Malmö 7 September 2021 **PRESS RELEASE**

Aptahem's collaboration with Örebro University defines a previously not shown unique modulation mechanism on coagulation and inflammation from Apta-1

Aptahem can today announce that further studies with Örebro University on Apta-1 show strong evidence in its features on the coagulation and inflammation by a unique modulation of Thrombin. This mechanism of action distinctly differs from current clinical used thrombin inhibitor drugs.

The Cardiovascular Research Centre at Örebro University and Aptahem research teams have with these clarifying data added a conclusive understanding to one of Apta-1's unique mechanisms.

Background information to give a better understanding of the unique impact on coagulation and inflammation by a new potent pathway of modulating Thrombin:

Sepsis is characterized by a number of abnormalities of hemostatic and immunological systems, leading to systemic inflammation, thrombosis, bleeding, and ultimately multiple organ dysfunction syndrome and death. In experimental models, Apta-1 significantly increases survival rate in sepsis-like conditions and inhibit formation of thrombosis without increased risk of bleeding. Hemostasis, defined as body´s normal defense against vessel trauma and bleeding, can be sub-divided into a rapid stage (primary hemostasis) and a slower, more powerful stage (secondary hemostasis). Primary hemostasis comprises activation of blood platelets leading to formation of a cellular plug at the damaged area of a blood vessel, whereas secondary hemostasis involves the sequential activation of plasma protein known as coagulation factors. Coagulation factor IIa (FIIa), is also known as thrombin. The mechanism behind thrombin activation of primary hemostasis relies on stimulation of cell surface receptors designated protease-activated receptors (PARs). These cell surface receptors are expressed on blood platelets, white blood cells and the blood vessel wall and cause pro-inflammatory and pro-thrombotic responses. In the presence of Apta-1, primary hemostasis as well as PAR receptors are functional, but thrombin loses its ability to activate PARs.

Thrombin comprises modulatory sites ("exosites") which can act as binding domain to heparin, resulting in altered enzymatic activity. Apta-1 interacts with a heparin-binding site on thrombin, and this is the basis for the incapability of thrombin to activate primary hemostasis via PAR receptors.

In conclusion, Apta-1 can be considered as a modulator of the serine protease thrombin by interacting with a heparin-binding site on the coagulation factor. Conversely, Apta-1 does not mimic the well-documented anti-coagulant effect of heparin, a pharmacological activity that increases the risk of bleeding. Primary and secondary hemostatic reactions are still functional in the presence of Apta-1 with one exception: thrombin cannot activate platelets. Incapability of thrombin to activate PARs will cause rapid anti-inflammatory and anti-thrombotic effects. The described mechanism of action of Apta-1 is distinctly different from that of clinically used thrombin inhibitors.

"The identified pharmacological mechanism for Apta-1 is a great discovery, as this will modulate one of the most important mechanisms that trigger pro-inflammatory and pro-thrombotic responses and without affecting others. This most likely means lesser negative side-effects compared to today's thrombin inhibitors / anticoagulants. For me this is a pivotal discovery that may just change our possibility to modulate thrombin in a safe way", says Magnus Grenegård, Professor in Physiology at Örebro University.

Malmö 7 September 2021 **PRESS RELEASE**

Dr. Luiza Jedlina, CSO at Aptahem, comments: "We are very happy for this discovery and clarification on one of Apta-1's mechanisms which now confirm our amazing results from previous studies and that we can better explain why and how it works" and she continues: "From a regulatory standpoint this is great and now we will continue with our efforts on unveiling the behavior of Apta-1 as well as preparing for getting these results peer reviewed in important scientific journals."

The joint research project between Aptahem AB and Cardiovascular Research Centre at Örebro University has obtained financing from the Swedish KK-foundation.

For further information:
Aptahem AB
Mikael Lindstam, CEO
Tel: +46 (0)766-33 36 99
E-mail: ml@aptahem.com

Forward-looking statements
This press release contains forward-looking statements that constitute subjective estimates and forecasts about the future. Assessments about the future are only valid on the date they are made and are, by their nature, similar to research and development work in the biotech field, associated with risk and uncertainty. In light of this, actual outcomes may differ substantially from what is described in this press release.

About Cardiovascular Research Centre (CVRC), Örebro University
Cardiovascular Research Centre (CVRC) is a research environment founded in 2014 at the Örebro University and consists of about 30 scientists at the university and Region Örebro. CVRC's overall goal is to increase the knowledge about disease mechanisms, more efficient diagnoses, treatment and prevention of cardiovascular diseases. Link to the CVRC at Örebro University: https://www.oru.se/english/research/research-environments/mh/cardiovascular-research-centre-cvrc/

About Aptahem
Aptahem AB (APTA) is a biotechnology company that develops aptamer-based pharmaceuticals for the treatment of life-threatening conditions in which a combination of coagulation and inflammation are involved. The company's primary pharmaceutical candidate, Apta-1, is being developed with the aim of preventing the high mortality rate caused by organ and tissue damage in sepsis patients, among others. The company possesses patent protection in strategic target markets and actively seeks business development opportunities with potential collaborators.