

## **Bioactive Adrenomedullin, measured with sphingotec's bio-ADM<sup>®</sup> assay plays a key role in septic shock patients as top-line results of AdrenOSS-2 Phase II Study indicate**

- Bioactive Adrenomedullin is a biomarker for endothelial dysfunction and allows the prediction of septic shock as elevated blood levels of bio-ADM<sup>®</sup> predict blood pressure break down and blood vessel leakage resulting in edema
- AdrenOSS-2 Phase II trial shows that modulating the Adrenomedullin plasma level with the therapeutic antibody Adrecizumab demonstrates an improvement of survival in patients with septic shock
- Increased bio-ADM<sup>®</sup> levels were used as inclusion criteria in the AdrenOSS-2 Phase II trial to identify patients with endothelial dysfunction
- sphingotec to launch IB10 sphingotest<sup>®</sup> bio-ADM<sup>®</sup> a rapid immunoassay for bioactive Adrenomedullin on its Nexus IB10 point-of-care platform mid 2020

**Hennigsdorf/Berlin, Germany, February 24, 2020** - Diagnostics company SphingoTec GmbH ("sphingotec", Hennigsdorf, Germany) today announced that data from the AdrenOSS-2 study indicate a modulating role of bioactive Adrenomedullin in septic shock. Topline results of the AdrenOSS-2 Phase II trial released on February 21, 2020 by its sponsor Adrenomed AG (Adrenomed) showed an increase in survival for patients with septic shock when treated with Adrecizumab. Adrecizumab targets bioactive Adrenomedullin and modulates endothelial function. Septic shock is the most severe form of sepsis, a medical emergency with high mortality. In the trial, blood levels of bioactive Adrenomedullin were measured with sphingotec's quantitative bio-ADM<sup>®</sup> immunoassay as inclusion criteria.

Bioactive Adrenomedullin has been previously validated in over 22,000 patients as an endothelial function biomarker whose detection in the blood provides dynamic information on the patients' progression in sepsis. High or rising blood levels of bioactive Adrenomedullin indicate a disbalance in the endothelial function leading to edema and shock while decreasing levels have been linked to improved patient outcomes. Based on this evidence, bioactive Adrenomedullin is not only a valid biomarker for endothelial function but was also qualified as a biotarget and led to the subsequent development of Adrecizumab, a therapeutic antibody to treat septic shock.

In the AdrenOSS-2 Phase II trial, which was designed to evaluate the safety, tolerability, and efficacy of Adrecizumab, increased bio-ADM<sup>®</sup> levels were used as an inclusion criterion to select those patients with septic shock, which have an endothelial dysfunction. The trial enrolled a total of 301 patients with septic shock and was carried out in multiple clinical trial centers in Belgium, France, Germany, and The Netherlands.

In this proof-of-concept trial, patients received Adrecizumab or placebo on top of standard of care treatment. The study achieved its primary endpoint: Adrecizumab demonstrated a

favorable safety profile and was well tolerated. In addition, a lower all-cause mortality for Adrecizumab-treated patients was observed when compared to placebo.

AdrenOSS-2' principal investigator Pierre-François Laterre commented: "Using bioactive Adrenomedullin blood levels as inclusion criteria allowed us to select the patients who have endothelial dysfunction. Measuring bioactive Adrenomedullin in a routine situation, furthermore allowed us to better understand the utility of this biomarker as a diagnostic tool as we saw that bioactive Adrenomedullin gave information on top of clinical standard parameters to assess patients' severity. We will now go ahead to further investigate use-cases of bioactive Adrenomedullin as a biomarker in the clinical routine."

Dr. Andreas Bergmann, founder and CEO of sphingotec commented: "Following our approach of diving deep into the biology of the disease, we have developed biomarkers that support clinicians in identifying the root causes of progression in sepsis. While the current trial indicates that using bioactive Adrenomedullin as a biomarker can help identifying those patients who could benefit in the future from Adrecizumab, the utility of this biomarker expands far beyond this and supports already today the early clinical decision making and monitoring of treatment success in sepsis."

