May I introduce you to bioactive Adrenomedullin (bio-ADM®)?
A unique biomarker for real-time assessment of vascular integrity

May I introduce you to Proenkephalin (penKid®)?
A unique biomarker for real-time assessment of kidney function

May I introduce you to Dipeptidyl Peptidase 3 (DPP3)?
A unique biomarker for interrupted signaling pathway communications

May I introduce you to PROCIZUMAB?
A personalized therapy under pre-clinical development to neutralize circulating Dipeptidyl Peptidase 3

May I introduce you to ADRECIZUMAB?
A personalized therapy under clinical development to restore vascular integrity in septic shock and beyond
“Our common goal is to improve the management of critically ill patients with first-in-class diagnostics and targeted therapy.”

Dr. Andreas Bergmann,
Founder of the Medicine4Future Initiative

www.medicine4future.com
Enkephalin, measurable via the prohormone fragment Proenkephalin (penKid®), was identified as the key regulator of renal function, changing dynamically as kidney function worsens or improves.

- Prediction and real-time monitoring of Acute Kidney Injury (AKI)
- Up to 2 days earlier response to kidney function than today's standard of care
- Independent of Inflammation and other comorbidities
- Ideal correlation to gold-standard methods of true GFR determination
- Validated in more than 30,000 patients
Bioactive Adrenomedullin (bio-ADM®), is a vasoprotective peptide hormone, freely diffusing between the blood and tissue compartment (extravascular space). In the blood-stream bio-ADM® stabilizes vascular integrity and prevents vascular leakage, in the extravascular space bio-ADM® acts as a vasodilator. Elevated blood bio-ADM® concentrations indicates edema, circulatory failure and subsequent organ dysfunction e.g. in septic shock or acute heart failure.

- Early prediction of shock and vasopressor demand in critically ill patients
- Monitoring of vascular integrity in critically ill patients
- Independent from inflammation or any other comorbidities
- Diagnosis of residual congestion
- Validated in more than 20,000 patients

Caution - The information contained in this communication does not constitute nor imply an offer to sell or transfer any sphingotec product in the USA or Canada due to regulatory reasons. For other countries, please check availability directly with SphingoTec GmbH, Germany. | 1 Mebazaa et. al. (2018) Critical care | 2 Ter Maaten et. al. (2019) Eur. J. Heart Fail.
**IB10 sphingotest® DPP3 –**
The Assay for Dipeptidyl Peptidase 3, a unique Biomarker for Signaling Pathway Disruptions Leading to Acute Organ Dysfunction¹

- Stratification of patients at high risk to develop short-term organ dysfunction
- Guidance for induction or escalation of therapy
- Monitoring of treatment success

**Disease state:**
DPP3 released from cells into circulation and subsequent organ dysfunction

- **DPP3**
  - Rising DPP3 blood concentrations, caused by cell death, indicates short-term organ dysfunction.

**Healthy state:**
DPP3 intracellular

- **DPP3**
  - Decreasing DPP3 blood concentrations indicate successful interventions whereas increasing or continuously elevated levels identify non-responders.

Dipeptidyl Peptidase 3 (DPP3) is an enzyme at the core of a recently discovered disease mechanism resulting in acute myocardial depression. The degradation of the cardiovascular and renal mediators angiotensin II and enkephalin by circulating DPP3 causes signaling pathway disruptions leading to short-term organ dysfunction.

**Consecutive IB10 sphingotest® DPP3 monitoring**

**Disease state:**
DPP3 released from cells into circulation and subsequent organ dysfunction

**Healthy state:**
DPP3 intracellular

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ADRECIZUMAB
A clinical-stage, first-in-class anti-Adrenomedullin antibody

Binding of ADRECIZUMAB to bioactive adrenomedullin (bio-ADM\textsuperscript{®}) stabilizes the molecule and translocates it to the blood. The accumulated ADRECIZUMAB-bio-ADM\textsuperscript{®} complex remains fully functional and thereby improves vascular integrity. ADRECIZUMAB is currently investigated in a biomarker-guided, proof-of-concept clinical phase II trial in septic shock patients, the AdrenOSS II study.

**Disease State**
The effects of vasoprotective bio-ADM\textsuperscript{®} depend on its localization.

1. Blood: Restore and maintain vascular integrity
2. Extravasal space: Vasodilatory effects affecting blood pressure.

**ADRECIZUMAB mode of action**

1. ADRECIZUMAB administration leads to accumulation of blood bio-ADM\textsuperscript{®}.
2. ADRECIZUMAB-bound bio-ADM\textsuperscript{®} is still functional and positively affects vascular integrity.

For more information visit our website www.adrenomed.com
Neutralization of circulating Dipeptidyl Peptidase 3 (DPP3) by PROCIZUMAB, reduces degradation of the cardiovascular and cardio-renal mediators angiotensin II and enkephalin, stabilizing organ function. PROCIZUMAB is under development as a treatment for patients with acute myocardial depression and currently investigated in pre-clinical models.