Press Release

Cerenis Therapeutics announces the publication of positive preclinical data in the world-renowned scientific journal PLOS ONE

- **CER-001 mimics native HDL**
- **Ability of CER-001 to inhibit the formation of atherosclerotic plaque with better efficacy at lower doses**
- **Confirmation of the optimal design of the Phase II CARAT clinical trial in the post Acute Coronary Syndrome (ACS) indication**

Toulouse, FRANCE and Ann Arbor, UNITED STATES, September 4, 2015 – **Cerenis Therapeutics (FR0012616852 - CEREN),** an international biopharmaceutical company dedicated to the discovery and development of innovative HDL therapies ("good cholesterol") for treating cardiovascular and metabolic diseases, today announces that important *in vitro* and *in vivo* preclinical data, evaluating the dose-dependent regulation of ABCA1 expression in the presence of CER-001 and native HDL (HDL3), has been published in the peer-reviewed journal PLOS ONE (http://dx.plos.org/10.1371/journal.pone.0137584).

This data shows the ability of CER-001 to promote plaque regression and the mechanism controlling plaque regression by HDL and HDL-mimetics. This data supports the CER-001 clinical development plan.

• Ability of CER-001 to inhibit the formation of atherosclerotic plaque with better efficacy at lower doses

The data confirms CER-001's efficacy at slowing the progression of atherosclerosis and demonstrates that high doses of HDL and CER-001 are less effective at slowing the progression of atherosclerotic plaque in apoE-/- mice compared with lower doses, following a U-shaped dose-response curve. A potential mechanism for this phenomenon is supported by the observation that high doses of HDL and CER-001 induce a rapid and strong down-regulation of the ABCA1 transporter (the cellular gatekeeper for eliminating excess tissue cholesterol) both *in vitro* and *in vivo*. Maximally efficient HDL- or CER-001-mediated cholesterol removal from atherosclerotic plaque is achieved by maximizing the macrophage-mediated efflux from the plaque while minimizing dose-dependent down-regulation of the ABCA1 expression.

With biologic products, it is often observed that "more is not always better", and too high a dose sometimes confers reduced efficacy due to the down-regulation of the expression of key elements controlling the pathway being engaged, in this case the "Reverse Lipid Transport" (RLT) pathway.

• Confirmation of the optimal design of the Phase II CARAT clinical trial in the post-ACS indication

The published preclinical data also supports the optimal dose of HDL-mimetics selected in the phase II clinical trial of atherosclerotic plaque regression, the CARAT study, testing 3mg/kg of CER-001 in post-Acute Coronary Syndrome (ACS) patients.

In the CHI SQUARE clinical study, the lower 3 mg/kg dose of CER-001 was shown to be more potent than the higher 6 and 12 mg/kg doses, which is consistent with the preclinical data and with the results observed by Professor Steven

Nissen with the apoA-I Milano complex in post-ACS patients (where the 15 mg/kg dose was more potent than the higher 45 mg/kg dose*).

Dr. Jean-Louis Dasseux, Founder and CEO of Cerenis, comments: "*We are delighted that these new positive results have been published in a world-renowned scientific journal. Understanding the biochemical mechanism controlling the cellular elimination of cholesterol within atherosclerotic plaque allows the Company to be well positioned to design the best treatment regimen to maximize the regression of atherosclerotic plaque in clinic. This is illustrated by the optimal design of the CARAT and TANGO studies* ".

** JAMA, November 5, 2003—Vol 290, No. 17 (2292-2300)*

Notes to editors

Atherosclerosis is a disease arising from formation of plaque, so-called atherosclerotic plaque, caused by deposits of lipids, especially cholesterol, in the vessel wall, which leads to the manifestation of cardiovascular diseases including myocardial infarction ("heart attack") and angina pectoris all designated by the term acute coronary syndrome (ACS). Atherosclerosis affects the entire vascular system and also leads to several other complications, including ischaemic stroke, renal failure and arteriopathy of the lower limbs.

The major carriers for cholesterol in the blood are lipoproteins, including the low-density lipoprotein (LDL) particles, and the high-density lipoprotein (HDL) particles. In a healthy human body, there is a balance between the delivery and removal of cholesterol. The LDL particles deliver cholesterol to organs, where it can be used to produce hormones, maintain healthy cells, and be transformed into natural products that assist in the digestion of lipids. The HDL particles remove cholesterol from arteries and tissues to transport it back to the liver for storage, recycling, and elimination through a pathway called "Reverse Lipid Transport" (RLT).

Epidemiological studies have historically demonstrated that the risk of developing cardiovascular diseases appeared to be higher in patients with low HDL-cholesterol independent of the level of LDL-cholesterol, even when patients are treated with the best available standard of care. This observation can be explained by the role the HDL particle plays in the RLT pathway, the only natural mechanism capable of removing cholesterol from peripheral tissues and delivering it back to the liver for elimination. HDL particles mediate the flux of cholesterol through the RLT and therefore act to counterbalance the delivery of cholesterol to the vessel wall by the LDL particles. The RLT is a pathway that may protect against atherosclerosis and cardiovascular diseases by clearing excess cholesterol from the arterial wall. The ATP-binding cassette transporter called ABCA1 is a protein that mediates the first step of RLT and acts as a gatekeeper for eliminating excess tissue cholesterol.

About Cerenis Therapeutics: www.cerenis.com

Cerenis Therapeutics is an international biopharmaceutical company dedicated to the discovery and development of innovative HDL therapies for the treatment of cardiovascular and metabolic diseases. HDL is the primary mediator of the reverse lipid transport, or RLT, the only natural pathway by which excess cholesterol is removed from arteries and is transported to the liver for elimination from the body.

Cerenis is developing a portfolio of HDL therapies, including HDL-mimetics for the rapid regression of atherosclerotic plaque in high-risk patients such as post-ACS patients and patients with HDL deficiency, and drugs which increase HDL for patients with low number of HDL particles to treat atherosclerosis and associated metabolic diseases.

Cerenis is well-positioned to become one of the leaders in the HDL therapeutic market, with a broad portfolio of programs being developed.

Since its inception in 2005, the company has been funded by top tier investors: Sofinnova Partners, HealthCap, Alta Partners, EDF Ventures, Daiwa Corporate Investment, TVM Capital, Orbimed, IRDI/IXO Private Equity and Bpifrance (Fund for Strategic Investment) and last March successfully completed an IPO on Euronext raising €53.4m.

About CER-001:

CER-001 is an engineered complex of recombinant human apoA-I, the major structural protein of HDL, and phospholipids. It has been designed to mimic the structure and function of natural, nascent HDL, also known as pre-beta HDL. Its mechanism of action is to increase apoA-I and the number of HDL particles transiently, to stimulate the removal of excess cholesterol and other lipids from tissues including the arterial wall and to transport them to the liver for elimination through a process called Reverse Lipid Transport.

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