NEWS RELEASE

Clinical Trial Evidence of Association between Antidopaminergic Medications and Clinical Measurements of Huntington's Disease Progression Published in Neurology®

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Post hoc analysis of 247 PROOF-HD placebo-arm participants was associated with greater worsening of measures of both overall clinical outcomes in Huntington's disease (HD) and individual domains of function, motor and cognition in those exposed to antidopaminergic medications (ADMs) at baseline and during the study compared to those who were not

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These newly published data represent clinical trial evidence of an association between ADM exposure and longitudinal clinical measurements of HD progression, and provided key insights informing the rationale and design of the ongoing confirmatory Phase 3 PRECISE-HD study

NAARDEN, Netherlands & WALTHAM, Mass. & BARCELONA, Spain--(BUSINESS WIRE)-- **Prilenia Therapeutics B.V.** and **Ferrer**[i] today announced the publication online, on October 22, 2026, of a new manuscript, in Neurology®, the medical journal of the American Academy of Neurology, presenting a post hoc analysis providing Phase 3 clinical trial evidence of the association between exposure to antidopaminergic medications (ADMs) and clinical outcome measures in Huntington's disease (HD) .

The manuscript, "**Antidopaminergic Medications and Clinical Outcomes in Huntington's Disease: Evidence from the PROOF-HD Placebo-Controlled Trial**"[iii], describes a post hoc analysis of 247 placebo-arm participants from the Phase 3 PROOF-HD study that shows an association between ADM exposure and longitudinal clinical outcome measures in HD, with worsening of both overall progression and measures of individual domains of function, motor and cognition.

"In this study, antidopaminergic medications appeared to have had an impact across various areas of the disease, with results showing a greater worsening of clinical measures in HD participants who were on ADMs, including Total Functional Capacity (TFC), composite UHDRS, Symbol Digit Modalities Test (SDMT), Stroop Word Reading (SWR) and Total Motor Score (TMS), compared to those who were not on ADMs" said Dr. Karen Anderson, Professor of Psychiatry and Neurology at Georgetown University, Director of the Huntington's Disease Care Education and Research Center at Georgetown MedStar Hospital and Georgetown University Medical Center, and publication lead author. "The important learning from this data, is to carefully consider the potential impact ADMs may have when designing or interpreting a clinical study. Taking ADMs may affect how someone scores on different HD measures, potentially influencing the outcome of the study, so we really need to think about ADMs not just as a concomitant medication that we record in a logbook, but as an integral part of the study design."

"The data from this study provided key insights for the rationale and design of the PRECISE-HD study that makes it different from other trials. It has been consciously designed to ensure that patients are not on ADMs at baseline, while maintaining, as part of the study protocol, the ability to use selected ADMs at doses described in product labeling when deemed medically necessary. This ensures that we decrease as much heterogeneity at baseline as possible, so that we increase our chances of observing a study result that is useful to the HD community within the bounds and duration of the study, while still allowing for standard of care in the management of developing clinical symptoms" said Prilenia's Chief Executive Officer, and manuscript co-author, Dr. Michael R. Hayden.

The PRECISE study is focused on generating data to further support regulatory evaluation and will assess the clinical effect of pridopidine on disease progression, functional capacity, motor function, cognition, speech and quality of life.

Dr Anderson has participated in clinical and patient advisory boards for Prilenia.

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[This press release is intended for informational purposes only. Pridopidine is an investigational medicine and is not approved for commercial use by any regulatory authority. Its safety and efficacy have not been established.

Information contained herein does not constitute medical advice. Patients should consult their healthcare provider for guidance regarding diagnosis or treatment options. Local regulations may vary; this release is not intended to promote or advertise any product.]

About HD

Huntington's disease (HD) is a rare, inherited, autosomal dominant, neurodegenerative disease that results in functional, motor, cognitive and behavioral symptoms, and ultimately leads to death. HD is caused by a mutation in the huntingtin (HTT) gene[iii], and each child of a parent with HD has a 50 percent chance of developing the disease[iv].

