AM-PHARMA PROVIDES BUSINESS UPDATE AND OUTCOME OF PRE-PLANNED INTERIM FUTILITY ANALYSIS OF PHASE 3 REVIVAL STUDY

- ***Phase 3 REVIVAL study stopped per recommendation of data monitoring committee after per-protocol pre-specified interim futility analysis on the study's primary endpoint, 28-day mortality, without any safety concern.***
- ***A significant reduction in Major Adverse Kidney Events by day 90 and no difference in overall mortality was observed after review of the data for all 649 patients in the study***
- ***Clear path forward for ilofotase alfa as potential treatment in acute kidney injury, based on consistent improvement of renal parameters observed in REVIVAL and other clinical studies***

Utrecht, The Netherlands, October 20, 2022 – AM-Pharma B.V., an emerging leader focused on developing therapeutics for severe medical conditions, today provided a business update and the outcome from its pre-planned 400-patient interim futility analysis for the pivotal phase 3 REVIVAL study, which has been stopped for futility based on the study's primary endpoint. The REVIVAL study evaluated AM-Pharma's proprietary recombinant alkaline phosphatase, ilofotase alfa, for the treatment of patients with sepsis-associated acute kidney injury (SA-AKI).

The data monitoring committee (DMC) reviewed unblinded safety data and 28-day all-cause mortality data – the primary endpoint of the study – for the first 400 patients enrolled in the main trial population and recommended to discontinue the clinical study. Importantly, the DMC concluded that there are no safety concerns.

AM-Pharma has now conducted a pre-specified analysis of the data from all 649 patients who were included in the phase 3 study combined population prior to termination, consisting of 567 patients in the main trial population, 49 patients with moderate-to-severe CKD and 33 patients with COVID-19, with all patients having sepsis and AKI. In the prespecified analysis of the secondary endpoint of Major Adverse Kidney Events by day 90 (MAKE90) a significant reduction of events was observed in the combined population with 206/319 events (65%) in the placebo group and 187/330 events (57%) in the ilofotase alfa group ($p<0.05$ KM proportion analysis). Additionally, in the COVID-19 cohort of the study, patients treated with ilofotase alfa experienced a reduction in 28-day all-cause mortality compared to those treated with placebo ($p<0.01$). The MAKE composite components were death, need for dialysis, substantial kidney function deterioration (>25% decline in estimated glomerular filtration rate (eGFR)) by day 90, and rehospitalization. MAKE90 is a potentially registrable primary endpoint.

"While futility was observed in the main trial population for the primary endpoint of all-cause mortality at day 28, the renal benefit observed in this study in ilofotase alfa treated patients cannot be ignored," said Peter Pickkers, principal investigator in the REVIVAL study and professor of Intensive Care Medicine in Radboud University Medical Center Nijmegen, The Netherlands. "MAKE90 is a clinically meaningful endpoint for patients with renal disease as it is predictive for poor long-term outcome for patients, including the development of end-stage renal disease (ESRD). I am encouraged by the potential for

ilofotase alfa for patients with AKI as we have now seen a MAKE90 benefit in two studies with close to 1000 patients evaluated."

"With a strong body of evidence behind us, we are confident that ilofotase alfa has a place in the treatment of patients with renal disease," said Erik van den Berg, Chief Executive Officer of AM-Pharma. "While we are disappointed with the outcome of the futility analysis, we intentionally designed the study with futility stopping rules to ensure that we had the most efficient development plan possible. With the encouraging data for preserving kidney function, we will look to further develop ilofotase alfa for patients with acute kidney injury, and potentially additional orphan indications."

"There are millions of patients affected by AKI across the globe without specific therapeutic treatment options available beyond supportive care," said Kathleen Liu, MD, PhD, Professor of Medicine and Anesthesia in the Divisions of Nephrology and Critical Care Medicine at the University of California, San Francisco (UCSF). "With the data generated from the REVIVAL study and earlier studies, I believe that ilofotase alfa has the potential to help patients affected by this disease."

About the REVIVAL study

The REVIVAL Phase 3 pivotal trial was a randomized, double-blind, placebo-controlled, two-arm, parallel-group, multi-center trial to evaluate the efficacy and safety of AM-Pharma's proprietary human recombinant alkaline phosphatase, ilofotase alfa, for the treatment of patients with SA-AKI. The study was designed to enroll up to 1400 patients with SA-AKI in the main study population. In two exploratory cohorts, up to 100 patients with moderate chronic kidney disease (CKD) and up to 100 patients with COVID-19 could also be enrolled. Patients in the study were randomized to receive 1.6mg/kg of ilofotase alfa or placebo. The primary endpoint of the study was 28-day all-cause mortality. Secondary endpoints included long-term Major Adverse Kidney Events (MAKE), the use of organ support, length of stay in the ICU and 90-day all-cause mortality. Further information on this study can be found at www.clinicaltrials.gov, NCT04411472 (REVIVAL).

About Ilofotase Alfa

Ilofotase alfa is a proprietary recombinant alkaline phosphatase, constructed from two human isoforms of alkaline phosphatase, that in multiple clinical trials was shown to be stable and highly active. 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.

About AM-Pharma

AM-Pharma strives to develop medicines for patients confronted with severe medical conditions. Our proprietary asset, Ilofotase alfa, is initially being developed for the treatment of patients with acute kidney injury and has been granted FDA fast-track status. With approximately 1000 patients 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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