

Press Release

Adrenomed Announces Positive Top-Line AdrenOSS-2 Phase II Results with Adrecizumab in Septic Shock

- **Adrecizumab, given on top of standard of care, was well tolerated and showed a favorable safety profile**
- **Adrecizumab demonstrates a positive trend on survival**
- **AdrenOSS-2 is a biomarker-guided (sphingotest bio-ADM^{®1}) trial in sepsis**
- **Mode of Action confirmed: Adrecizumab modulates plasma level of bioactive Adrenomedullin (bio-ADM), a key hormone for vascular integrity and endothelial function**

Hennigsdorf/Berlin (Germany), February 21, 2020 – Adrenomed AG, the vascular integrity company, today reported positive top-line results from its proof-of-concept AdrenOSS-2 Phase II trial. AdrenOSS-2 evaluated the safety, tolerability and efficacy of Adrecizumab, a first-in-class monoclonal antibody targeting the vasoprotective peptide Adrenomedullin to restore and maintain vascular integrity in patients with early septic shock. Septic shock is a life-threatening condition with very limited treatment options. Sepsis is the main cause of death in hospitals worldwide.²

The biomarker-guided, randomized, international, multicenter, double-blind, placebo-controlled AdrenOSS-2 Phase II trial ([NCT03085758](#)³) enrolled a total of 301 patients with early septic shock and elevated blood levels of bio-ADM[®] throughout Belgium, France, Germany and The Netherlands.⁴ In addition to standard of care, patients received Adrecizumab or placebo. Coordinating investigators for each involved country and chairpersons of the Steering Committee are Prof. A. Mebazaa, France, Prof. P.F. Laterre, Belgium, Prof. G. Marx, Germany and Prof. P. Pickkers, The Netherlands.

The study achieved its primary endpoint: Adrecizumab demonstrated a favorable safety profile and was well tolerated. The safety and tolerability of Adrecizumab in septic shock patients were consistent with observations from the previous Phase I trials.⁵ In addition, the mortality rate in the 28-day follow-up in the placebo group was 28%, and a trend of lower all-cause mortality for Adrecizumab-treated patients compared to placebo was observed.

Dr. Jens Zimmermann, CMO of Adrenomed said: “These are very promising results and consistent data. The outcome of the AdrenOSS-2 trial indicates that Adrecizumab is of benefit for septic shock patients. By restoring and maintaining vascular integrity, Adrecizumab may represent a new treatment option for septic shock.”

Prof. Pierre-François Laterre, MD, Head of the medical-surgical intensive care unit at Saint Luc University Hospital at the Université Catholique de Louvain, Brussels (Belgium), said: “For the first time, we have seen a positive effect on early death in septic shock. The outcome of AdrenOSS-2 is an important step towards successful treatment of sepsis. The data support Adrecizumab being

an effective therapeutic agent with an innovative mode of action which may improve survival of patients in the early stage of septic shock. We eagerly await the confirmation of these positive results in the future clinical development of Adrecizumab.”

“Septic shock is a challenging syndrome with a high mortality rate,” said Prof. Alexandre Mebazaa, MD, PhD, Chair of Department of Anesthesiology and Critical Care in Paris at the Hôpital Lariboisière, Université de Paris (France). “Safe and efficacious treatments are urgently needed to change the course of this complex condition. Undoubtedly, AdrenOSS-2 exhibited benefits on survival in septic shock patients, suggesting great potential for endothelial modulation on septic shock outcomes.”

Dr. Andreas Bergmann, CSO and co-founder of Adrenomed commented: “Endothelial dysfunction is the major driver for organ dysfunction and mortality in sepsis. The biomarker bio-ADM specifically enables the identification of sepsis patients with endothelial dysfunction, who potentially may benefit the most from Adrecizumab treatment. Biomarker guidance of specific drugs will lead to new directions for fighting multi-complex diseases like sepsis.”

Dr. Jens Schneider-Mergener, CEO of Adrenomed, said: “We are looking forward to further discussions with regulatory authorities and partners regarding the future development of Adrecizumab. With this successful proof-of-concept trial, we believe Adrecizumab has great potential not only in septic shock but also in other serious or life-threatening conditions associated with vascular leakage. We would like to take this opportunity to thank the investigators, study personnel, patients and their families for their participation in the AdrenOSS-2 trial.”

Detailed data from the AdrenOSS-2 study will be submitted for publication in a peer-reviewed journal later this year.

About Sepsis and Septic Shock

Sepsis is a life-threatening condition that results in organ dysfunction caused by a dysregulated host response to infection. Septic shock is the most severe form of sepsis characterized by a rapid fall in blood pressure requiring vasopressor treatment; profound circulatory, cellular and metabolic abnormalities; diminished oxygen supply to organs and finally, multiple organ failure. Septic shock is driven by severe loss of vascular integrity: a breakdown of the endothelial barrier, which results in uncontrolled leakage of intravascular fluid and other compounds into the extravascular space leading to congestion and edema.

Today, sepsis and septic shock are major healthcare problems, representing a high unmet medical need affecting millions of people around the world every year. In the United States, sepsis causes or contributes to between one-third and one-half of all deaths occurring in hospitals. With an unacceptably high mortality rate,² sepsis represents an enormous public health burden. The current standard of care for sepsis patients is based on early treatment with antibiotics and administration of fluids and vasopressors (hemodynamic support).

About Adrecizumab and Adrenomedullin⁶

Adrenomedullin (ADM) is a free-circulating peptide that is mainly expressed and secreted by vascular endothelial cells. It shows vasoprotective activity inside blood vessels, where it closes the gaps between endothelial cells, subsequently preventing intravascular fluid and other

compounds from uncontrolled leakage into the interstitium/extravascular space (= vascular leakage). In the interstitium, however, ADM has vasodilatory properties and causes hypotension when present in higher concentrations, which, in sepsis patients, leads to worsening and progression of the disease. Adrenomed's first-in-class drug candidate, Adrecizumab, targets bioactive Adrenomedullin (bio-ADM) to restore endothelial barrier function (= vascular integrity). Binding of the monoclonal antibody Adrecizumab to ADM in the blood traps and stabilizes the peptide-hormone, resulting in increased ADM concentrations within the blood vessels. The complex of ADM and Adrecizumab in the blood is still active. This way, Adrecizumab treatment boosts ADM's protective effects on the endothelial barrier.

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 first-in-class monoclonal antibody. Adrecizumab targets the vasoprotective peptide Adrenomedullin, an essential regulator of vascular integrity. Adrecizumab has successfully completed a biomarker-guided, double-blinded, placebo-controlled, randomized, multicenter proof-of-concept Phase II trial with 301 patients suffering from septic shock. For further information, please visit www.adrenomed.com and follow us on [LinkedIn](#) and [Twitter](#).

Contact

Adrenomed AG

Frauke Hein, Ph.D. (Chief Business Officer)
phone: +49 (0)3302 2077814
fhein@adrenomed.com

Media Inquiries

MC Services AG

Eva Bauer / Julia von Hummel
phone: +49 (0)89 21022880
adrenomed@mc-services.eu

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- ¹ bio-ADM® is a registered trademark of sphingotec GmbH
 - ² [JAMA, 2014;312\(1\):90-92](#)
 - ³ clinicaltrials.gov/ct2/show/NCT03085758?term=NCT03085758&rank=1
 - ⁴ [BMJ Open, 2019;9:e024475](#)
 - ⁵ [BJCP, 2018;84\(9\):2129-2141](#)
 - ⁶ [Shock, 2018;50\(6\):648-654](#)