4TEEN4's first-in-class therapeutic antibody Procizumab restores heart function in life-threatening cardiac depression induced by sepsis

- 4TEEN4 reports on the efficacy of Procizumab in a preclinical model of sepsis
- Procizumab targets the cardiac depressant factor Dipeptidyl Peptidase 3 (DPP3) and restores cardiac function in a septic cardiomyopathy model
- Current data confirm that DPP3 is involved in pathophysiological processes driving septic cardiomyopathy

Hennigsdorf/ Berlin, Germany, September 16, 2020 - 4TEEN4 Pharmaceuticals GmbH ("4TEEN4") announces data on the efficacy of its lead product, Procizumab, that promptly restored cardiac dysfunction in a preclinical sepsis model by inhibiting the cardiac depressant factor DPP3. The current findings indicate that DPP3 plays an important role in septic cardiomyopathy. Sepsis is a dysregulated host response to an infection that ultimately leads to organ dysfunction.

The study data (1) from the team lead by Prof. Alexandre Mebazaa have shown that high DPP3 blood values are associated with decreased heart function in a preclinical sepsis model. In this randomized, controlled study, the administration of Procizumab immediately and significantly improved heart function by increasing cardiac output, stroke volume, and left ventricular shortening fraction. Inactivation of the cardiac depressant factor DPP3 fully restored cardiac contraction and improved survival.

DPP3 is at the core of a recently discovered disease mechanism, which was previously demonstrated to be a leading cause of circulatory failure (2,3,4). The release of the cardiac depressant factor DPP3 into the bloodstream causes the inactivation of the heart-stimulating hormone, Angiotensin II, a process leading to cardiac depression, hemodynamic instability and shock.

"These findings demonstrate for the first time that DPP3 plays a role in sepsis. By inhibiting DPP3 with our antibody Procizumab, we are able to restore cardiac function in preclinical sepsis models. This paves the way for future investigations on the utility of Procizumab as a possible therapeutic option in patients with sepsis and septic shock" said Dr. Andreas Bergmann, CEO of 4TEEN4.

The antibody Procizumab offers a new approach for the treatment of life-threatening diseases related to acute circulatory failure. Preclinical safety and toxicity studies of the antibody as well as the initiation of the first-in-man studies are planned for 2021.

References

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(2) 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

(3) 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

(4) 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

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About 4TEEN4

4TEEN4 Pharmaceuticals GmbH is a biopharmaceutical company developing Procizumab, a humanized antibody targeting human Dipeptidyl Peptidase 3 (DPP3) for the treatment of acute cardiovascular diseases. 4TEEN4 licenses its proprietary biomarker DPP3 to make it available for diagnostic use in indications as acute heart failure, myocardial infarction, cardiogenic shock and septic shock. 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 Procizumab

Procizumab is a humanized monoclonal antibody in preclinical development specifically binding circulating Dipeptidyl Peptidase 3 (DPP3). It will be a first-in-class drug that targets and modulates DPP3 as an essential regulator of cardiovascular function. Procizumab has an innovative mode of action, relevant in acute diseases. Massive cell death and release of DPP3 into the bloodstream lead to degradation of its substrates, including angiotensin II and enkephalin, that are responsible for cardiac and renal function regulation. Procizumab inhibits the activity of DPP3, thereby reducing bioactive peptide degradation, stabilizing cardiovascular function and potentially increasing survival chances e.g. in acute heart failure and septic shock. Preclinical studies of Procizumab in models of cardiovascular failure showed instant efficacy.

About DPP3

Dipeptidyl Peptidase 3 (DPP3) is 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 cardiac depression and consequently hemodynamic instability and consequently cardiac depression. The DPP3 release is a newly identified disease mechanism explaining short-term organ failure in critically ill patients.

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