NEWS RELEASE

Pridopidine Pivotal Phase 3 ALS Study Unveiled at NEALS 2025 Annual Meeting

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Prilenia and Ferrer will unveil their planned pivotal Phase 3 study of pridopidine in ALS at the upcoming Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS) 2025 Annual Meeting, Florida, October 7-10, 2025

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Aimed at confirming the encouraging post hoc Phase 2 data for pridopidine in global function (ALSFRS-R scores), speech, respiratory function and survival[i], the pivotal Phase 3 study is expected to start enrolling participants early in 2026

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In vivo data demonstrating pridopidine's potential to enhance neuronal survival by mitigating ER stress, an early hallmark of ALS and other neurodegenerative diseases, will also be presented

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Pridopidine is an investigational, non-invasive, orally administered, small molecule, sigma-1 receptor (S1R) agonist. Pridopidine has demonstrated a favorable safety and tolerability profile from placebo-controlled studies and clinical experience involving more than 1600 people and extending up to seven years

NAARDEN, Netherlands & WALTHAM, Mass. & BARCELONA, Spain--(BUSINESS WIRE)-- **Prilenia Therapeutics B.V.** and **Ferrer** today announced the presentation of their planned pivotal Phase 3 study of pridopidine in Amyotrophic Lateral Sclerosis (ALS) at the upcoming Northeast Amyotrophic Lateral Sclerosis Consortium (NEALS) 2025 Annual Meeting, Florida, October 7-10, 2025.

“The opportunity to potentially bring a much-needed new therapy for a disease as intractable as ALS is exciting and daunting in equal measure. The ALS community deserves to see progress in the management of the disease – we hope to make some of that progress. Early next year we expect to initiate the study at some of the leading ALS centers in the world, allowing us to begin enrolling participants with early and rapidly progressive ALS,” said Dr. Michael R. Hayden, CEO of Prilenia.

“In the phase 2 HEALEY ALS platform trial we have seen important improvements in global function (ALSFRS-R scores), speech, respiratory function and survival with pridopidine in people with early and rapidly progressive disease. Personally, the benefits in terms of speech were of special significance - helping patients to maintain the ability to communicate with their families at such fragile times brings a value that cannot be expressed clinically,” said Oscar Pérez, Chief Scientific Officer at Ferrer. “These signals provide hope that a sigma-1 receptor agonist like pridopidine can have a major positive impact for people living with ALS, and being on the cusp of being able to further explore that potential is a privilege.”

Details of the pivotal Phase 3 study and the in vivo neuronal survival data will be presented in two posters at NEALS:

Poster 1: A Planned Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Pridopidine in Participants with ALS (poster #191 to be presented by Sabrina Paganoni, Healey Center for ALS at MGH, Boston, Thursday October 9th 2025).

The study will have an initial 48-week double-blind treatment period followed by a 48-week open-label extension phase, with a primary endpoint of change from baseline in ALSFRS-R adjusted for mortality at 48 weeks. Secondary endpoints will include the effect of pridopidine on survival, measures of speech, respiratory (SVC) and bulbar function, and quality of life (ALSAQ-40). The study will also evaluate patient-reported outcomes of communication, as well as plasma biomarkers. Enrollment of participants with early and rapidly progressive ALS[ii] is expected to start in January 2026, subject to regulatory acceptance, at leading ALS treatment centers in the US, Canada and European countries (site opening will be on a rolling basis and subject to local regulatory requirements). The study population is defined to enable determination of a therapeutic effect within the limited timeframe of the trial.

Poster 2: Pridopidine exerts neuroprotective effects through the activation of the Sigma-1 receptor (S1R) by modulating ER stress in iPSC-derived neural progenitor cells (poster #192 to be presented by May Meltzer, Prilenia, Thursday October 9th, 2025).

Prolonged endoplasmic reticulum (ER) stress is an early hallmark of ALS and many other neurodegenerative diseases, implicated in increased mitochondrial dysfunction and reduced neuronal survival. S1R plays a role in pathways that help mitigate ER stress and mitochondrial dysfunction, translating into enhanced neuronal survival. Pridopidine significantly reduced expression of two key markers of ER stress, BiP and CHOP[iii], by 72% and 52% respectively ($p<0.0001$), correlating with improved cell viability and growth (50% increase, $p<0.0001$). A selective S1R antagonist was then used to block pridopidine's effect and demonstrate that restoration of mitochondrial function and cell survival was indeed S1R-dependent.

About pridopidine

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

Pridopidine has demonstrated a favorable safety and tolerability profile throughout its extensive development program, involving more than 1,600 people to date.

Pridopidine is also being utilized in the Accelerating Access to Critical Therapies for ALS (ACT) for ALS Expanded Access Program (EAP), supported by a grant from the National Institutes of Health (NIH) - Neurological Disorders and Stroke (NINDS), being run by the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital (**NCT06069934**)[v]. This ongoing EAP has completed enrollment of 200 people with ALS who were not eligible for other clinical trials.

In addition to ALS, pridopidine is in late-stage clinical development for HD, with Prilenia and Ferrer planning to initiate in 2026 a confirmatory study in HD designed to confirm pridopidine's effects and support global regulatory approval pathway discussions.

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

About ALS

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease or motor neuron disease (MND), is a rare, chronic, progressive neurodegenerative disease that affects approximately 500,000 people worldwide. There are approximately 140,000 new cases diagnosed worldwide each year. The average life span from the onset of symptoms is approximately 2 to 5 years.

In people living 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. People living with ALS rapidly lose their ability to walk, speak, eat and breathe, and become fully dependent on their caretakers. Treatment options are limited.

Dysfunction of the S1R has been associated with multiple forms of ALS, and maintaining S1R functionality may play a key role in protecting neuronal function.

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 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**

[i] **https://www.neurology.org/doi/10.1212/WNL.0000000000206526**

[ii] Participants with definite or probable ALS by EEC and early in the disease (<18 months since symptom onset).

[iii] Binding Immunoglobulin Protein (BiP) and C/EBP Homologous Protein (CHOP)

[iv] Naia, L., Ly, P., Mota, S.I. et al. The Sigma-1 Receptor Mediates Pridopidine Rescue of Mitochondrial Function in Huntington Disease Models. Neurotherapeutics 18, 1017–1038 (2021). **https://doi.org/10.1007/s13311-021-01022-9**

[v] A Second Intermediate-Size Expanded Access Protocol (EAP) for Pridopidine in People With Amyotrophic Lateral Sclerosis (Pridopidine EAP 2) **https://clinicaltrials.gov/study/NCT06069934?cond=ALS&intr=pridopidine&rank=2**

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