To support the critical care community in the timely assessment of endothelial function in sepsis and other acute and critical care conditions, sphingotec will launch IB10 sphingotest® bio-ADM®, a rapid test for bioactive Adrenomedullin that will be deployed on the company's proprietary point-of-care platform, the Nexus IB10 immunoassay analyzer.

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#### **About sphingotec**

SphingoTec GmbH ("sphingotec"; Hennigsdorf near Berlin, Germany) develops and markets innovative in vitro diagnostic (IVD) tests for novel and proprietary biomarkers for the diagnosis, prediction and monitoring of acute medical conditions, such as sepsis, acute heart failure, circulatory shock, and acute kidney injury in order to support patient management and provide guidance for treatment strategies. sphingotec's proprietary biomarker portfolio includes Bioactive Adrenomedullin (bio-ADM®), a unique biomarker for real-time assessment of endothelial function in conditions like sepsis or congestive heart failure, Proenkephalin (penKid®), a unique biomarker for real-time assessment of kidney function, and Dipeptidyl Peptidase 3 (DPP3), a unique biomarker for cardio-renal pathway disruptions leading to acute organ dysfunction. In addition, sphingotec develops a portfolio of novel biomarkers, which predict the risks of developing obesity, breast cancer and cardiovascular diseases. IVD tests for sphingotec's proprietary biomarkers are made available as sphingotest® microtiterplate tests as well as point-of-care tests on the Nexus IB10 immunoassay platform by sphingotec's subsidiary Nexus Dx Inc. (San Diego, CA, USA) alongside a broad menu of IB10 tests for established biomarkers for acute and critical care.

#### **About Nexus Dx Inc. and the IB10 Platform**

Nexus Dx Inc., a wholly-owned subsidiary of sphingotec, headquartered in San Diego, CA, USA, is a global provider of a near patient testing system and advanced diagnostic solution. The company is improving patient care by providing the medical community with rapid and reliable information at the point of care (POC), delivering patient information when and where it is needed most. The company has invested over \$160m to develop and market the IB10 analyzer system which, without the need for sample preparation, automatically separates plasma from whole blood with subsequent reliable and quantitative detection of biomarkers in the plasma by means of antibodies. With a hands-on-time of less than 3 minutes the easy-to-use system provides in only 20 minutes test results for biomarkers that are crucial in the management of critical care patients. The portfolio of IB10 assays includes tests for established critical care parameters such as Procalcitonin, Troponin I, CK-MB, Myoglobin, NT-proBNP, and D-Dimer as well as tests for sphingotec's proprietary biomarkers such as DPP3, an assay for Dipeptidyl Peptidase 3, a unique and proprietary biomarker for cardio-renal pathway disruptions leading to acute organ dysfunction, and Proenkephalin (penKid®), a unique and proprietary biomarker for real-time assessment of kidney function. An IB10 assay for bioactive Adrenomedullin (bio-ADM®), a unique and proprietary biomarker for endothelial function is expected to be launched later in 2020.

#### **About bio-ADM®**

sphingotest® bio-ADM® measures blood levels of bioactive adrenomedullin (bio-ADM®), a hormone maintaining endothelial function. The endothelium contributes to blood pressure and separates blood from the surrounding tissue. Elevated blood levels of bio-ADM® predict blood pressure break down and leaky vessels resulting in oedema. Imbalanced endothelial function is the major cause of shock ultimately resulting in organ dysfunction and death. Early identification of an imbalance in endothelial function allows guidance of vasopressor and diuretic therapy in critically ill patients to improve outcomes.

#### **About Adrecizumab**

Adrenomed's first-in-class drug candidate Adrecizumab targets adrenomedullin (ADM) to rescue 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 Adrenomedullin's protective effects on the endothelial barrier. [www.adrenomed.com](http://www.adrenomed.com)

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