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Santhera Signs Agreements in Gene Therapy Research for Congenital Muscular Dystrophy with Rutgers University

Pratteln, Switzerland, May 06, 2020 – Santhera Pharmaceuticals (SIX: SANN) announces the signing of two agreements with Rutgers, The State University of New Jersey as part of its program to advance gene therapy research for the treatment of LAMA2-deficient congenital muscular dystrophy (LAMA2 MD or MDC1A). Under the agreements, Santhera gains rights to intellectual property developed at Rutgers on certain gene constructs that will be further studied under a collaboration agreement.

Santhera has entered into a license agreement with Rutgers, The State University of New Jersey and a collaboration with Prof. Peter Yurchenco, a pioneer in a novel gene therapy approach for the treatment of LAMA2 MD. These agreements complement the ongoing collaboration of Santhera with Prof. Markus Rüegg from the Biozentrum of the University of Basel [1]. Previous collaborative work by Prof. Rüegg and Prof. Yurchenco has established the potential of this approach in animal models.

The novel gene therapy strategy developed by these leading experts uses two linker proteins that are composed of domains derived from extracellular matrix proteins agrin, laminin and nidogen [2-5]. In animal models for LAMA2 MD, this approach has led to restoration of muscle fiber basement membranes, recovery of muscle force and size, increased overall body weight and markedly prolonged survival thus demonstrating strong evidence for disease modifying potential [2].

The coordinated work of both collaborations will further advance Santhera´s effort to bring this innovative gene therapy approach to patients with LAMA2 MD.

“Gene replacement is a promising therapeutic option for the treatment of LAMA2 MD,” said **Peter D. Yurchenco, MD, PhD, Professor at Rutgers Robert Wood Johnson Medical School, USA**. “We have been working on continuously optimizing linker proteins engineered from extracellular matrix proteins which will aid in advancing such gene therapy approach towards clinical use.”

“Santhera is excited to extend its collaborative network for this therapeutic approach, now including experts from Rutgers University,” added **Kristina Sjöblom Nygren, MD, Chief Medical Officer and Head of Development of Santhera**. “This will add value to our gene therapy program for LAMA2 MD and complements the work already under way with the Biozentrum at the University of Basel, which was awarded a grant by Innosuisse in 2019. Both of our collaboration partners have pioneered this field and will work closely with Santhera, clinical experts and the patient community to establish the best way to bring this approach to clinical use.”

About LAMA2 MD (CMD Type 1A or MDC1A) and Emerging Therapy Approaches

Congenital muscular dystrophies (CMDs) are inherited neuromuscular diseases characterized by early-onset weakness and hypotonia alongside associated dystrophic findings in muscle biopsy. Progressive muscle weakness, joint contractures and respiratory insufficiency characterize most CMDs. Laminins are proteins of the extracellular matrix that help maintain muscle fiber stability by binding to other proteins. LAMA2-related muscular dystrophy (LAMA2 MD, also called MDC1A), is one of the most common forms of CMD. It is caused by mutations in the LAMA2 gene encoding the alpha2 subunit of laminin-211. Most LAMA2 MD patients show complete absence of laminin-alpha 2, are hypotonic (floppy) at birth, fail to ambulate, and succumb to respiratory complications.

Previous work has demonstrated that two linker proteins, engineered with domains derived from the extracellular matrix proteins agrin, laminin and nidogen, could compensate for the lack of laminin-alpha2 and restore the muscle basement membrane [2-5]. Through simultaneous expression of artificial linkers ("SEAL"), this gene therapy approach aims to overcome the genetic defect by substituting laminin-alpha2 deficiency with small linker proteins containing necessary binding domains to re-establish muscle fiber integrity. In a transgenic mouse model, the linker expression increased the lifespan of LAMA2-deficient mice 5-fold to a median of 81 weeks compared to 15.5 weeks in the disease model without the therapeutic linker expression [2]. Recently, it was demonstrated that such linker constructs could be applied by standard adeno-associated virus (AAV) vectors [6, 7]. First results using the AAV technology have been presented by Prof Rüegg [8].

References

[1] Santhera press release on gene collaboration with Biozentrum Basel (May 21, 2019), accessible here
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[8] Reinhard, J. et al. (2019) Neuromuscular Disorders, Volume 29, S164

About Rutgers, The State University of New Jersey

Rutgers, The State University of New Jersey, is a leading national research university and the state of New Jersey's preeminent, comprehensive public institution of higher education. Established in 1766, the university is the eighth-oldest higher education institution in the United States. More than 71,000 students and 23,000 faculty and staff learn, work and serve the public at Rutgers University-New Brunswick, Rutgers University-Newark, Rutgers University-Camden, and Rutgers Biomedical and Health Sciences.

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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