NEWS RELEASE

Nature Medicine Publishes Phase 3 Data on Pridopidine in Early-Stage Huntington's Disease, Highlighting Impact on Clinical Progression

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Treatment with pridopidine slowed clinical progression and maintained function, cognition, and motor performance in pre-defined analyses of a subgroup of early-stage Huntington's disease (HD) patients who were not taking antidopaminergic medicines (ADMs). The PROOF-HD study did not meet its overall primary or secondary endpoints in the full population

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In the group of patients who were not taking ADMs, pridopidine demonstrated clinically meaningful improvement from baseline for one year, and slowing of decline thereafter, as measured by cUHDRS

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ADMs may cause side effects that cannot be distinguished from HD progression and can negatively impact clinical outcome measures and confound treatment-related effects in a clinical trial[i]

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This randomized, double-blind, placebo-controlled study represents the first Phase 3 trial in HD to deliver a consistent pattern of meaningful benefits across multiple outcome measures of efficacy including cognition (SWR)

and motor function (Q-Motor), in a subgroup of subjects, as well as a favorable safety profile

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A planned confirmatory study in early HD patients, designed to confirm pridopidine's effects and support global regulatory approval pathway discussions, is expected to start next year

NAARDEN, Netherlands & WALTHAM, Mass. & BARCELONA, Spain--(BUSINESS WIRE)-- **Prilenia Therapeutics B.V.** and **Ferrer** today announced the publication, in the journal Nature Medicine, of a manuscript entitled "**Pridopidine in Early-Stage Manifest Huntington Disease: A Phase 3 Trial**"[ii]. The publication describes data showing that treatment with pridopidine slowed clinical progression in Huntington's disease (HD) patients not taking antidopaminergic medicines (ADMs).

The published data, from pre-defined analyses of a subgroup of patients not taking ADMs from pridopidine's Phase 3 PROOF-HD trial, show that treatment with pridopidine achieved a clinically meaningful improvement from baseline for one year and slowing of decline thereafter, as measured by cUHDRS, with change vs placebo of 0.46, -0.45, 0.41 and 0.27 at 26, 39, 52 and 65 weeks (the end of the double-blind trial). Annual reductions in cUHDRS of 0.1–0.3 points have been associated with a clinically meaningful benefit in HD[iii].

Importantly, the benefits in cUHDRS in this subgroup of subjects with HD were seen across domains of function, cognition, and motor performance. Pridopidine also achieved similar maintenance of cognition with no deterioration, as measured by Stroop Word Reading Test (SWR), and motor performance, as measured by Quantitative Motor (Q-Motor).

Ralf Reilmann, MD, FAAN, Founding Director, George Huntington Institute and publication lead author, said: "The published data represents the first Phase 3 HD trial to deliver consistent and meaningful benefits on progression across multiple clinical domains of HD such as function, cognition and motor performance, while also confirming pridopidine's favorable safety and tolerability profile. Upcoming studies can now refine patient selection and account for the impact of ADM exposure, which obscured the true drug-related benefits. Appropriate stratification and dosage strategies will control for this confounding factor and allow demonstration of pridopidine's positive treatment effects on clinical progression of symptoms. I would like to express my gratitude for the continued commitment of everyone working to support the next data-driven steps to making this well-tolerated and easily administered treatment option available to HD patients."

Dina de Sousa, European Huntington Association (EHA) Board member, remarked: "We have no options to help slow down our decline. Nothing to help people feed themselves a little longer, button a shirt a little longer, walk a little longer, or maybe even dance a little longer. Treatment options are needed now that can enable

maintenance of independence for as long as possible. These results provide hope that there are therapies that can go further than just symptom control, and hope that we can take a step forward toward availability of a disease-modifying treatment able to slow down the inexorable march of this dreadful disease."

"These data provide a clear path forward for next year's planned global confirmatory study in early HD patients, aimed at confirming pridopidine's effect and supporting ongoing global regulatory discussions," said Dr. Michael R. Hayden, CEO of Prilenia.

"Nature Medicine is one of the world's leading peer-reviewed medical journals, and this important publication adds to the weight of evidence in support of the sigma-1 receptor agonist approach and the development of pridopidine for the treatment of neurodegenerative diseases such as HD and ALS," said Oscar Pérez, Chief Scientific Officer at Ferrer.

About pridopidine

Pridopidine (45 mg twice daily) is a potent and selective, orally administered sigma-1 receptor (S1R) agonist which stimulates key neuroprotective mechanisms impaired in neurodegenerative diseases such as HD and ALS[iv].

Pridopidine's extensive development program involved approximately 1,600 people, demonstrating a favorable safety and tolerability profile.

In addition to HD, pridopidine is in late-stage clinical development for ALS, with Prilenia and Ferrer planning to initiate a single, pivotal Phase 3 trial in ALS early in 2026, building on the findings in the population with early and rapid progressing disease from the Phase 2 HEALEY ALS Platform Trial.

Pridopidine has Orphan Drug designation in HD and ALS in the US and EU, and FDA Fast Track designation for the treatment of HD[v].

About Huntington's Disease

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

HD affects approximately 4.88 out of 100,000 people around the world with an additional 300,000 people at risk of developing HD[viii,ix]. It is usually diagnosed between the ages of 30 and 50, 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 15

to 20 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 nothing impacting measures of overall progression.

About Prilenia

Prilenia is a private biopharmaceutical company driven by an unwavering commitment to scientific excellence and accelerating progress for people affected by Huntington's disease (HD), amyotrophic lateral sclerosis (ALS) and other children and adults with 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 partnered with Ferrer for the commercialization and co-development of pridopidine in Europe and other select markets, retaining full commercialization and development rights to pridopidine in North America, Japan and Asia Pacific.

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

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

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 in adults and children. 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**

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