NEWS RELEASE

Prilenia and Ferrer Announce FDA Clearance to Start the “PREVAiLS” Pivotal Phase 3 Study with Pridopidine in ALS

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FDA clearance received to start the pivotal, 500-patient, placebo-controlled Phase 3 “PREVAiLS” study of pridopidine in participants with early, rapidly progressive ALS; US recruitment set to begin early 2026

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PREVAiLS (Pridopidine Phase 3 Study to Evaluate Efficacy & Safety in ALS), will be conducted in up to 60 leading ALS treatment centers globally

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Study aims to confirm Phase 2 data from HEALEY trial participants with rapidly progressive ALS, early in their disease course, showing the potential for clinically meaningful improvements with pridopidine in multiple domains of disease progression, speech and survival

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Manuscript describing these subgroup analyses from the HEALY ALS Platform Trial accepted for publication in Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration (ALS & FTD)[i]

NAARDEN, The Netherlands & WALTHAM, Mass. & BARCELONA, Spain--(BUSINESS WIRE)-- **Prilenia Therapeutics B.V.** and **Ferrer** today announced that the US Food and Drug Administration (FDA) has cleared the start of the pivotal, 500-patient, randomized, placebo-controlled Phase 3 study of pridopidine in participants with rapidly progressive amyotrophic lateral sclerosis (ALS) early in their disease course. Recruitment is planned to begin at the first US clinical trial sites in early 2026, with sites in Europe and other regions to follow, pending local clinical trial clearance.

PREVAiLS (Pridopidine Phase 3 Study to Evaluate Efficacy and Safety in ALS) will be conducted in up to 60 leading ALS treatment centers across the US, Canada, EU, UK and Israel[ii]. Aiming to confirm pridopidine's Phase 2 data, the study will target the same subgroup population, enrolling participants with definite or probable ALS (El Escorial Criteria) and who are within 18 months from first onset of disease symptoms.

The study will consist of an initial 48-week double-blind placebo-controlled phase, randomized on a 3:2 (pridopidine:placebo) basis, followed by a 48-week open-label extension phase. The primary endpoint will be the change from baseline in ALSFRS-R adjusted for mortality at 48 weeks. Secondary and exploratory endpoints will include measures of speech, respiratory function, bulbar function, quality of life and effect of pridopidine on survival, as well as patient-reported outcomes of communication and plasma biomarkers[iii]. A study website providing more details will be launched soon at **https://prevailstrial.com/**.

PREVAiLS is predicated on subgroup analyses of data from 284 subjects with rapidly progressive ALS early in their disease course (120 in the pridopidine group and 164 in the shared placebo group) from the Phase 2 HEALEY ALS Platform trial, showing potentially clinically meaningful improvements with pridopidine in multiple domains of disease progression, speech and survival.

These subgroup analyses from the HEALY ALS Platform Trial, described in a manuscript accepted for publication in the peer-reviewed journal Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration (ALS & FTD), showed a 32% slowing of overall progression (ALSFRS-R, p=0.03), a 62% slowing of respiratory function worsening (p=0.03) and slowing of decline of dyspnea by 88% (p=0.005), with articulation and speaking rate deterioration reduced by 93% (p=0.0007) and 70% (p=0.002) respectively, at 24 weeks (p-values nominal).

These data also showed a 57% improvement in survival benefit for patients taking pridopidine, prolonging median survival time from 300 to 600 days (n=49, 37 pridopidine-to-pridopidine, early start group, 12 placebo-to-pridopidine, delayed start group)[iv], and a favorable safety profile[i].

"This study has the clear aim of evaluating the efficacy and safety of a much-needed new treatment option for ALS," said Sabrina Paganoni, MD, PhD, Co-Director, MGH Neurological Clinical Research Institute (NCRI) and PREVAiLS Steering Committee member and investigator. "Early detection and management are essential for preserving

function, with slowing of functional decline, maintaining speech and prolonging survival being ALS therapeutic priorities. This makes pridopidine's S1R activation mechanism of particular interest, holding promise in ALS by enhancing key cellular mechanisms and promoting neuroprotection".

"These data show the potential for benefits with pridopidine - seen across multiple functional domains including overall progression, respiratory, bulbar and speech functionality. This together with the signal of improved survival provides strong rationale to proceed to Phase 3 evaluation of pridopidine," said Merit E. Cudkowicz, MD, MSC, Executive Director Mass General Brigham Neuroscience Institute, Director of the Sean M. Healey & AMG Center for ALS at Mass General Brigham, PREVAiLS Steering Committee member and author on the ALS & FTD paper.

"The FDA's clearance to start PREVAiLS is significant, providing an immediate opportunity to begin a pivotal Phase 3 study with the aim of bringing a promising, oral, well tolerated new therapy to patients," said Henk Schuring, Prilenia's Chief Regulatory and Commercialization Officer. "The publication of the data by ALS & FTD will provide the ALS community with a clear view of the basis for the design of PREVAiLS and our confidence in pridopidine's capabilities, as we aim to confirm pridopidine's results in this population of people living with ALS."

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[v]. It has a favorable safety and tolerability profile, demonstrated in a safety database of more than 1,600 people, extending, in some cases, up to seven years on active treatment.

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**)[vi]. 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 a confirmatory study in HD designed to confirm pridopidine's effects and support global regulatory approval pathway discussions. Study is expected to start recruitment in the first half of 2026.

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 often referred to as 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.

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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[i] Geva M, et al. Pridopidine Treatment in ALS: Subgroup Analyses from the HEALEY ALS Platform Trial" Amyotroph Lateral Scler Frontotemporal Degener. In press.
[ii] Ex-US enrollment is planned to begin following relevant local regulatory approvals.
[iii] van den Berg L, et al. A planned Phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of pridopidine in participants with ALS
36th International Symposium on ALS/MND, San Diego, CA, USA, December 2025.
[iv] The early-start group (pridopidine-to-pridopidine) had a median survival time of 600 days, compared to 300 days in the delayed start group (placebo-to-pridopidine). At 300 days, the survival probability in the early-start pridopidine group was 85%, with a log rank test p-value of 0.069. In addition, Cox regression analysis adjusted from ENCALS score only yielded a HR of 0.429 (p=0.052), indicating a 57% relative reduction in hazard for the early start group compared with the delayed start group.
[v] 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**
[vi] 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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