AM-PHARMA ANNOUNCES POSITIVE CLINICAL DATA FROM PHASE 1B STUDY EVALUATING ILOFOTASE ALFA IN HYPOPHOSPHATASIA PATIENTS

- **Ilofotase alfa demonstrates pharmacologically relevant effect on disease specific biomarkers and a positive safety profile in adult patients with hypophosphatasia;**
- **Data to be presented by Lothar Seefried, MD, at the American Society for Bone and Mineral Research's Symposium on Rare Bone Diseases on Thursday, October 12, 2023**

Utrecht, The Netherlands, October 11, 2023 – AM-Pharma B.V. today announced positive clinical results from the Phase 1b study evaluating the company's proprietary recombinant alkaline phosphatase, ilofotase alfa, as potential enzyme replacement therapy in adult hypophosphatasia (HPP) patients. HPP is an inherited metabolic disease, characterized by low activity of tissue non-specific alkaline phosphatase (TNAP), caused by mutations at the *ALPL* gene. This low activity leads to accumulation of inorganic pyrophosphate (PPi), a strong inhibitor of mineralization, as well as pyridoxal-5'-phosphate (PLP), an important cofactor for enzymes. The disease can range widely in severity, however most adults with HPP suffer from recurrent fractures, muscle weakness, joint diseases and pain.[1]

In the open-label pilot trial, a total of 12 patients were randomly assigned to one of two treatment arms and received a single intravenous dose of either 0.8 mg/kg or 3.2 mg/kg. Patients were followed for 10 days after dosing to evaluate changes in the biochemical fingerprint of HPP, safety and tolerability. The primary objectives for the study were changes in serum levels of PLP and PPi as compared to baseline. For PLP, the maximum proportional reduction was 35% in the 0.8 mg/kg cohort and 66% in the 3.2 mg/kg cohort. The mean time to return to 90% of baseline was 55 hours in the low-dose cohort and 168 hours in the high-dose cohort. The maximal proportional reduction for PPi was 36% in the 0.8 mg/kg cohort and 77% in the 3.2 mg/kg cohort. The mean time to return to 90% of baseline was 9.3 hours in the low-dose cohort and 53 hours in the high-dose cohort. In addition, ilofotase alfa was well-tolerated with pharmacokinetics consistent with observations from previous clinical studies.

"The pronounced effect on all HPP disease relevant biomarkers together with a positive safety and tolerability profile, consistent with previous clinical studies with ilofotase alfa, supports its further development as a treatment option for adult HPP patients who are currently underserved," **said Juliane Bernholz, PhD, Chief Executive Officer of AM-Pharma.**

The full dataset will be presented at the American Society for Bone and Mineral Research – Rare Bone Disease Alliance (ASBMR-RBDA) Symposium at the Vancouver Convention Centre in Vancouver, BC, Canada. The presentation by Lothar Seefried, MD, from the University of Wuerzburg, lead investigator of the trial, is scheduled for 3:00 pm PDT on Thursday, October 12, 2023, in session III: Latest in Clinical trials.

"Considering the wide range of clinical manifestations of HPP, there's an unequivocal need to expand therapeutic opportunities for these patients," ***added Lothar Seefried, MD.*** *"The encouraging early results confirming dose-dependent reductions of PLP and PPi levels upon treatment with ilofotase alfa underline*

[1] Tournis, S., Yavropoulou, M. P., Polyzos, S. A., & Doulgeraki, A. (2021). Hypophosphatasia. *Journal of Clinical Medicine*, *10*(23), 5676.

the compound's therapeutic potential in that indication and I'm looking forward to evaluating ilofotase alfa in next stage clinical studies."

About ilofotase alfa

Ilofotase alfa is a proprietary recombinant alkaline phosphatase, constructed from two human isoforms of alkaline phosphatase, that has been shown to be stable and highly active in multiple clinical trials. The recombinant enzyme displays exquisite activity towards dephosphorylating and detoxifying damage-associated molecular patterns (DAMPs) and pathogen-associated molecular patterns (PAMPs) such as lipopolysaccharide (LPS), ATP, ADP and other extracellular substrates that drive acute inflammation, coagulation and microvascular ischemia found in kidney following sepsis or ischemia-induced damage. Research has shown that ATP dephosphorylation has a double effect in protecting against kidney injury. When the pro-inflammatory ATP is dephosphorylated, the resulting adenosine further reduces inflammation through the activation of the immunosuppressive adenosine A2a receptor pathway. In hypophosphatasia, ilofotase alfa addresses elevated levels of pyridoxal-5'-phosphate (PLP), inorganic pyrophosphates (PPi), two disease related biomarkers that are related to, for example, bone mineralization and pain sensation.

About hypophosphatasia

HPP is a rare inherited disease characterized by a deficiency in alkaline phosphatase which is essential for bone mineralization and general functions. HPP patients of all ages can exhibit a wide variety of symptoms that worsen overtime, including bone injury, severe muscle pain and weakness. The disease can also lead to life-threatening complications in infants. The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) granted AM-Pharma Orphan Drug Designation (ODD) for ilofotase alfa in HPP. In preclinical models, ilofotase alfa was able to achieve improved overall survival of severe disease, as well as restoration of phenotypes associated with HPP.

About AM-Pharma

AM-Pharma strives to develop medicines for patients confronted with severe medical conditions. Our proprietary asset, ilofotase alfa, is being developed for the treatment of patients with acute kidney injury and has been granted FDA fast-track status. We also develop ilofotase alfa in the severe rare disease hypophosphatasia where ilofotase alfa has orphan drug status in the US and EU. With approximately 1,000 subjects evaluated to date in clinical trials, ilofotase alfa has a proven safety profile and a demonstrated kidney benefit. We are a dedicated team driven to bring treatment options to severely ill patients, their families and acute care professionals. Find out more about us online at: www.am-pharma.com.

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