AM-Pharma Announces Enrollment and Financing of COVID-19 Cohort in Phase III REVIVAL Trial

- First patients with COVID-19 enrolled in the REVIVAL Phase III study

- COVID-19 patients with sepsis-associated acute kidney injury will be included in an exploratory cohort in the pivotal trial enrolling up to 1,600 SA-AKI patients overall

- RVO, an agency of the Dutch Ministry of Economic Affairs and Climate Policy, provides a loan of up to €5 million for the COVID-19 cohort clinical study

Utrecht, The Netherlands, 7 January 2021 – AM-Pharma B.V., an emerging leader focused on the treatment of kidney disease, sepsis and organ injury, today announced that the first patients with COVID-19 infection and sepsis-associated acute kidney injury (SA-AKI) have been enrolled in the Company's Phase III REVIVAL pivotal trial in an exploratory cohort to assess the safety, tolerability and clinical benefit of recombinant alkaline phosphatase.

Patients with severe COVID-19 infection often present with acute severe inflammation and organ failure. Recent studies conducted in the US demonstrated that up to 90% of the COVID-19 patients that received mechanical ventilation also suffered from AKI and that the development of AKI in these patients is associated with poor prognosis.[1] AM-Pharma received an innovation credit of up to EUR 5 million from the "Netherlands Enterprise Agency" (RVO.nl), which has been established by the Dutch Ministry of Economic Affairs and Climate Policy to support the development of innovative programs with promising market potential.

"The ongoing coronavirus pandemic and the lack of treatment options for severe cases has been devastating for patients, their families and medical communities around the world," **commented Erik van den Berg, Chief Executive Officer at AM-Pharma.** *"The prevalence of COVID-19 infections and the high AKI comorbidity support our decision to include this additional cohort into our Phase III REVIVAL pivotal study. By providing our proprietary recombinant alkaline phosphatase to clinicians for evaluation in severe COVID-19 cases, we aim to make our novel treatment option available for these patients."*

The REVIVAL Phase III pivotal trial is 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 for the treatment of patients with SA-AKI. The study will enroll approximately 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 will be enrolled. The primary aim of the study is to confirm the improvement on the primary endpoint of 28-day all-cause mortality, as observed in the Phase II STOP-AKI study. Secondary endpoints include the treatment effect on long-term Major Adverse Kidney Events (MAKE), on the use of organ support, length of stay in the ICU and on 90-day all-cause mortality. Further information on this study can be found at www.clinicaltrials.gov, NCT04411472 (REVIVAL).

[1] Hirsch, J.S. et al. Kidney International, 2020; DOI: 10.1016/j.kint.2020.05.006

"We have seen the potential of AM-Pharma's proprietary recombinant human alkaline phosphatase to benefit patients with sepsis and acute kidney injury, as demonstrated in the Phase II STOP-AKI study," **said John A. Kellum, M.D., Professor, Vice Chair Department of Critical Care Medicine and Director at the Center for Critical Care Nephrology at University of Pittsburgh**. *"This is very relevant for severe COVID-19 patients as many of these patients also experience AKI, with increased AKI severity being correlated with increased mortality."*

Professor Peter Pickkers, M.D., Ph.D., Chair of Experimental Intensive Care Medicine, Radboud University Medical Center, and principal investigator of the REVIVAL study added: *"The relative reduction in mortality of 40% and significant improvement in renal function over the course of the Phase II STOP-AKI study period support the hypothesis that AM-Pharma's drug candidate might provide a unique treatment opportunity for severe COVID-19 patients with acute kidney injury. I am excited to continue our collaboration with AM-Pharma for this trial."*

For the Phase III REVIVAL trial, potentially over 100 sites across Europe and North America are actively recruiting patients with SA-AKI in the trial. Enrollment completion of the first 400 patients in the main study population is expected by the end of 2021. The company expects to complete target enrollment and to announce data on the primary endpoint of 28-day all-cause mortality in 2023.

About AKI, Sepsis and COVID-19

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 Europe, the US 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 ranges from 10% to as high as 60%. In the US alone, hospitals spend around $10 billion each year on managing this major medical problem.[2,3,4]

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, while the healthcare burden for sepsis in the US alone is $16.7 billion on an annual basis.[5]

In patients with COVID-19 requiring ICU care, the prevalence of AKI is 46% and up to 90% in COVID-19 patients who need mechanical ventilation. Development of AKI is associated with a poor prognosis with a mortality rate of approximately 50%. There is currently no treatment available for COVID-19 patients with AKI other than renal replacement therapy. Non-surviving patients have severe inflammation and excessive immune activation.[6,7,8]

About recombinant alkaline phosphatase

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 via dephosphorylation of

[2] Murugan R. and Kellum J.A. Nature Reviews Nephrology, 2011; 7(4): 209-217
[3] Heung M. and Chawla L.S. Nephron Clinical Practice, 2014; 127 (1-4): 30-34
[4] Chertow, G.M. et al. Journal of the American Society of Nephrology, 2005; 16(11): 3365-3370
[5] Alobaidi, R. et al. Seminars in Nephrology, 2015; 35(1): 2-11
[6] Hirsch, J.S. et al. Kidney International, 2020; DOI: 10.1016/j.kint.2020.05.006
[7] Stevens, J.S., et al. PloS one, 2020, 15.12: e0244131.
[8] Silver, S.A., et al. Kidney Medicine, 2020; DOI: 10.1016/j.xkme.2020.11.008

lipopolysaccharides (LPS) and extracellular ATP. AM-Pharma has shown that treatment of patients with exogenous AP not only reduces local and systemic inflammation but also protects the kidney against further damage.

About AM-Pharma
AM-Pharma's purpose is to save and improve the lives of patients confronted with kidney disease, sepsis and organ injury. Our initial focus is sepsis-associated acute kidney injury, the cause of death for hundreds of thousands of people hospitalized each year. Our proprietary recombinant human alkaline phosphatase 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.

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