Press Release

Cerenis Therapeutics featured prominently at the 25th Conference of the ASIAN PACIFIC ASSOCIATION FOR THE STUDY OF THE LIVER (APASL)

Experimental results demonstrate an active role to treat atherosclerosis and non-alcoholic steatohepatitis (NASH) for CER-209 as an agonist of the P2Y13 receptor

Toulouse, FRANCE, Ann Arbor, UNITED STATES, February 25, 2016 – 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 reported two poster presentations featuring Cerenis Therapeutics' innovative HDL therapy, CER-209, during the 25th Conference of the APASL held in Tokyo, February 20-24, 2016.

- **CER-209, an agonist of the P2Y13 receptor, is potentially well suited to the treatment of atherosclerosis and non-alcoholic steatohepatitis (NASH)**

In a poster presentation ("P2Y13 receptor agonist CER-209 decreases both atherosclerosis and liver steatosis in vivo"), Cerenis presented results of CER-209, a selective novel agonist of the P2Y13 receptor (P2Y13R) that caused an increased uptake of high-density lipoprotein-cholesterol (HDL-c) in the liver which is associated with stimulation of bile acid secretion. Repeated dose administration of CER-209 stimulated the apoA-I synthesis and formation of small HDL particles, known to be atheroprotective. CER-209-treated plasma samples had high cholesterol efflux capacity for the mobilization of cellular cholesterol in vitro compared with the placebo group. CER-209 induced a decrease in atherosclerotic plaques in aorta and carotids as well as a remarkable decrease in the steatosis in a validated preclinical model.

HDL is known to protect against atherosclerosis by promoting the reverse lipid transport. A new pathway for the regulation of HDL-c recognition by the liver involving F1-ATPase and P2Y13 receptor (P2Y13R) has been described in vitro, and recently in mice. An increase in the expression of liver mRNA coding for apoA-I and plasma apoA-I concentration of treated animals was observed. The uptake of large, mature HDL particles loaded with cholesterol by the liver also stimulates de novo synthesis of nascent HDL particles, thereby enhancing the cholesterol efflux capacity of the serum. The overall implication of this increase is not only to allow the removal of cholesterol from atherosclerotic plaques, but also to regulate lipid homeostasis in the liver.

In another poster presentation ("P2Y13 receptor agonist CER-209, an anti-atherosclerotic compound, decreases liver steatosis in vivo"), Cerenis presented further results with the selective novel agonist of the P2Y13R, CER-209. In this preclinical model, CER-209 resulted in a marked reduction in overall steatohepatitis as determined by reductions in cholesterol, trigylcerides and fatty acids compared with placebo. Furthermore, CER-209 produced considerable decreases in liver enzymes (ALT and AST) in the plasma. These effects suggest the restoration of liver integrity and indicate a strong potential for CER-209 to treat liver disease such as NASH and non-alcoholic fatty liver disease (NAFLD) associated with cardiovascular disease.

These are important findings given the current lack of treatment options for NASH and introduces P2Y13R as a new therapeutic target for this disorder. CER-209 exerts its beneficial effect on liver steatosis via a specific action on the cholesterol elimination pathways. Therefore, CER-209 has a strong potential for the treatment of NASH and NAFLD.

Dr. Jean-Louis Dasseux, Founder and CEO of Cerenis comments*: "These results show that CER-209 has the potential to be an effective treatment for atherosclerosis and associated non-alcoholic steatohepatitis (NASH). They also demonstrate the ability of the Cerenis scientists to advance critically our understanding of HDL metabolism which could lead to several entirely new classes of therapeutic agents".*

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 (or LDL) particles, and the high-density lipoprotein (or 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 disease 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 Reverse Lipid Transport (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 disease 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.

Non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) are components of the worldwide epidemic of obesity. NAFLD, the most prevalent chronic liver disease, affects 20–40% of the population. Approximately one-third of patients with NAFLD will progress to non-alcoholic steatohepatitis (NASH). Many studies demonstrate a direct link between NAFLD and CVD. The clinical implication is that patients with NAFLD are at an increased risk of cardiovascular disease (CVD) While no specific treatments are currently available, recent guidelines recommend weight loss, increased physical activity, control of hyperglycaemia and statins to lower lipids through regulation of LDL-cholesterol. RLT, driven by HDL metabolism, controls the transfer of cholesterol from non-hepatic cells to the liver, where it is excreted from the body in the form of bile acids and unesterified cholesterol. HDL-directed lipid elimination by the liver could impact atherosclerosis as well as fatty liver and steatohepatitis, providing therapeutic potential in NAFLD and NASH patients with high risk of CVD.

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-209:

CER-209 is the first drug candidate in the category of oral P2Y13 receptor agonists. The P2Y13 receptor is a member of the P2Y receptor family, a well-known receptor family including the P2Y12 receptor which is the target of successful drugs such as the anti-thrombotic agent Clopidogrel (Plavix®). In preclinical studies CER-209 promotes HDL recognition by the liver and increase the activity of Reverse Lipid Transport (RLT), and thus has an impact on atherosclerosis regression. Because of the favorable metabolic effects observed in the liver, CER-209 may also offer a new mechanism for the treatment of non-alcoholic steato-hepatitis (NASH).

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. Previous Phase II studies have provided important data demonstrating the efficacy of CER-001 in regressing atherosclerosis in several distinct vascular beds in patients representing the entire spectrum of cholesterol homeostasis. The totality of the data to date indicates that CER-001 performs all of the functions of natural pre-beta HDL particles and has the potential to be the best-in-class HDL mimetic in the market.

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