale-Total Functional Capacity score (TFC), or the key secondary endpoint, measured by the Composite Unified Huntington's Disease Rating Scale (cUHDRS). Effects on both of these measures were reduced by the use of concomitant medications.

Pre-specified analyses that excluded participants taking neuroleptics and chorea medications showed clinically meaningful and nominally significant benefits for participants on pridopidine across multiple measures, including disease progression (cUHDRS) and cognition (Stroop Word Reading Test, SWR), at various timepoints. There were also positive trends in motor (TMS) and function (TFC). For many of these measures, this represented improvement from baseline values.

Additionally, important secondary endpoints measuring Q-Motor, a quantitative, objective, rater-bias independent, computerized assessment of motor function, showed robust and nominally significant beneficial effects for participants on pridopidine and improvement from baseline. The effect was further strengthened when excluding participants taking neuroleptics and chorea medications.

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.

"These preliminary findings reflect the potential of pridopidine across a variety of important clinical measures, for a large subset of patients in the study," said Ralf Reilmann, M.D., Founding Director and CEO, George Huntington Institute (GHI), Muenster, and the European Lead Principal Investigator for the PROOF-HD study. "The Q-Motor findings in PROOF-HD replicate what was seen in the prior Phase 2 PRIDE-HD study and are highly correlated to cUHDRS and TFC. The totality of these data will hopefully bring pridopidine closer to becoming a new treatment for HD."

“The potential represented in these preliminary results warrants further investigation of pridopidine given the highly complex nature of HD, the 100,000 patients affected by it worldwide, and the lack of an approved treatment that slows its clinical progression,” said Andrew Feigin, M.D., Chief Medical Officer at The Huntington Study Group, Professor, Department of Neurology at NYU Grossman School of Medicine, and North American Lead Principal Investigator for the PROOF-HD study. “PROOF-HD marks the first time in HD that we have had a study suggest benefit on multiple important clinical measures, including progression, cognition, and motor findings.”

Dr. Feigin presented “Topline results of the PROOF-HD pivotal phase 3 trial: PRidopidine's Outcome On Function in Huntington Disease,” at AAN on Tuesday, April 25, 2023 as part of the Clinical Trials Plenary Session. These initial results also will be presented at the CHDI Foundation’s 18th Annual Huntington’s Disease Therapeutics Conference taking place April 24-27, 2023, in Dubrovnik, Croatia.

“We are pleased to see initial results of PROOF-HD that suggest pridopidine provided meaningful benefits to certain HD patients,” said Dr. Michael R. Hayden, CEO and Founder of Prilenia. “While of course we are not satisfied by not reaching the primary endpoint of this study, PROOF-HD has provided key findings that will be important to patients and families with HD and offer hope for progressing pridopidine for this devastating illness. We are deeply grateful to the global HD community, study investigators, and most importantly, the people who participated in this study and their families for making this important research possible.”

Detailed analyses of the PROOF-HD data, including additional pre-specified and post-hoc results, are planned for presentation at future scientific meetings.

The Company intends to continue providing patients with access to pridopidine as part of the current PROOF-HD Open Label Extension or via Expanded Access programs.

The PROOF-HD study was conducted with the **Huntington Study Group (HSG)**, a world leader in clinical research for HD and valued collaborator for Prilenia.

Pridopidine in ALS: First Scientific Presentation of Initial Data from the HEALEY ALS Platform Trial

Sabrina Paganoni, M.D., Ph.D., of Massachusetts General Hospital, presented “Results from the First Four Regimens of the HEALEY ALS Platform Trial,” at AAN on Tuesday, April 25, 2023 as part of the Clinical Trials Plenary Session.

This was the first scientific presentation of topline results from the pridopidine arm (Regimen D) of the HEALEY ALS Platform Trial, which were **previously announced by Prilenia** and the **Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital**, in February 2023. The pridopidine arm of the study showed notable, nominally

significant effects on several clinical outcome measures, including rate of progression (ALSFRS-R), respiration (dyspnea), speech (aural analytics), and quality of life (ALSAQ-40), in fast-progressing patients who were early in their disease.

“Pridopidine showed encouraging results for the potential treatment of ALS that deserve further exploration,” 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. “The impact of pridopidine on rater-independent speech measures was especially notable, likely due to its S1R mechanism of action. Speech is a highly clinically relevant endpoint in ALS studies, and more than 80 percent of ALS patients become speech impaired, which significantly impacts their quality of life.”

The Company is exploring the potential for a Phase 3 clinical study of pridopidine in ALS.

“The Prilenia team’s dedication and drive as they work to develop novel treatments that can slow the progression of neurodegenerative diseases like HD and ALS is truly remarkable,” said Geert-Jan Mulder, Chairman of the Board of Directors of Prilenia and Managing Partner at Forbion. “The Company is committed to advancing pridopidine in both HD and ALS, as well as additional indications.”

About Pridopidine

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.

Prilenia holds Orphan Drug designation for pridopidine in HD and ALS 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.

About PROOF-HD

PROOF-HD, a Phase 3, randomized, double-blind, placebo-controlled study, evaluated the safety and efficacy of pridopidine (45 mg twice daily for 65-78 weeks), an oral, highly selective, and potent investigational S1R agonist, in individuals with manifest HD (TFC 7-13 at baseline). The aim of the study was to evaluate pridopidine’s ability to preserve the functional ability of individuals living with HD, with a primary endpoint of a change from baseline in

the UHDRS-TFC score at 65 weeks. The highest ranked secondary endpoints were cUHDRS, which includes measures of TFC, SWR, Total Motor Score and Symbol Digit Modalities Test, as well as Q-Motor. The study enrolled 499 individuals and was conducted in the U.S., Canada, Austria, Czech Republic, France, Germany, Italy, the Netherlands, Poland, Spain and the United Kingdom.

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.

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**.

For a copy of this release, visit Prilenia's website at **www.prilenia.com**.

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