Press release

2018 Annual Results and clinical update

- **Cash position of €11.5 million at December 31, 2018**
- **Results of the Phase I study, assessing CER-209 in NAFLD/NASH, confirm the drug candidate's favorable safety and tolerance profile**
- **Success of the TARGET Phase II study demonstrates the ability of CER-001, an HDL mimetic, to target tumors in patients with esophageal cancer**
- **Missed primary endpoint in the TANGO Phase III study**

Toulouse, FRANCE, Lakeland, UNITED STATES, January 24, 2019, 7:00 pm CET – **CERENIS Therapeutics** (**FR0012616852 – CEREN – PEA-PME eligible**), an international biopharmaceutical company dedicated to the discovery and development of innovative therapies for treating cardiovascular and metabolic diseases, as well as new HDL-based vectors for targeted drug delivery in the field of oncology, today announces its 2018 annual results, as approved by the Board of Directors on January 24, 2019, and issues clinical update. Audit procedures on statutory and consolidated accounts have been performed by the auditors, and the certification report is currently being issued.

Richard Pasternak, **Chairman and CEO** of **CERENIS**, says: "*During the 2018 financial year, major clinical results were disclosed regarding the negative TANGO study with CER-001, the Phase I study with CER-209, and information regarding the HDL platform's activity with the TARGET study. The data from the second Phase I study with CER-209, in the treatment of Non-Alcoholic Steato-Hepatitis (NASH) and Non-Alcoholic Fatty Liver Disease (NAFLD) confirms the favorable safety and tolerance profile and highlight the potential of the mechanism of action via the P2Y13 receptor. The TARGET study with CER-001, meanwhile, demonstrated the ability of HDL particles to act as carriers, thus strengthening the targeted drug delivery platform's potential. CERENIS now has a promising portfolio enabling multiple therapeutic areas to be addressed. In order to activate this potential and finance the CER-209 and CER-001 HDL platform, CERENIS is currently assessing the best strategic opportunities*".

Selected financial information (at December 31, 2018/ IFRS consolidated accounts)

€ millions	2017	2018
Revenue	0	0.2
R&D expenditure	-4.9	-4.3
General & Administrative expenses	-1.7	-2.9
Operating income	**-6.6**	**-7.1**
Financial income	2.5	1.0
Financial expenses	-0.8	-0.3
Financial result	**1.7**	**0.7**
Net income	**-5.0**	**-6.3**
Net earnings per share (€)	-0.27	-0.34
Net cash flow from operating activities	-9.0	-6.0
Net cash flow from financing activities	0.9	1.2
Change in the cash position	**-8.4**	**-4.8**
Cash and cash equivalents at end of period	**16.3**	**11.5**

Details of the main income statement changes

In line with expectations, CERENIS Therapeutics did not generate any revenue from its products in 2018, as these products are at the Research & Development stage. The revenue of €174 thousand corresponds to the invoicing of license revenue associated with the license retrocession agreement concluded in 2007 with Nippon Chemiphar.

Research & Development expenses totaled €4.295 million over the year, compared with €4.899 million in 2017. The decrease reflects the end of the CARAT and TANGO studies. There was an associated fall in R&D study costs and personnel costs following the restructuring plan initiated in 2017, after the end of the CARAT study. In 2018, the expense relating to share-based payments was marginal, while in 2017 the Company had recorded income because of the reversal of the 2016 expense in the income statement. This was related to the non-allocation of free performance-based shares following the end of the CARAT study in 2017. Lastly, the cost associated with depreciation and provisions increased due to the restructuring provision. The changes in share payments and provisions thus explain the limited fall in R&D expenditure with the end of the CARAT and TANGO studies.

General & Administrative expenses totaled €2.931 million in 2018, versus €1.738 million the previous year. This increase was a result of higher depreciation and provisions within the framework of the job-protection plan; 2017 general and administrative expenses were reduced by the reversal of a provision associated with the end of the dispute with the Montreal Heart Institute (MHI) in Canada.

Once these elements are taken into account, the Company recorded a **net loss** of €7.052 million over the year to December 31, 2018, versus a net loss of €6.637 million the previous year.

