Santhera and Cold Spring Harbor Laboratory to Investigate Lonodelestat (POL6014) in COVID-19-related Acute Respiratory Distress Syndrome (ARDS)

Pratteln, Switzerland, April 27, 2020 – Santhera Pharmaceuticals (SIX: SANN) has entered into a collaboration agreement with Cold Spring Harbor Laboratory (CSHL) to investigate the potential of lonodelestat (POL6014), a potent inhibitor of human neutrophil elastase (hNE), as a therapeutic intervention for COVID-19-related acute respiratory distress syndrome (ARDS).

Researchers at CSHL are part of a recently formed consortium of international non-clinical and clinical experts called the ‘NETwork to target neutrophils in COVID-19’. This NETwork will study the role of neutrophils and neutrophil extracellular traps (NETs) in the pathology of COVID-19 as well as hNE and other targets for intervention for the purpose of treating COVID-19 [1, 2].

NETs are macromolecular structures of DNA and proteins that neutrophils can expel, for example during severe inflammation. hNE is released by neutrophils when they form NETs. There are clear similarities between the clinical presentation of severe COVID-19 and diseases known to involve NETs, such as ARDS. On this basis, the NETwork has developed the rationale that excess NETs may play a major role in COVID-19 and that inhibition of hNE may be a therapeutic strategy to antagonize NETs in COVID-19 patients.

Santhera will provide lonodelestat and intellectual support for the scientists at CSHL who will conduct the non-clinical research program. The work is expected to further validate hNE as a target and shed light on this clinical stage compound as a potential agent also in COVID-19.

“There is a strong scientific rationale that inhibition of hNE may interrupt a neutrophil-driven inflammatory cascade that leads to ARDS in COVID-19 patients” explained Mikala Egeblad, PhD, Associate Professor at Cold Spring Harbor Laboratory, New York. “Based on previous work with lonodelestat in models of ARDS and acute lung injury, we were very encouraged about the potential of lonodelestat. Our own research in non-clinical models will start immediately and we are delighted that Santhera has offered their support in our efforts to find a potential novel treatment that could be investigated in patients with COVID-19.”

“We would like to thank CSHL and collaborating clinicians that have approached us to support their efforts to further explore and understand the role of hNE in relation to ARDS in COVID-19,” said Kristina Sjöblom Nygren, MD, Chief Medical Officer and Head of Development of Santhera.

About lonodelestat (POL6014)
Lonodelestat (previously known as POL6014) is a highly potent and selective peptide inhibitor of human neutrophil elastase (hNE). In preclinical studies lonodelestat was effective in animal models of neutrophil activation in lung tissue and of acute lung injury (ALI) [3, 4]. Lonodelestat is an investigational drug which completed Phase 1 single dose escalation studies in healthy volunteers and patients with cystic fibrosis (CF) and is currently investigated in a multiple ascending dose study in CF patients. Current data demonstrated that single dose inhalation of lonodelestat can lead to high drug concentrations within the lung, resulting in inhibition of hNE in sputum of patients, an enzyme associated with lung tissue inflammation [5].
About human neutrophil elastase (hNE), acute respiratory distress syndrome (ARDS) and COVID-19
Activated or necrotic neutrophils liberate human neutrophil elastase (hNE) in the lung which causes damage to the pulmonary microenvironment. hNE is also a critical enzyme in neutrophils and it is required for neutrophils to form NETs (neutrophil extracellular traps) as part of the body’s immune response. Under conditions of severe inflammation, neutrophils can expel NETs which can aggravate pulmonary inflammation and may contribute to the development of acute respiratory distress syndrome (ARDS). Inhibition of hNE activity may therefore display a dual action: it may block the toxicity of hNE in the lung tissue, prevent the formation of NETs and therefore may allow combating ARDS in patients with COVID-19.

About Cold Spring Harbor Laboratory
Founded in 1890, Cold Spring Harbor Laboratory has shaped contemporary biomedical research and education with programs in cancer, neuroscience, plant biology and quantitative biology. Home to eight Nobel Prize winners, the private, not-for-profit Laboratory is a National Cancer Institute designated Cancer Center employing 1,100 people including 600 scientists, students and technicians. The Meetings & Courses Program hosts more than 12,000 scientists from around the world each year on its campuses in Long Island and in Suzhou, China. The Laboratory’s education arm also includes an academic publishing house, a graduate school and programs for middle and high school students and teachers. For more information, visit www.cshl.edu

About the ‘NETwork to target neutrophils in COVID-19’
In the urgent battle to treat COVID-19 patients, a group of eleven international medical research organizations is investigating whether overactive immune cells – specifically neutrophils – via production of neutrophil extracellular traps (NETs) cause the most severe cases. The group, called the NETwork, includes Cold Spring Harbor Laboratory, the Feinstein Institutes for Medical Research, McGill University Health Centre, Weill Cornell Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Centre Hospitalier Universitaire de Nancy, University of Michigan, University of California, San Francisco, University of Texas MD Anderson Cancer Center, University of Utah School of Medicine, and Northwell Health [1].

About Santhera
Santhera Pharmaceuticals (SIX: SANN) is a Swiss specialty pharmaceutical company focused on the development and commercialization of innovative medicines for rare neuromuscular and pulmonary diseases with high unmet medical need. Santhera is building a Duchenne muscular dystrophy (DMD) product portfolio to treat patients irrespective of causative mutations, disease stage or age. A marketing
authorization application for Puldysa® (idebenone) is currently under review by the European Medicines Agency. Santhera has an option to license vamorolone, a first-in-class anti-inflammatory drug candidate with novel mode of action, currently investigated in a pivotal study in patients with DMD to replace standard corticosteroids. The clinical stage pipeline also includes lonodelestat (POL6014) to treat cystic fibrosis (CF) and other neutrophilic pulmonary diseases, as well as omigapil and an exploratory gene therapy approach targeting congenital muscular dystrophies. Santhera out-licensed ex-North American rights to its first approved product, Raxone® (idebenone), for the treatment of Leber’s hereditary optic neuropathy (LHON) to Chiesi Group. For further information, please visit www.santhera.com.

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