PRESS RELEASE

Chiesi Global Rare Diseases Announces Publication of Results from Phase 3 BRIGHT Study of Pegunigalsidase Alfa ▼ in Fabry Disease

- *Data published in Journal of Inherited Metabolic Disease*
- *This article is created and funded by Chiesi*

PARMA, 29th, 2024 – Chiesi Global Rare Diseases, a business unit of the Chiesi Group established to deliver innovative therapies and solutions for people living with rare diseases, today announced the publication of results from the Chiesi Phase 3 BRIGHT study of pegunigalsidase alfa 2 mg/kg administered every four weeks for 52 weeks in adult patients with Fabry disease who were previously treated with agalsidase alfa or beta administered every two weeks. The data are published in the *Journal of Inherited Metabolic Disease.*[1]

"We are delighted to see the publication of these data in the Journal of Inherited Metabolic Disease," said ***Dr Kamran Iqbal, Head of Medical Affairs (UK and Ireland) - Global Rare Diseases at Chiesi****. "While the findings are encouraging, further studies will be important to better understand the implications of this investigational 4 weekly dosing regimen with pegunigalsidase alfa, for suitable patients living with Fabry disease."*

Pegunigalsidase alfa is a PEGylated α-Gal A enzyme replacement therapy (ERT) that is approved for the treatment of adults with Fabry disease in the United States, European Union and Great Britain at the recommended dose of 1 mg/kg of body weight administered once every two weeks. The regimen of pegunigalsidase alfa 2mg/kg administered every four weeks is investigational and not approved by the EMA or other regulatory authorities. Interactions with regulatory authorities to investigate the feasibility of introducing every four weeks posology as an alternative dosing regimen are underway.

A total of 29 patients (23 men, 6 women) completed the Phase 3 open-label, single arm, switchover, 12-month BRIGHT study that was designed to assess the safety and efficacy of pegunigalsidase alfa (2 mg/kg) administered intravenously every four weeks in Fabry patients who had previously been treated with agalsidase alfa (0.2 mg/kg) or agalsidase beta (1 mg/kg) every two weeks for at least three years.

The primary endpoint was the number of treatment-emergent adverse events (TEAEs), Other key safety endpoints included occurrence of infusion-related reactions and the development of ADAs directed against pegunigalsidase alfa. Key efficacy endpoints included change in eGFR (calculated using the CKD-EPI equation) and change in plasma concentrations of globotriaosylsphingosine (lyso-Gb3) over the trial period. Additional assessments included patient-reported outcomes and pharmacokinetics.

Results from the Phase 3 BRIGHT study showed:

- There were no new safety concerns among adult patients treated with pegunigalsidase alfa.
  - Overall, 33 (18%) out of a total of 182 TEAEs, reported in 9 (30%) patients in the safety population, were considered treatment-related,

and the majority of patients (7/9) with treatment-related TEAEs were male
    - All treatment-related events were mild or moderate in severity, and there were no TEAEs leading to study discontinuation or death
    - 5/30 (16.7%) patients experienced at least one infusion-related reaction, all of which were mild or moderate
    - No patients developed de novo anti-drug antibodies (ADAs)

- Median estimated glomerular filtration rate (eGFR) change from baseline was -1.9 mL/min/1.73m^2/year (-2.4 in males, -0.7 in females) after 12 months of treatment with pegunigalsidase alfa.
- Plasma lyso-Gb3 concentrations were low and stable in women treated with pegunigalsidase alfa (0/6 ADA-positive), with a slight increase observed in treated men (9/24 ADA-positive) compared to baseline.
- Pegunigalsidase alfa median plasma concentrations at the end of each 4-week dosing interval were above the lower limit of quantification.

"The availability of ERTs for Fabry disease has improved clinical outcomes and disease management for many patients, but there is still room for improvement and a need for additional treatment options. For example, the bi-weekly infusion schedule can often represent a burden for some patients," said Ales Linhart, professor, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic, author of the publication*. "The BRIGHT study results show that 2 mg/kg of pegunigalsidase alfa administered every four weeks is generally well tolerated in adult patients and that this schedule deserves further exploration".*

"Fabry disease is a complex, life-altering condition that profoundly affects quality of life. While existing treatments have, over the years, enhanced patient autonomy and lightened the load on caregivers, many challenges remain, one of them being the infusion frequency", said Mary Pavlou, President of Fabry International Network*. "From a patient's perspective, reducing the frequency of infusions could significantly improve care and enhanced quality of life for both patients and their families, resulting in better health outcomes".*

About Chiesi Global Rare Diseases

Chiesi Global Rare Diseases is a business unit of the Chiesi Group established to deliver innovative therapies and solutions for people affected by rare diseases. As a family business, Chiesi Group strives to create a world where it is common to have a therapy for all diseases and acts as a force for good, for society and the planet. The goal of the Global Rare Diseases unit is to ensure equal access so as many people as possible can experience their most fulfilling life. The unit collaborates with the rare disease community around the globe to bring voice to underserved people in the health care system.

About Chiesi Group

Chiesi is a research-oriented international biopharmaceutical group that develops and markets innovative therapeutic solutions in respiratory health, rare diseases, and specialty care. The company's mission is to improve people's quality of life and act responsibly towards both the community and the environment.

By changing its legal status to a Benefit Corporation in Italy, the US, and France, Chiesi's commitment to create shared value for society as a whole is legally binding and central to

company-wide decision-making. As a certified B Corp since 2019, we're part of a global community of businesses that meet high standards of social and environmental impact. The company aims to reach Net-Zero greenhouse gases (GHG) emissions by 2035.

With over 85 years of experience, Chiesi is headquartered in Parma (Italy), with 31 affiliates worldwide, and counts more than 7,000 employees. The Group's research and development centre in Parma works alongside 6 other important R&D hubs in France, the US, Canada, China, the UK, and Sweden.

For further information please visit www.chiesi.uk.com.

References

1. Holida M, Linhart A, Pisani A, Longo N, François Eyskens, Ozlem Goker-Alpan, et al. A phase III, open-label clinical trial evaluating pegunigalsidase alfa administered every 4 weeks in adults with Fabry disease previously treated with other enzyme replacement therapies. Journal of Inherited Metabolic Disease. 2024 Oct 9;