CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN

BIH Berlin Institute of Health @Charité

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SpliSense
Making Sense of Splicing

Short profile

Name: Splisense

Medical field	Pulmonary diseases
Product type	Antisense oligonucleotide treatment development
Growth stage	Development
Team	Profile of Executive Team Members: Gili Hart PhD – CEO. A biotech executive with extensive experience in global drug development from pre-clinical through successful Phase 3 trials. Former CEO of Mitoconix Bio and OPKO Biologics. Batsheva Kerem PhD -Co-founder & CSO. Prof. in the Hebrew University of Jerusalem. 30 years of leading research in CF genetics starting with the discovery of the CFTR gene. Prof. Eitan Kerem MD -CMO. A pulmonologist; Head of the Pediatric Pulmonology Unit of HMC Jerusalem, Chairman of the Israeli CF Foundation CAB. Oren Gez, MBA- CBO. An experienced and appreciated financer with over 18 years of experience in the global capital market working at local and international investment banking Efrat Ozeri Galai PhD, MBA- VP Research Leading the research team overseeing early discovery, screening for lead drug candidates and preclinical pharmacology. Experienced in human genetics specifically in pulmonary diseases and RNA modulation for over 15 years. Splisense has a trong team leading the research and development with a track record in the development of ASO drugs from discovery to clinical studies and a team of researchers performing in-house experiments in established methods.

Description of product:

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ASOs are small synthetic nucleic acid molecules, able to bind specific sequences within target RNA molecules. ASOs are used for a variety of applications, i.e. reducing RNA levels, inducing protein restoration and the generation of modified proteins.
This project is focusing on two ASO products:
1. SPL5B is an ASO drug reducing MUC5B mucin for the treatment of Idiopathic Pulmonary Fibrosis (IPF). Excess of MUC5B in IPF was shown to cause bronchiolar plugging and impair mucosal host defense. The reduction of MUC5B levels improves Muco-Ciliary Clearance (MCC), reducing infection and inflammation and potentially prevent further progression of the fibrosis and decline in lung function.
2. SPL5AC is an ASO drug targeting MUC5AC mucin for the treatment of Muco-obstruction diseases (Asthma, COPD and NCFB). In muco-obstructive diseases MUC5AC levels are increased leading to plugging of the airways. Reduction of MUC5AC levels will allow mucus lung clearance improving the patient's lung function and quality of life.

Desired project goal: *Please also elaborate on the primary outcome*

Splisense completed lead ASO selection for the reduction of MUC5B and MUC5AC in a screening system followed by a PoC in primary respiratory epithelial cells and a WT mice. Splisense is sampling bronchial primary epithelial cells from patients to provide a PoC for the ASOs effect in patient derived cells. Splisense have submitted a patent that protects the concept of reducing MUC5B and MUC5AC levels in pulmonary diseases using ASOs. A specific list of ASO sequences is also protected in this patent. The current proposed study will confirm SPL5B and SPL5AC effects in an applicable disease mice models. This induced disease model will allow to test the effect of the ASO candidates a preventive treatment as well as an interventive treatment that will be given at different stages of disease.

Desired project type: *Please also elaborate on the following points, if applicable: population, intervention, study design etc.*

Type of project: Contract research

Splisense already selected and validated lead ASO (SPL5B and SPL5AC) that were found to efficiently reduce the levels of MUC5B or MUC5AC in cellular as well as initial in vivo systems. The experiment will be performed at the Charite as well as at Splisense.

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We are interested in working with prof. Marcus Mall from the Charite. In the last years prof. Mall established a novel genetic mice model that is based on inhibiting the Nedd4 gene. This mice model recapitulates the phenotype of the lung fibrosis seen in IPF patients including the overexpression of MUC5B. Other common mice models used to model lung fibrosis do not show all the fibrotic characteristics of IPF and do not show MUC5B over expression and thus cannot be used for a validation for SPL5B effect in a disease mice model. Most importantly, the increase of MUC5B in the Nedd4 mice model created by Prof. Mall is in correlation to fibrosis progression in the mice. Thus, this model is an adequate model system to validate the activity of SPL5B in a disease mice model. In addition, Prof. Mall published several peer reviewed manuscripts on genetic mouse models impairing the MCC that uniquely show mucus obstruction and allergen hyperresponsiveness as typical in muco-obstructive diseases.

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