There was a **financial income** of €0.7 million in 2018, compared with €1.7 million in 2017. **Financial income and expenses** correspond to the application of IFRS to BPI repayable advances. The change between the two years was the result of the booking of net financial income of €1.601 million at December 31, 2017, following the updating of the repayment schedule for BPI advances dependent on clinical prospects at end-2017. Based on the latest estimates, the rescheduling of these repayments generated a financial income of €666 thousand in 2018.

Once this financial income is taken into account, the **net loss was** -€6.305 million at the end of 2018, compared with -€4.978 million at the end of 2017.

Cash and cash equivalents totaled €11.457 million at December 31, 2018.

Update on the Company's clinical developments in 2018

Negative results of TANGO clinical study evaluating CER-001 in patients with HDL deficiency

The objective of the study was to assess the impact of 6 months of treatment with CER-001 on the mean vascular wall area (MVWA) of the carotid artery as determined by MRI. Analysis of the study data did not show a statistically significant reduction in atheroma plaque between the CER-001 and placebo groups.

However, no major treatment-related adverse events were observed, confirming the safety and good tolerance profile of CER-001.

CER-209: Results of the Phase I study which assessed the daily administration of repeated and increasing doses of CER-209 over a 28-day period in patients with a high risk of NAFLD/NASH

CER-209 was safe and well tolerated following the administration of multiple doses in patients at high risk for NAFLD/NASH based on the presence of visceral obesity and/or dyslipidemia. Pharmacokinetic and pharmacodynamic endpoints were also studied in order to help define the optimal dose for future studies.

Mechanism of action via the P2Y13 receptor supported by changes in HDL cholesterol

The observed absorption of CER-209 was fast (within thirty minutes) and proportional to the administered dose.

Although the duration of the administration of CER-209 in this study was too short to observe any metabolic changes, there were dose dependent decreases in fasted HDL-C on Day 28 compared to Day 1 which is consistent with the innovative mechanism of action of CER-209. This activation by CER-209 of the P2Y13 receptor promotes HDL recognition and lipid elimination by the liver.

The next steps will include the development of a formulation with optimal bioavailability in preparation for a Phase II clinical study in patients with NASH over a longer period of time.

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, in these models 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 also reducing the risks associated with cardiovascular disease.

CER-001: Final results of TARGET PHASE II study demonstrate the ability of CER-001, an HDL mimetic, to target tumor in patients with esophageal cancer

TARGET was the first clinical study performed to assess radioactively labeled HDL tumor uptake in cancer patients and in doing so, the first clinical study to test the ability of HDL to target tumor in patients after interacting with cellular HDL receptors.

In TARGET, CER-001, a pre-beta HDL mimetic, was labeled with Zirconium-89 for serial PET/CT[1] imaging in patients. It has been previously demonstrated that CER-001 has the same structure and function as a natural pre-beta HDL. It was therefore reasoned that labeled CER-001 could be used as a tumor imaging product to target tumors via HDL receptors. A number of preclinical studies have already validated the concept[2], showing that HDL nanoparticles can act as a specific drug delivery platform targeting tumor cells or targeting immune cells.

CER-001 has been shown to be safe and well tolerated in multiple previous clinical trials with more than 5,000 administrations among the different studies and with repeated administrations of up to 18 months.

About CERENIS

Founded in 2005, Cerenis Therapeutics is an international biopharmaceutical company dedicated to the discovery and development of HDL-based innovative therapies. CERENIS' expertise has translated into a rich portfolio of programs for the treatment of cardiovascular disease and associated metabolic diseases such as NAFLD and NASH as well as a HDL targeted drug delivery platform in oncology, more specifically in immuno-oncology and chemotherapy.

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. 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 Targeted HDL 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 an HDL-based targeted drug delivery platform dedicated to the oncology market, including immuno-oncology and chemotherapy.

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PET/CT: ***Positron emission tomography–computed tomography*** *is a nuclear medicine technique which combines, in a single gantry, a positron emission tomography (PET) scanner and an x-ray computed tomography (CT) scanner, to acquire sequential images from both devices in the same session, which are combined into a single superposed (co-registered) image. Thus, functional imaging obtained by PET, which depicts the spatial distribution of metabolic or biochemical activity in the body can be more precisely aligned or correlated with anatomic imaging obtained by CT scanning. Two- and three-dimensional image reconstruction may be rendered as a function of a common software and control system.*

2 *J Nucl Med August 1, 2015 vol. 56 no. 8 1272-1277 / Front. Pharmacol.* **7**, 466 (2016).

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