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AM-Pharma and Kyowa Kirin Sign Exclusive License Agreement for Commercialization of Ilofotase Alfa in Japan

- *AM-Pharma to receive EUR 20 million upfront payment, and EUR 30 million related to milestones prior to regulatory submission, and up to EUR 195 million upon submission, NHI price listing and sales milestone payments bringing the overall deal value to EUR 245 million.*
- *Kyowa Kirin gains exclusive rights to develop and commercialize ilofotase alfa in Japan.*

Utrecht, The Netherlands, and Tokyo, Japan, September 8, 2021 – AM-Pharma B.V., an emerging leader focused on developing therapeutics for severe medical conditions, and Kyowa Kirin Co., Ltd. (TSE: 4151, Kyowa Kirin), a global specialty pharmaceutical company that strives to create new value through the pursuit of advances in life sciences and technologies, today announced that they have entered into an exclusive license agreement under which Kyowa Kirin gains the rights to develop and commercialize ilofotase alfa, AM-Pharma's proprietary recombinant human alkaline phosphatase. Ilofotase alfa is currently being evaluated in the global pivotal REVIVAL Phase III clinical study as the potential first disease-altering treatment for sepsis-associated acute kidney injury (SA-AKI). In July of this year, AM-Pharma announced the enrollment of the first patient in Japan as part of the ongoing REVIVAL trial.

"Kyowa Kirin is a leading Japanese specialty pharmaceutical company deeply rooted in science that shares our commitment to addressing high unmet medical needs. Based on the number of successful international partnerships they have, they are the ideal partner to support the commercialization of ilofotase alfa in Japan," **stated Erik van den Berg, Chief Executive Officer at AM-Pharma.** *"This is a significant milestone for AM-Pharma as this agreement will optimize the commercialization of ilofotase alfa in the Japanese market and expedite our ability to bring our therapeutic candidate to a substantial patient population in Japan post-approval."*

"As an organization centered around research, development and partnerships with innovative drug discovery organizations around the globe, we are excited to initiate this relationship with AM-Pharma to potentially improve the lives of patients and families affected by sepsis-associated acute kidney injury," **added Tomohiro Sudo, Executive Officer, Head of Global Product Strategy Department at Kyowa Kirin**. *"Ilofotase alfa has demonstrated its therapeutic potential in AM-Pharma's Phase II STOP-AKI study, and we look forward to being a strategic partner supporting the commercialization and thereby patient access of ilofotase alfa upon successful completion of the pivotal REVIVAL study."*

Under the terms of the agreement, AM-Pharma will receive EUR 20 million upfront payment, and EUR 30 million related to milestones prior to regulatory submission, and up to EUR 195 million upon submission, NHI price listing and sales milestone payments bringing the overall deal value to EUR 245 million. In addition, AM-Pharma is entitled to tiered double-digit royalties on sales and a drug supply fee. Kyowa Kirin will gain the exclusive right to develop and commercialize ilofotase alfa in Japan. AM-Pharma is responsible for the completion of the REVIVAL pivotal Phase III study, as well as a Phase I pharmacokinetics, safety and tolerability study in Japan and drug supply, whereas Kyowa Kirin will be responsible for the regulatory approval process and commercialization of ilofotase alfa in Japan.

About REVIVAL

The REVIVAL trial is a Phase III pivotal study evaluating AM-Pharma's proprietary recombinant alkaline phosphatase, ilofotase alfa, for the treatment of patients with SA-AKI. The primary endpoint of the study is all-cause mortality 28 days post-treatment start with ilofotase alfa at a dose of 1.6 mg/kg. In the Phase II study of ilofotase alfa, the patient group treated with this dose experienced a statistically significant 46% relative reduction in mortality compared to the group treated with placebo (p= 0.022). REVIVAL was initiated in November 2020 and is enrolling up to 1,600 patients in North America, Europe and Japan. As per the study protocol, four interim analyses for futility and/or efficacy will be conducted when enrollment hits certain levels and the first futility analysis will occur when 400 patients have been treated.

Up to about 120 clinical sites worldwide, including as many as 11 sites in Japan, will enroll patients into the single global pivotal Phase III REVIVAL trial in SA-AKI patients. The U.S. Food and Drug Administration, European Medicines Agency and Japanese Pharmaceuticals and Medical Devices Agency have all approved the REVIVAL protocol.

In addition to the REVIVAL study, the PMDA has approved enrollment into a Phase I pharmacokinetics (PK), safety and tolerability study in healthy Japanese subjects, which is being conducted in parallel to REVIVAL in Japan.

About ilofotase alfa

AM-Pharma's therapeutic candidate is a proprietary recombinant human Alkaline Phosphatase (AP) constructed from two naturally occurring human isoforms of the AP enzyme. The Company's compound is highly stable and active and has a dual mechanism of action. The recombinant enzyme displays exquisite activity towards dephosphorylating and detoxifying damage-associated molecular patterns (DAMPs) and pathogen-associated molecular patterns (PAMPs) such as, ATP, ADP, lipopolysaccharide (LPS) and other extracellular substrates that drive acute inflammation, coagulation and microvascular ischemia. 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 (A2aR). AM-Pharma has shown that treatment of patients with ilofotase alfa not only reduces local and systemic inflammation but also protects the kidney, and possibly other organs, against further damage.

About AKI and Sepsis

Acute Kidney Injury (AKI) involves inflammatory processes in the kidney which can lead to complete loss of renal function. Hospital-acquired AKI affects annually around 3 million patients in the US, Europe, and Japan, and is associated with mortality in roughly 700,000 patients. It occurs in 40-60% of critical care admissions. Depending on the severity and cause of renal injury, mortality occurs in up to 60% of the cases. In the US alone, hospitals spend around $10 billion each year on managing this major medical problem.[1,2,3]

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[1] Murugan R. and Kellum J.A. Nature Reviews Nephrology, 2011; 7(4): 209-217

[2] Heung M. and Chawla L.S. Nephron Clinical Practice, 2014; 127 (1-4): 30-34

[3] Chertow, G.M. et al. Journal of the American Society of Nephrology, 2005; 16(11): 3365-3370

Sepsis is a condition that is responsible for 1 out of 3 deaths in hospitals and is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. The kidney is the most commonly affected organ, resulting in SA-AKI and significantly increasing the risk for mortality and morbidity in sepsis. No singular effective therapy to alter the progression of these devastating conditions has been approved.[4]

About AM-Pharma
AM-Pharma's purpose is to save and improve the lives of patients confronted with severe medical conditions. Our initial focus is sepsis-associated acute kidney injury, the cause of death for hundreds of thousands of people hospitalized each year. Our proprietary compound, ilofotase alfa, has the potential to become the first treatment for sepsis-associated acute kidney injury and is now in a global pivotal Phase III clinical trial. 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.

About Kyowa Kirin
Kyowa Kirin strives to create and deliver novel medicines with life-changing value. As a Japan-based Global Specialty Pharmaceutical Company with a more than 70-year heritage, the company applies cutting-edge science including an expertise in antibody research and engineering, to address the needs of patients and society across multiple therapeutic areas including Nephrology, Oncology, Immunology/Allergy and Neurology. Across our four regions – Japan, Asia Pacific, North America and EMEA/International – we focus on our purpose, to make people smile, and are united by our shared values of commitment to life, teamwork/Wa, innovation, and integrity. You can learn more about the business of Kyowa Kirin at: https://www.kyowakirin.com.

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[4] Alobaidi, R. et al. Seminars in Nephrology, 2015; 35(1): 2-11