Press Release

Adrenomed AG doses first patient in proof of concept study with Adrecizumab to treat patients with early septic shock

- First patient enrolled in Phase II study ADR-02 (AdrenOSS-2), designed to demonstrate safety and efficacy of Adrecizumab in patients with early septic shock
- Study to be conducted in Germany, the Netherlands, Belgium, and France
- Population of biomarker-predicted responders will be dosed with Adrecizumab to improve overall survival
- Phase II study with Adrecizumab in patients with congestive heart failure starting next year

Hennigsdorf/Berlin (Germany) December 11, 2017 – German vascular integrity specialist Adrenomed AG, announced today that the first patient with early septic shock has been dosed in the ADR-02 Phase-II study (AdrenOSS-2, NCT03085758) conducted in Germany, Belgium, France and the Netherlands. In the double-blind, placebo-controlled, randomised, multicenter study, Adrenomed will assess safety, tolerability and efficacy of two dose levels (2mg/kg and 4mg/kg) of its humanized monoclonal antibody Adrecizumab in 300 patients with early septic shock, who show elevated blood levels of adrenomedullin. Adrecizumab specifically targets adrenomedullin, a key regulator of endothelial barrier function, blood pressure and vascular tone. The breakdown of vascular integrity plays a pivotal role in the development of vascular leakage and organ dysfunction leading to septic shock.

Specifically, Adrenomed will compare mortality over 28 days in patients diagnosed with early septic shock receiving Adrecizumab plus standard of care vs standard of care. Furthermore, tolerability and treatment-emergent adverse events over 90 days will be assessed (primary outcomes).

The primary efficacy endpoint of this study is the Sepsis Support Index (SSI) defined as days with organ support or death within 14 day follow up. Further patient-relevant outcomes include SSI at 28 day follow-up; persistent organ dysfunction or death at 14 and 28 day follow-up, mortality rate at day 28 and day 90; SSI components (hemodynamic, respiratory and renal failure); Sequential Organ Failure Assessment (SOFA) Score and its changes over time until day 90, improvement in renal function, Length of stay at ICU/ hospital, and functional biomarkers.
In a sub-study key pharmacokinetic parameters are to be determined in 80 patients.

In preclinical studies, Adrecizumab reduced mortality from sepsis and septic shock (Struck et al, 2013). In addition, Adrecizumab positively impacted the vasoactive adrenomedullin system leading to stabilization of blood pressure (Blet et al. 2015), renal function and improved catecholamine responsiveness (Wagner et al 2013). Two Phase-I studies demonstrated excellent tolerability and safety of Adrecizumab without any severe adverse effects (NCT02991508, NCT03083171).

„The hope is to demonstrate the potential of Adrecizumab to reduce the high mortality rates from sepsis," said Andreas Bergmann, PhD., Chief Scientific Officer (CSO) of Adrenomed. „Sepsis affects millions of people globally. To date, there is no causative treatment for the systemic inflammation that leads to multi- organ failure". Besides septic shock, Adrenomed is currently evaluating the potential of Adrecizumab's mode of action in decompensated heart failure. A Phase II proof-of-concept study in patients with elevated bio-ADM plasma concentrations who experience worsening heart failure (WHF) requiring hospitalization is expected to start next year.

About Adrenomed

Adrenomed AG is a privately financed biopharmaceutical company, based in Hennigsdorf near Berlin, Germany, with a clear mission to improve survival by improving vascular integrity in critically ill patients. Its lead candidate, Adrecizumab, a monoclonal antibody therapy targeting the vasoactive Adrenomedullin system, is in clinical testing for septic shock. Impaired vascular integrity is a pathology that serves a variety of medical conditions. A further indication besides sepsis is acute decompensated heart failure.

About Adrenomedullin and Adrecizumab

Adrenomedullin is a strong vasodilatory hormone released by endothelial cells. It is a key regulator of blood pressure and vascular tone and plays a pivotal role in the development of septic shock. Adrecizumab is a proprietary humanized monoclonal Adrenomedullin-specific antibody, as first-in-class therapy for the treatment and prevention of impaired vascular integrity, which is a hallmark of septic shock. Adrecizumab showed excellent safety & tolerability as well as high efficacy in a variety of preclinical animal models, mimicking human standard of care treatment on ICU. In several resuscitated vascular integrity models (mouse, rat, pig), Adrecizumab reduced vascular leakage, stabilized the circulation, by restoring blood pressure, normalized fluid balance and reduced vasopressor demand,

improved renal function and reduced mortality from septic shock by 50%. The excellent tolerability and safety of Adrecizumab was confirmed in clinical Phase-I studies in healthy subjects with and without LPS challenge.

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