Press release

First patients enter TARGET study, recently initiated by Cerenis Therapeutics to evaluate HDL nanoparticles in patients with esophageal cancer

Toulouse, FRANCE, Lakeland, UNITED-STATES, November 22, 2017, 8.00 am 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, today announces further evolution of its use of HDL with the enrollment of the first patients in the TARGET study, recently initiated to evaluate HDL nanoparticles in patients with esophageal cancer.

TARGET is the first ever performed clinical study testing the potential of labelled HDL to visualize tumors in cancer patients. A number of preclinical studies have already validated the concept, however this study will support the opportunity to treat cancer patients using HDL nanoparticles as a specific drug delivery platform targeting tumors.

Cerenis' CER-001 allied with NanoDisk® technology, an engineered complex of recombinant human apoA-I, will target malignant cells to bring potent drugs to their intended site of action, while sparing healthy cells.

Dr. Jean-Louis Dasseux, Founder and CEO of Cerenis, comments: *« Following the acquisition of the LYPRO Nanodisk® technology, Cerenis has initiated a study to obtain compelling clinical data in order to support our HDL Drug Delivery platform. TARGET is our first step in the clinic and this imaging study in patients will validate HDL selective tumor targeting by demonstrating that cancer cells which over-express HDL receptors facilitate HDL Targeted Drug Delivery. We intend to leverage our know-how and our proprietary Intellectual property to move forward into immuno-oncology and chemotherapy.*
We also remain dedicated to our efforts in patients with genetic HDL deficiencies, through the fully enrolled TANGO study, and with our advancement of CER-209 for patients with Non-Alcoholic Steato-Hepatitis (NASH) or Non-Alcoholic Fatty Liver Disease (NAFLD).
This evolution has been included in this year's budget and does not have a significant impact on Cerenis' cash position. Fully committed to this exciting stage of Cerenis' development, we look forward to pursuing the clinical advances of our innovative HDL therapies' portfolio."

The aim of the TARGET study is to assess the concentrations of Zirconium 89 (89Zr) labeled CER-001 in tumor tissue. Recent pre-clinical studies have demonstrated that reconstituted radio-labeled HDL nanoparticles may be used to label tumors, with specificity for tumor associated macrophages. Furthermore, in cancer patients, 89Zr-labeled HDL mimetic CER-001 will allow for non-invasive evaluation of the potential of drug delivery strategies in selected cancers. Success will pave the way for loading of HDL nanoparticles with immune-oncology and chemotherapeutic agents.

The secondary objective of the TARGET study is to evaluate the biodistribution of 89Zr-labeled CER-001, the correlation between 89Zr-labeled CER-001 and tumor microcirculation as assessed with Dynamic Contrast Enhanced-MRI (CE-MRI), as well as Diffusion Weighted Imaging/Intravoxel Incoherend Motion (DWI/IVIM) MRI. This information could provide proof of concept for the tumor selectivity of this strategy. The study will also evaluate the relationship between histological markers from the tumor biopsy and the 89Zr-PET signal and MRI parameters.

The TARGET study is a single-center observational trial enrolling adult subjects with a pathologically proven diagnosis of primary esophageal carcinoma in situ. Patients are all T2 staged according to the TNM classification. A total of 10 patients will undergo all study procedures. The study is expected to be completed by the end of Q2 2018.

The investigational product is CER-001, a pre-beta HDL mimetic labeled with Zirconium-89 for serial PET/CT imaging in patients. It has been demonstrated that CER-001 pre-beta HDL mimetic has the same structure and function as a natural pre-beta HDL and could be used as a specific tumor imaging product to validate that HDL specifically target tumors via HDL receptors in patients. CER-001 is also in a phase III clinical trial for patients with a genetic HDL deficiency ("TANGO"), and has a very favorable safety and tolerance profile as demonstrated in previous clinical trials.

CER-001 particles associated to Nanodisk® technology have the future potential to serve as carriers of multiple anti-cancer drugs, antigens, interfering RNA (siRNA's), and anti-sense oligonucleotides (ASOs) opening the path to attractive partnerships for the Cerenis platform.

The two principal investigators of the TARGET study are Professor Dr. Erik Stroes, MD, PhD, Chair of the Department of Vascular Medicine, Amsterdam Medical Center (AMC) and Professor Dr. Hanneke Van Laarhoven, MD, PhD, Department of Medical Oncology, Amsterdam Medical Center (AMC).

Professor Dr. Erik Stroes, comments: "*More and more scientific data support the role of HDL as a universal transporter to carry the building blocks necessary to the growth and multiplication of cancer cells. HDL interacts with a number of HDL receptors such as the scavenger receptor B-I (SR-BI). We look forward to testing, in cancer patients, CER-001 known to have the structure and function of natural pre-beta HDL mimetic.*"

Professor Dr. Hanneke Van Laarhoven, MD, PhD, concludes: *"CER-001 targeting particles associated with the NanoDisk® technology hold the promise to treat cancer with lowered systemic toxicity. The fact that a wide variety of drugs can be embedded in HDL nanoparticles could increase efficacy compared to available drug delivery technologies and open a new generation of drugs in oncology."*

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). 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 with results expected at the end of Q1, '18. 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, a well-known receptor family including the P2Y12 receptor which is the target of successful drugs such as the anti-thrombotic agent Clopidogrel (Plavix®). CER-209 is a specific agonist of P2Y13 receptor and is not interacting 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. Because of the favorable metabolic effects observed in the liver, CER-209 may also offer a new mechanism for the treatment of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steato-hepatitis (NASH).

About HDL targeting Drug Delivery

CER-001 targeting particles associated with the NanoDisk® technology 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 which will target markers specific to cancer cells and bring these potent drugs to their intended site of action, with lowered systemic toxicity. Cerenis intent to develop the first HDL particle delivery platform dedicated to the oncology market, including immuno-oncology and novel chemotherapeutic delivery technologies.

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