Press Release

Cerenis Therapeutics receives EMA Orphan Drug Designation for CER-001 for the treatment of apaoA-I and ABCA-1 deficiencies

Toulouse, FRANCE, Ann Arbor, UNITED STATES, September 3, 2014 - Cerenis Therapeutics, the biopharmaceutical company developing CER-001, an engineered human apoA-I-containing pre-beta HDL mimetic, for the treatment of cardiovascular disease, announced today that it has received two separate Orphan Drug Designations from the European Medicines Agency (EMA) for the use of CER-001 in the treatment of patients with rare genetic defects in HDL synthesis/maturation pathways, specifically apoA-I deficiency and ABCA1 deficiency.

Inherited defects in the apoA-I gene or the ABCA1 gene in both homozygous and heterozygous forms can act in a dominant manner to cause Familial Primary HypoAlphalipoproteinemia (FPHA), a rare syndrome characterised by the absence of or a severe deficiency of HDL particles in the circulation. Due to either the impaired production/maturation or the premature destruction of HDL particles, the Reverse Lipid Transport (RLT) pathway, the body's only natural mechanism for the elimination of cholesterol, is compromised. Patients experience a rapid accumulation of cholesterol, particularly in blood vessels, which often results in accelerated atherosclerosis and premature cardiovascular disease.

John J.P. Kastelein, MD, PhD, of the Department of Vascular Medicine at the Academic Medical Center in Amsterdam, The Netherlands, said: "These patients accumulate cholesterol and experience premature cardiovascular events despite essentially 'normal' levels of LDL-C or despite having been placed on optimized statin therapy. The mechanism of action of statins does not directly target this pathophysiology in these patients with FPHA; as a result the benefit derived from statins will be at best indirect and incomplete. There is no treatment currently available which can directly restore normal HDL levels or normal levels of apoA-I. Despite receiving the best standard of care, many patients have a persistent and extremely high risk of adverse cardiovascular events and premature death, underscoring the unmet medical need for novel therapies. An orphan designation opens up a pathway for CER-001 to be a potential new therapeutic strategy to add to currently available lipid lowering agents to address this elevated risk."

Proof-of-mechanism data supporting the orphan designation application were obtained from the SAMBA Phase II efficacy and safety trial of CER-001 in patients with FPHA and were presented at the European Atherosclerosis Society in June 2014. The data from this trial showed that CER-001 reconstituted the RLT pathway in individuals who have defects in the natural HDL pathway and facilitated elimination of cholesterol from the body. Importantly, one month of treatment with 9 doses of CER-001, provided on top of optimized standard of care for LDL-c-lowering therapy, resulted in a statistically significant reduction in carotid artery Mean Vessel Wall Area, as measured by Magnetic Resonance Imaging (3T-MRI). CER-001 was well-tolerated.

Erik S.G. Stroes, MD, PhD, Professor of Medicine, Head of the Department of Vascular Medicine at the Academic Medical Center in Amsterdam, The Netherlands, and Principal Investigator of the SAMBA trial, commented, "We observed that CER-001 stimulated cholesterol removal on all essential levels of the reverse cholesterol transport pathway, eventually resulting in increased cholesterol excretion into the faeces. More importantly, this increased lipid removal was accompanied by marked reductions in the vessel wall dimensions of atherosclerotic arteries in patients with genetically-determined low HDL cholesterol. This is in line with the observed reduction in vessel wall dimension in patients following 24 weeks of bi-weekly CER-001 infusion in patients with Familial Hypercholesterolemia in the MODE study. The results of these two studies support the future use of CER-001 for chronic administration aiming to reduce the elevated cardiovascular risk in low HDL patients with a high unmet clinical need.

John F. Paolini, MD, PhD, FACC, Chief Medical Officer of Cerenis, said, "CER-001 has now been shown in Phase II trials to provide benefit to patients suffering from accelerated cardiovascular disease caused by genetic defects at both ends

of the spectrum of cholesterol homeostasis. The product has a good safety profile as observed in all studies performed thus far."

Jean-Louis Dasseux, PhD, MBA, and Chief Executive Officer of Cerenis, concluded: "CER-001 has the potential to be an important therapy not only for patients with rare diseases, such as FPHA, for which there is currently no other therapeutic option, but also for larger patient populations such as post-ACS patients. These two orphan drug designations from the EMA validate our approach and will enable us to accelerate the development of CER-001 and provide this new treatment option to patients."

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