The cardiac depressant factor DPP3 is predicting organ failure in burn patients

- DPP3 is a highly dynamic marker for predicting and monitoring cardiac depression in burn patients
- High DPP3 blood concentrations are indicating multiple organ failure and poor outcomes
- sphingotec commercializes a rapid CE-IVD test for DPP3 on its proprietary point-of-care platform Nexus IB10

Hennigsdorf/Berlin, Germany, May 14, 2020 – Diagnostics company SphingoTec GmbH ("sphingotec") and 4TEEN4 Pharmaceuticals GmbH ("4TEEN4") announced today the publication of new data showing that high blood levels of Dipeptidyl Peptidase 3 (DPP3) are indicating upcoming multiple organ failure and mortality risk in burn patients. DPP3 is a proprietary biomarker of 4TEEN4 for hemodynamic instability and cardiac depression. sphingotec has in-licensed global rights to develop and commercialize in vitro diagnostic (IVD) tests for the DPP3 biomarker from 4TEEN4 and made it available on its proprietary Nexus IB10 point-of-care platform.

The results from the recent study[1] provide evidence that DPP3 blood concentrations in severely ill burn patients are indicating fatal outcomes. The data also shows that high DPP3 concentration in the blood is linked to circulatory failure, cardiac depression, and acute kidney injury. Decreasing DPP3 levels in the blood, on the other hand, indicate a substantially reduced risk of mortality.

According to a newly identified disease mechanism, the release of the cardiac depressant factor DPP3 into the bloodstream is a major cause of short-term organ failure: DPP3 is an enzyme that is present in many cell types and normally plays an important role in the recycling of cellular proteins.
When massive uncontrolled cell death occurs, like in the case of burn patients, DPP3 is released into the bloodstream where it degrades angiotensin II, a peptide hormone controlling the heart function. Unphysiologically low levels of angiotensin II rapidly lead to cardiac depression and ultimately organ failure. Previously published data[2,3] provided evidence that poor outcome of patients with severe heart failure or cardiogenic shock are caused by DPP3. Furthermore, the causal role of DPP3 in cardiac depression could be reproduced in several model systems.

"The new data adds to the growing body of evidence that places the cardiac depressant factor DPP3 in strong connection with short-term organ failure and high mortality in critical care settings. We have already started a collaboration with the critical care community to provide our fully automated DPP3 point-of-care test to support the management of acute care patients," said Dr. Andreas Bergmann, CEO and founder of sphingotec.

The IVD test for DPP3 is commercialized under the brand name IB10 sphingotest® DPP3 and is designed and validated for use in conjunction with sphingotec's fully automated Nexus IB10 whole blood point-of-care platform, delivering results within 20 minutes. This new test complements a wide-range of assays for acute care settings that are already available on this widely used point-of-care platform that can be

flexibly deployed in laboratory as well as near-patient settings such as emergency departments and intensive care units.

(1) Dépret (2020) Circulating dipeptidyl peptidase-3 at admission is associated with circulatory failure, acute kidney injury and death in severely ill burn patients, Critical Care. doi: 10.1186/s13054-020-02888-5.
(2) Takagi (2019) Circulating dipeptidyl-peptidase 3 and alteration in hemodynamics in cardiogenic shock: Results from the OptimaCC Trial, European Journal of Heart Failure, doi: 10.1002/ejhf.1600
(3) Deniau (2019) Circulating dipeptidyl peptidase-3 is a myocardial depressant factor: DPP3 inhibition rapidly and sustainably improves hemodynamics, European Journal of Heart Failure, doi: 10.1002/ejhf.1601

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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 cardiac depression. 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 established and commonly used tests for acute and critical care.

About 4TEEN4

4TEEN4 Pharmaceuticals GmbH ("4TEEN4") is a biopharmaceutical company developing Procizumab, a humanized antibody targeting human Dipeptidyl Peptidase 3 (DPP3) for the treatment of critically ill patients suffering from cardiac depression and multiple organ failure. 4TEEN4 licenses its proprietary biomarker DPP3 to make it available for diagnostic use in indications as acute heart failure, cardiogenic shock, septic shock and other critical care conditions. The company was established in 2013 in Hennigsdorf near Berlin, Germany, by Dr. Andreas Bergmann, CEO of 4TEEN4, as part of his Medicine4Future Initiative.

About DPP3

IB10 sphingotest® DPP3 is a rapid point-of-care (POC) immunoassay for the in vitro quantitative determination of Dipeptidyl peptidase 3 an active enzyme which, when released into the blood, inactivates angiotensin II, a hormone that is important for the heart function. This inactivation leads to hemodynamic instability and consequently cardiac depression. The DPP3 release is a newly identified disease mechanism explaining short-term organ failure in critically ill patients. Early identification of DPP3 release may allow better patient stratification and earlier therapy escalation to improve outcomes.

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