Across the world an estimated 100,000 people have HD[v], with an additional 300,000 people at risk of developing HD[vi,vii]. It is usually diagnosed between the ages of 35 and 55[viiiix], although HD can occur at any age, including in children and young adults (known as juvenile onset HD or JHD). The disease progresses slowly over 10 to 30[x] years, with patients slowly losing their ability to work, communicate, manage day-to-day life and take care of themselves. This increasing disability leads to full reliance on a caregiver and, ultimately, death.

The only currently available treatments for HD focus on symptomatic relief and palliative care, with no approved therapies shown to impact measures of overall disease progression.

About pridopidine

Pridopidine is an investigational highly selective, oral sigma-1 receptor (S1R) agonist. S1R has been shown to play a role in stimulating multiple neuroprotective pathways impaired in neurodegenerative diseases, such as Huntington's disease (HD) and amyotrophic lateral sclerosis (ALS)[xi].

In clinical studies to date, pridopidine (taken as an oral capsule twice a day) has shown a generally favorable safety and tolerability profile, with data from more than 1,600 people (mostly from HD studies), some of whom have received active treatment for up to seven years[xii].

Pridopidine is currently in late-stage clinical development for HD and ALS. It has Orphan Drug Designation in HD and ALS in the US and EU, and FDA Fast Track designation in the US for the treatment of HD. These designations do not imply that pridopidine has been approved or that safety and efficacy have been established.

About the PRECISE-HD Study

PRECISE-HD (Pridopidine Phase 3 Study to Establish Clinical Impact and Safety in Huntington's Disease) is a confirmatory, global, 400-participant, randomized, double-blind, placebo-controlled study designed to further

evaluate the efficacy and safety of pridopidine, an investigational medicinal product, in people living with Huntington's disease (HD), from early to mid-stage disease (TFC 7-13).

Focused on generating data to further support regulatory evaluation, the study will assess the clinical effect of pridopidine on disease progression, functional capacity, motor function, cognition, speech and quality of life. It incorporates learnings from prior research, advice and input from the HD patient and research community, and regulatory authorities.

PRECISE-HD comprises two consecutive stages: a 52-week placebo-controlled stage, with participants randomized to receive either pridopidine or placebo on a 1:1 basis, followed by a 104-week open-label extension stage in which all eligible participants will receive pridopidine. The primary endpoint is the change from baseline to Week 52 in the combined Unified Huntington's Disease Rating Scale (cUHDRS) score.

PRECISE-HD will be undertaken at up to 75 sites globally, including sites in the United States, European Union, United Kingdom and Canada. Further details are available at **www.clinicaltrials.gov** (**NCT07609108**), **www.clinicaltrialsregister.eu/** (EU CT number: 2026-526093-16-00).

About Prilenia

Prilenia is a private biopharmaceutical company driven by an unwavering commitment to scientific excellence and accelerating progress for people affected by HD, amyotrophic lateral sclerosis (ALS) and other neurodegenerative disorders. Our mission is simple but urgent: to develop and provide sustainable access to transformative medicines for people affected by devastating neurodegenerative diseases.

Prilenia is incorporated in the Netherlands and backed by leading life sciences investors.

Prilenia and Ferrer are partners in co-development and commercialisation of pridopidine.

For more information, please visit **www.prilenia.com**, and connect with us on **LinkedIn**, **X** or **Instagram**.

About Ferrer

At Ferrer, we use business to fight for social justice. We have long been a company that wants to do things differently; instead of maximizing shareholder returns, we reinvest much of our profit in initiatives that give back to society. Back where it belongs. We go beyond compliance and are guided by the highest standards of sustainability, ethics and integrity. As such, since 2022, we are a B Corp.

Founded in Barcelona in 1959, Ferrer offers transformative solutions for life-threatening diseases in more than one

hundred countries. In line with our purpose, we have an increasing focus on pulmonary vascular and interstitial lung diseases and rare neurological disorders. Our 1,800-strong team is driven by a clear conviction: our business is not an end in itself, but a way to change lives.

We are Ferrer. Ferrer for good. **www.ferrer.com**

[i] In April 2025, Prilenia and Ferrer signed a commercialization and co-development agreement for pridopidine. **https://news.prilenia.com/press-releases/press-release-details/2025/Prilenia-Enters-into-a-Collaboration-and-License-Agreement-with-Ferrer-for-the-Commercialization-and-Co-Development-of-Pridopidine-in-Europe-and-Other-Select-Markets/default.aspx**

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