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Santhera Announces Publication of Phase I Clinical Data with POL6014 in Journal of Cystic Fibrosis

Pratteln, Switzerland, September 10, 2019 – Santhera Pharmaceuticals (SIX: SANN) announces the online publication of Phase I data with its human neutrophil elastase (hNE) inhibitor POL6014 in the *Journal of Cystic Fibrosis* [1]. These data demonstrated that single dose inhalation of POL6014 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.

POL6014 is an innovative, potent and selective inhibitor of human neutrophil elastase (hNE) in clinical development for the treatment of cystic fibrosis (CF). In CF, excessive release of enzymes like hNE accelerates lung tissue inflammation and damage, leading to an incapacitating and progressive decline in pulmonary function. The two double-blind, placebo-controlled studies now published evaluated the safety, tolerability and pharmacokinetics of single ascending doses of inhaled POL6014 in healthy volunteers and CF patients.

In the two studies, a total of 48 healthy volunteers and 24 patients with CF were randomly allocated to various doses of POL6014 or placebo. Healthy volunteers received POL6014 at doses ranging from 20 mg to 960 mg; CF patients were dosed at 80 mg, 160 mg or 320 mg. Shortly after inhalation of POL6014, a clear reduction of active hNE in sputum was observed at all doses tested in patients with CF. Furthermore, levels of POL6014 in sputum for these patients appeared to be up to 1000-fold higher compared to plasma levels at 3 and 24 hours post inhalation, indicating high exposure to POL6014 in the lung, with very limited systemic drug exposure. Doses of up to 480 mg POL6014 were assessed as safe and well tolerated.

“We are encouraged by these early data in healthy volunteers and patients with cystic fibrosis. POL6014 brings new promise to current CF treatment which, despite recent developments, is still lacking a solution to lung tissue inflammation, a cause of pulmonary exacerbations. In addition, inhalation of POL6014 shows a strong advantage over the oral route as it delivers the drug directly to the lung with a low systemic burden,” said **Kristina Sjöblom Nygren, MD, Chief Medical Officer and Head of Development** at Santhera. “As an innovative inhibitor of human neutrophil elastase, POL6014 could have potential in a range of other pulmonary diseases.”

On the basis of the successful Phase I data, Santhera is currently conducting a Phase Ib/IIa MAD (multiple ascending dose) study designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of orally inhaled multiple doses of POL6014 in patients with CF.

Santhera obtained the worldwide, exclusive rights from Polyphor AG to develop and commercialize POL6014 in CF and other pulmonary diseases. The Cystic Fibrosis Foundation (CFF) is providing funding support for the conduct of the safety trials with POL6014.

Reference:
[1] Barth P. et al (2019). Single dose escalation studies with inhaled POL6014, a potent novel selective reversible inhibitor of human neutrophil elastase, in healthy volunteers and subjects with cystic fibrosis. Journal of cystic fibrosis 2019. DOI: https://doi.org/10.1016/j.jcf.2019.08.020

About POL6014

POL6014 is a highly potent and selective inhibitor of human neutrophil elastase (hNE) and was shown to reach high concentrations in the lung when administered by inhalation via an optimized eFlow® nebulizer (PARI Pharma GmbH). POL6014 may also show therapeutic benefit for a range of neutrophilic pulmonary diseases with high medical need such as non-cystic fibrosis bronchiectasis (NCFB), alpha-1 antitrypsin deficiency (AATD) or primary ciliary dyskinesia (PCD). POL6014 has EU orphan drug designations (ODD) for the treatment of AATD, PCD and CF.

About cystic fibrosis and human neutrophil elastase (hNE)

Cystic fibrosis (CF) is a rare, hereditary, life-threatening, progressive disease affecting approximately 70,000 patients in the U.S. and Europe and is characterized by persistent lung infection and chronic inflammation thereby limiting the ability to breathe over time. Activated or necrotic neutrophils liberate human neutrophil elastase (hNE) in the lung that causes damage to structural, cellular and soluble components of the pulmonary microenvironment. High levels of hNE play a central role in the pathophysiology of CF and correlate with disease severity as measured by functional lung parameters. Inhibition of hNE is expected to reduce airway inflammation and slow the damage to lung tissue and may help to improve the overall quality of life for individuals with CF.

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 leading Duchenne muscular dystrophy (DMD) franchise. 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 dissociative steroid currently investigated in a pivotal study in patients with DMD to replace standard corticosteroids. The clinical stage pipeline also includes 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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