Press Release

Adrenomed AG announces publication of Phase II trial design of Adrecizumab to treat septic shock

- **Ongoing proof-of-concept trial AdrenOSS-II testing Adrecizumab in early septic shock**
- **Adrecizumab is a first-in-class antibody targeting Adrenomedullin, to rescue vascular function**
- **Vascular integrity, regulated by Adrenomedullin, is key to preventing vascular leakage and septic shock**

Hennigsdorf (Germany) February, 7, 2019 – Adrenomed AG, the vascular integrity company, today announced that the Phase II clinical trial design of AdrenOSS-II was published by the peer-reviewed open access journal *BMJ Open*. The currently ongoing Phase II trial is conducted to assess the safety and efficacy of the monoclonal antibody Adrecizumab in patients with early septic shock, a life-threatening condition with very high unmet medical need.

The biomarker-guided, randomized, double-blind, placebo-controlled, multicenter proof-of-concept AdrenOSS-II trial is evaluating the safety, tolerability and efficacy of Adrecizumab in 300 patients with early septic shock and elevated blood levels of the vasoprotective peptide Adrenomedullin (bio-ADM®). The primary endpoints are safety and tolerability of Adrecizumab over a 90-day period. A key secondary endpoint is the Sepsis Support Index (SSI) defined as days with organ support or death within 14 days. The AdrenOSS-II trial started in December 2017 and is currently running in about 30 centers throughout Germany, Belgium, France and the Netherlands (NCT03085758).[1] To date, 150 patients have been enrolled. Full details of the Phase II trial design have now been published on *BMJ Open*.[2]

Adrenomed's first-in-class antibody Adrecizumab specifically targets Adrenomedullin, an essential regulator of vascular integrity to treat life-threatening conditions associated with increased vascular leakage, congestion and shock.[3] Adrenomedullin (bio-ADM®) was validated as critical biomarker and target in the AdrenOSS-I study, which demonstrated a correlation between high plasma levels of bio-ADM® and organ dysfunction as well as higher mortality rates in patients with sepsis and septic shock (NCT02393781).[4] The full article was recently published in *Critical Care*.[5] Adrecizumab demonstrated an excellent safety profile in two Phase I trials (NCT02991508, NCT03083171, *British Journal of Clinical Pharmacology*).[6, 7, 8]

About Adrenomed

Adrenomed AG is a German privately-financed, clinical stage biopharmaceutical company. Adrenomed´s mission is to rescue vascular integrity in order to save the lives of critically ill patients with limited treatment options. Founded in 2009 by a management team with decades of in-depth experience in sepsis and deep knowledge in diagnostics and drug development, the Company's lead product candidate Adrecizumab is a clinical-stage, first-in-class monoclonal antibody. Adrecizumab targets the vasoprotective peptide Adrenomedullin, an essential

regulator of vascular integrity. Adrecizumab is currently under clinical evaluation in a biomarker-guided, double-blinded, placebo-controlled, randomized, multicenter proof-of-concept Phase II study with 300 patients suffering septic shock. Excellent safety and tolerability were demonstrated in two Phase I trials.

About Adrenomedullin (bio-ADM®)

Adrenomedullin is a free-circulating peptide that is mainly expressed and secreted by vascular endothelial cells. It shows vasodilatory effects in the interstitium and vasoprotective activity in the circulation, where it closes the gaps between endothelial cells, subsequently preventing vascular leakage. The diagnostic specialist sphingotec GmbH developed sphingotest® bio-ADM®, a reliable commercially available IVD to measure biologically active Adrenomedullin. The test was used to validate Adrenomedullin as biomarker and therapeutic target through an analysis of over 20.000 well-defined acute care patient samples.

About Adrecizumab's mode of action

Adrenomed's lead product candidate Adrecizumab is a clinical stage first-in-class drug candidate targeting Adrenomedullin an essential regulator of vascular integrity, to rescue endothelial barrier function. The binding of the monoclonal antibody Adrecizumab to Adrenomedullin in the blood traps and stabilizes the hormone resulting in increased Adrenomedullin concentrations within the circulation. The complex of Adrecizumab and Adrenomedullin is still functional, thus antibody-bound Adrenomedullin can still act on the endothelium. Consequently, Adrecizumab treatment boosts Adrenomedullin's protective effects on the endothelial barrier.

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