NEWS RELEASE

Prilenia Enrolls First Subject in Europe in its PROOF-HD Phase 3 Clinical Trial for Huntington's Disease

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- PROOF-HD, a Phase 3 clinical trial in Huntington's Disease (HD), is currently recruiting in Europe
- The trial is designed to replicate previous findings of pridopidine demonstrating maintenance of functional capacity in early HD patients and could lead to the registration of pridopidine
- PROOF-HD trial is endorsed by the European Huntington's Disease Network

NAARDEN, Netherlands--(**BUSINESS WIRE**)--Prilenia Therapeutics B.V., a clinical stage biotech company focused on developing novel treatments for neurodegenerative and neurodevelopmental disorders, today announces the enrollment of the first participant in Europe in its global Phase 3 clinical trial for HD. The study is being conducted in 60 sites in collaboration with the **Huntington Study Group** (HSG) in North America and Europe. The **first US subjects in the PROOF-HD** trial were enrolled in October 2020.

"The design of the PROOF-HD study is based on strong scientific and clinical data, including in vivo target engagement for the selected dose, prior clinical efficacy results and extensive long-term safety data in our target population. Enrolling our first patients in Europe is a significant milestone."

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PROOF-HD will take place at 30 sites across nine countries in Europe: Austria, Czech Republic, France, Germany, Italy, the Netherlands, Spain, Poland, and the UK. National approval has been granted in all European countries. The first participant was enrolled at **George Huntington Institute (GHI)** in Münster, Germany. The innovative protocol design, including virtual visits, will allow the study to continue undisrupted in case of any potential

lockdown situations during the ongoing COVID-19 pandemic.

The study is a randomized, double-blind, placebo-controlled, Phase 3 study evaluating the efficacy and safety of pridopidine 45 mg bid in patients with early-stage HD. The primary endpoint is Total Functional Capacity. The global study will enroll a total of 480 participants aged 25 years or older with a clinical diagnosis of adult-onset HD in North America and Europe. The treatment period will last up to 78 weeks and there will be an optional open-label extension.

PROOF-HD is designed to replicate previous findings demonstrating that pridopidine shows a beneficial effect on the maintenance of functional capacity in patients with early HD. The trial treatment dose (45 mg bid) has a favorable safety profile based on over 1,000 patient years in previous HD trials.

Ralf Reilmann, MD, PhD, FAAN, Founding Director of the George-Huntington-Institute and European Principal Investigator of the study, said: “PROOF-HD is currently the only Phase 3 study available to early-HD patients in Europe, opening up an exciting opportunity for the patient community with an orally available drug. Pridopidine has shown a positive safety profile and promising results in earlier studies, making me confident of its potential to have a positive effect on everyday function and quality of life for patients.”

Michael R. Hayden, CEO of Prilenia and world-renowned scientist in Huntington’s Disease research, commented: “The design of the PROOF-HD study is based on strong scientific and clinical data, including in vivo target engagement for the selected dose, prior clinical efficacy results and extensive long-term safety data in our target population. Enrolling our first patients in Europe is a significant milestone.”

Pridopidine is a first-in-class highly selective Sigma 1-receptor (S1R) agonist developed by Prilenia for the treatment of neurodegenerative disorders such as HD and Amyotrophic Lateral Sclerosis (ALS). Pridopidine binds and activates the S1R, a protein that is expressed at high levels within the brain and regulates key cellular pathways, commonly impaired in neurodegeneration. Recent analyses of previous **PRIDE-HD** and **Open-HART** trial results have shown positive data with regards to pridopidine on Total Function Capacity.

Further details of the trial can be found here:

- **PROOF-HD Study website**
- **ClinicalTrials.gov**
- **EU clinical trial register**

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Notes to Editors

About Prilenia (**www.prilenia.com**)

Prilenia is a clinical stage biotech startup founded in 2018 with the purpose of improving the lives of patients and their families by developing treatments for neurodegenerative and neurodevelopmental disorders. Prilenia raised $ 88.5 million thus far and is backed by a group of well-respected investors: Talisman, Forbion, Morningside and Sectoral and ALS Investment Fund. The Company is based in Naarden, the Netherlands, Herzliya, Israel and Boston, MA in the U.S.

About Pridopidine

Prilenia's lead asset is Pridopidine, a first-in-class drug candidate with an established safety profile and therapeutic potential in several neurodegenerative diseases affecting adults and children. The highly selective S1R agonist was acquired from Teva in 2018.

Pridopidine's favorable safety profile has been established in clinical trials in >1300 study participants, exposed to various doses for a total of ~1300 patient years.

Pridopidine for Huntington's Disease

HD is a fatal, inherited, neurodegenerative disorder. Every offspring of an HD patient has a 50% chance of inheriting the gene. Usually starting at around 40 years of age, HD patients suffer from movement disorder, progressive functional and cognitive decline, psychiatric disturbances and behavioral symptoms. Following diagnosis, functional, motor and cognitive functions decline steadily, ultimately leading to immobility, dementia and premature death.

Pridopidine has demonstrated maintenance of functional capacity in HD patients, as measured by Total Functional Capacity (TFC), in a clinical trial. This effect was most prominent in early-stage HD patients (HD1 and HD2), who showed functional benefit from pridopidine 45 mg, taken twice a day.

There is extensive preclinical evidence that further supports pridopidine's potential beneficial effect in HD. The therapeutic effect has been shown to be mediated exquisitely by the sigma-1 receptor (S1R) using multiple deletion and antagonist models.

Analyses of previous PRIDE-HD and Open-HART trial results have shown positive data with regards to pridopidine. Exploratory additional efficacy data show pridopidine (45 mg bid) to be the first drug to exert a significant and clinically meaningful beneficial effect on TFC. In addition, results from the Open-HART trial demonstrate potential

durability of the effect of pridopidine with less TFC decline over 5 years compared to historical placebo group, as well as positive safety and tolerability data.

Results were published in The Journal of Huntington's Disease:

- **Effects of Pridopidine on Functional Capacity in Early-Stage Participants from the PRIDE-HD Study**
- **Additional Safety and Exploratory Efficacy Data at 48 and 60 Months from Open-HART, an Open-Label Extension Study of Pridopidine in Huntington Disease**

Prilenia has an orphan drug designation for pridopidine for the treatment of HD in both the US and Europe.

About PROOF-HD

PROOF-HD is a Phase 3, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of pridopidine in patients with early stage of Huntington's Disease. The purpose of the study is to evaluate the effect of pridopidine 45mg bid on functional capacity, as well as on motor and behavioral features.

For more information about PROOF-HD, including inquiries regarding participation, please visit the study's website: **https://huntingtonstudygroup.org/proof-hd/**

About Huntington Study Group Clinical Research

Founded in 1993 in Rochester, NY, the Huntington Study Group (HSG) is a not-for-profit organization comprised of the world's first collaborative network of experts in Huntington's Disease. HSG Clinical Research, Inc. is a wholly-owned for-profit subsidiary of the HSG, conducts clinical trials to benefit the HSG and its mission of seeking treatments that make a difference for those affected by HD. There are 700 credentialed HD experts at more than 120 HSG credentialed research sites worldwide. The HSG also offers educational services like CME4HD™ for healthcare professionals and care providers on treating patients with HD. For more information, visit **www.huntingtonstudygroup.org**.

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