NEWS RELEASE

Prilenia Announces Topline Results for Pridopidine in Phase 2 ALS Study

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- The primary and key secondary endpoints did not reach statistical significance
- Beneficial effects were observed across several secondary and exploratory endpoints
- Both pre-specified and post-hoc analyses in early, fast progressors showed benefit in the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) and neurofilament light (NfL)
- These results provide valuable insights, which will inform future clinical development for pridopidine 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 and neurodevelopmental disorders, today announced initial results from the pridopidine arm of the Phase 2 HEALEY ALS Platform Trial. Pridopidine is an oral, small molecule, highly selective and potent Sigma-1 Receptor (S1R) agonist. It is an investigational drug, and its safety and efficacy have not been determined by the FDA.

While pridopidine did not meet the primary endpoint of change from baseline to week 24 in the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R), there were consistent, positive trends observed among participants receiving pridopidine across several pre-specified secondary and exploratory measures.

In post-hoc analyses, rapidly declining participants on pridopidine with definite or probable ALS who were early in the disease (less than 18 months from symptom onset) had substantially less decline in the ALSFRS-R total score

(-7.51 points) compared to placebo (-12.71 points, unadjusted p-value=0.04).

Trends for less decline in the ALSFRS-R respiratory sub-scale were also seen in all participants (p=0.06). In pre-specified analyses of all study participants, benefits were observed in quantitative speech measures with significant improvement in speaking rate (p=0.028) and articulation rate (p=0.013).

Neurofilament light (NfL) is a well-recognized biomarker of ongoing neuronal injury that is increased in neurodegenerative diseases including ALS, Huntington's disease (HD), multiple sclerosis, and Alzheimer's disease. Pridopidine reduced NfL levels in rapidly declining patients with disease duration less than 18 months (average reduction of 40%) at 24 weeks compared to placebo in post-hoc analyses.

Data from this and other clinical studies show that pridopidine was well-tolerated, with a safety profile comparable to placebo. There were no new safety indicators as compared to previous clinical studies where pridopidine was similarly safe and well-tolerated.

"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, Chief of the Department of Neurology at Massachusetts General Hospital and the Julieanne Dorn Professor of Neurology at Harvard Medical School. "In particular, the impact of pridopidine on speech measures was 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."[1]

"Pre-clinical data in mice and other species strongly indicated that S1R activity can mitigate the features of ALS and loss of function mutations in the Sigma-1 gene that cause ALS in humans. This study showed for the first time in humans that S1R agonism with pridopidine has the potential to impact ALS," said Dr. Michael R. Hayden, CEO and Founder of Prilenia. "This study adds to the growing body of evidence that S1R activation has beneficial neuroprotective effects, and this gives us a compelling rationale for further development of pridopidine in ALS. Prilenia intends to continue its evaluation of pridopidine in ALS, and our future clinical program will build on the important learnings from the HEALEY ALS Platform Trial."

Dr. Hayden continued, "We would like to extend our deepest appreciation to the team at the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital, the clinical trial investigators and staff at the Northeast ALS Consortium sites, and most importantly to the people living with ALS who participated in this trial and their families whose time and commitment made this research possible."

Prilenia is exploring potential next steps for pridopidine in ALS. Additional analyses are underway, including from

the open-label extension study, and complete study results will be presented at upcoming scientific meetings.

About the HEALEY ALS Platform Study

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 amyotrophic lateral sclerosis (ALS).

For additional data from the pridopidine regimen and for information about the trial design, **please see this press release** issued by the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital.

About ALS

ALS, also known as Lou Gehrig's Disease or Motor Neuron Disease, is a chronic progressive neurodegenerative disease that affects people worldwide, with approximately 20,000 in the U.S. alone. The majority of ALS cases (~90%) are sporadic. However, ~10% of ALS cases are caused by genetic mutations. Several genes have been discovered that are causative for ALS, including the gene encoding the Sigma-1 Receptor (S1R).

In patients with ALS, motor neurons in the brain and spinal cord that convey messages to the muscles degenerate, affecting the brain's ability to communicate with muscles. This leads to muscle wasting and progressive paralysis. Patients rapidly lose their ability to walk, speak, eat and breathe and become fully dependent on their caretakers.

About Pridopidine

Pridopidine (45mg twice daily) is an oral, highly selective S1R agonist that has exhibited a safety and tolerability profile similar to placebo in clinical studies to date. It is an investigational drug, and its safety and efficacy have not been determined by the FDA. The S1R is highly expressed in the brain and spinal cord where it regulates several processes that are commonly impaired in various neurodegenerative diseases. Activation of the S1R by pridopidine stimulates multiple cellular pathways, including autophagy, which are essential to neuronal function and survival, and may lead to neuroprotective effects.

Pridopidine is currently being assessed as a potential treatment for people living with HD in PROOF-HD, a global Phase 3 clinical trial. Results from the study, which includes 59 sites and 499 participants, are expected in Q2 2023.

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 Prilenia

Prilenia is a clinical stage biotechnology company focused on developing novel treatments 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, Mass. 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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[1] Armon et al, J Neurol Sci. 1998; 160 and del Aguila et al, Neurology. 2003.

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