Press release

Approval to launch the Phase I Study of repeated and increasing doses to assess CER-209 in NASH/NAFLD

Presentation of CER-209 at the 2nd annual H.C. Wainwright NASH Investor Conference on March 19, 2018

- **Regulatory authority approval to begin enrollment in the study**
- **Daily administration of increasing doses of CER-209 over a 28-day period in patients with a high risk of NAFLD/NASH**
- **First clinical assessment of the mechanism of action associated with the P2Y13 receptor including liver-related measures of fat accumulation**

Toulouse, FRANCE, Lakeland, UNITED STATES, March 7, 2018, 6 pm CET – **CERENIS Therapeutics** (**FR0012616852 – CEREN – PEA-PME eligible**), an international biopharmaceutical company dedicated to the discovery and development of HDL-based innovative therapies for treating cardiovascular and metabolic diseases, as well as new HDL-based vectors for targeted drug delivery in the field of oncology, announces the approval and the upcoming launch of the second Phase I study to assess the daily administration of increasing doses of CER-209 over a 28-day period in patients with a high risk of developing Non-Alcoholic Steato-Hepatitis (NASH) and/or Non-Alcoholic Fatty Liver Disease (NAFLD).

Moreover, during the second annual H.C. Wainwright NASH Investor Conference in New York on March 19, 2018, Jean-Louis Dasseux will discuss the scientific aspects and clinical strategy of CER-209.

Jean-Louis Dasseux, **founder** and **CEO** of **Cerenis**, commented: "*We are eager to validate CER-209's safety and tolerance profile via the multiple dose Phase I study whose results are expected in Q4 2018. As well as the standard tolerance, safety and pharmacokinetic parameters examined in this study, the first pharmacodynamic data regarding CER-209's mechanism of action should confirm our drug candidate's therapeutic potential. CER-209, by activating the natural metabolic pathways mediated by the P2Y13 receptor, promotes HDL recognition and lipid elimination by the liver. It is precisely this objective of reducing hepatic fat that the Phase II study – the next stage in CER-209's clinical development – will evaluate. This will represent a major milestone in the development of this treatment that aims to address NASH and NAFLD, which are among the leading causes of cirrhosis in the United States, and associated cardiovascular diseases that represent the main cause of death among patients with liver steatosis*".

Daily administration of repeated and increasing doses of CER-209 over a 28-day period in patients with a high risk of NAFLD/NASH

The regulatory authorities have given their approval to initiate the enrollment of subjects that will begin by end-March 2018. The primary endpoints concern safety and tolerance following the administration of multiple doses of CER-209. Pharmacokinetic and pharmacodynamic endpoints will also be studied in order to define the optimal dose for the next studies.

The subjects included in the study have large waist circumferences and high triglyceride levels, parameters associated with a high risk of subsequently developing metabolic diseases such as NAFLD and NASH.

The protocol for this randomized, double blind and placebo controlled trial foresees the enrollment of 6 cohorts of subjects. Multiple doses of CER-209 will be administered in 6 cohorts of 5 subjects each. Daily doses of 10, 30, and 60 mg of CER-209 will be given for 28 days. In all cohorts 4 subjects will receive active drug.

First clinical assessment of the mechanism of action associated with the P2Y13 receptor

The profile of the study's subjects will enable assessment of two parameters associated with the mechanism of action of CER-209:

- Changes in the level of lipids in the liver, measured using magnetic resonance imaging (MRI-PDFF);
- The rate of fecal elimination of cholesterol and bile acids.

Positive efficacy signals, demonstrating improvement in these parameters, would enable validation of previous findings, and would strengthen CER-209's therapeutic potential, already highlighted in preclinical studies.

The mechanism of action of CER-209, an agonist of the P2Y13 receptor

In preclinical models, CER-209 results in a marked reduction in steatohepatitis as determined by a reduction in the levels of cholesterol, triglycerides and fatty acids in the liver compared with the placebo, as well as a reduction in atherosclerosis. Furthermore, CER-209 produces significant decreases in liver enzymes (ALT and AST) in the plasma. These effects suggest the restoration of liver integrity and indicate CER-209's strong potential for treating NAFLD and NASH while reducing the risks associated with cardiovascular disease.

About CERENIS: www.cerenis.com

CERENIS Therapeutics is an international biopharmaceutical company dedicated to the discovery and development of innovative lipid metabolism 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 lipids is removed from arteries and is transported to the liver for elimination from the body.

CERENIS is developing a portfolio of lipid metabolism therapies, including HDL mimetics for patients with genetic HDL deficiency, as well as drugs which increase HDL for patients with a low number of HDL particles to treat atherosclerosis and associated metabolic diseases including Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steato-Hepatitis (NASH). Capitalizing on its expertise, Cerenis is developing the first HDL-based targeting drug delivery platform dedicated to the oncology field (immuno-oncology and chemotherapy).

CERENIS is well positioned to become one of the leaders in the HDL therapeutic market, with a broad portfolio of programs in development.

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. SAMBA, the clinical Phase 2 study in patients with hypoalphalipoproteinemia due to genetic defects, has provided important data demonstrating the efficacy of CER-001 in regressing atherosclerosis in several distinct vascular beds, and leading to the TANGO study. 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 on the market.

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, well-known receptors including the P2Y12 receptor which is the target of successful drugs such as the anti-platelet agent Clopidogrel (Plavix®). CER-209 is a specific agonist of P2Y13 receptor and does not interact with the P2Y12 receptor. 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 as well as liver fat. Thus the favorable metabolic effects of CER-209 in the liver offers a new mechanism for the treatment of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steato-hepatitis (NASH).

About HDL targeting Drug Delivery

HDL particles, loaded with an active agent, hold the promise to target and selectively kill malignant cells while sparing healthy ones. A wide variety of drugs can be embedded in these particles targeting markers specific to cancer cells and bring these potent drugs to their intended site of action, with lowered systemic toxicity. Cerenis intends to develop the first HDL-based targeting drug delivery platform dedicated to the oncology market, including immuno-oncology and chemotherapy.

Financial Agenda:
Cash position and revenue for Q1 2018
April 19th, 2018

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