SpliSense Reports Positive Results from Phase 2 Study of SPL84 in Cystic Fibrosis

Results mark first evidence of potential clinical benefit of antisense oligonucleotide therapy in a pulmonary disease

Encouraging safety profile with no identified safety signals to date

Improvement in lung function observed in up to 70% of participants treated with SPL84

The readout validates SpliSense' platform, supporting advancement of the Company's additional pulmonary programs, for muco-obstructive diseases and idiopathic pulmonary fibrosis, into the clinic in early 2026

JERUSALEM, ISRAEL – September 3, 2025 – SpliSense, a clinical-stage biotechnology company developing transformative RNA-based therapies for pulmonary diseases, today announced positive results from SPL84-002, its ongoing global Phase 2 study evaluating SPL84, the Company's lead antisense oligonucleotide (ASO), for the treatment of people with cystic fibrosis (CF) carrying the 3849+10 kilobase (Kb) C->T splicing mutation in the CFTR gene.

The SPL84-002 study is ongoing in a number of centers in the US and Europe. The data, based on the complete evaluation of Cohorts 1 and 2 (n= 12) of the study, demonstrated:

- **Safety** – No safety signals or trends of concern were identified to date among participants. No treatment related Severe Adverse Events (SAEs) were observed.
- **Efficacy** – Improvement in lung function (ppFEV1) was observed in up to 70% of SPL84-treated participants. The estimated mean absolute change in ppFEV1 for SPL84 compared with placebo was 10.

"The SPL84-002 data mark an important milestone, not only for SpliSense but for the entire field of pulmonary ASO therapeutics," said Gili Hart, PhD, CEO of SpliSense. "They represent the first time an antisense oligonucleotide administered directly to the lungs by inhalation has demonstrated potential efficacy in treating a pulmonary disease."

"The favorable safety and efficacy profile emerging from our SPL84 program provides clinical validation of our ASO platform. Importantly, this readout supports advancement of our additional pipeline programs – SPL5AC for muco-obstructive diseases such as Chronic Obstructive Pulmonary Disease (COPD), asthma, Non-Cystic Fibrosis Bronchiectasis (NCFB) and CF, and SPL5B for Idiopathic Pulmonary Fibrosis (IPF) – with first-in-human studies expected to begin in early 2026. We remain focused on our mission of developing new treatment options for people suffering from serious pulmonary conditions," added Dr. Hart.

About the SPL84-002 Study

SPL84-002 is a global randomized, double-blind, placebo-controlled Phase 2 trial evaluating the safety, tolerability, and efficacy of SPL84 in people with CF carrying the 3849+10 Kb C->T mutation. The study was designed in three sequential cohorts assessing different dose levels of inhaled SPL84 (25, 50, 100mg), administered once weekly for 9 weeks. The study endpoints are based on safety assessment and efficacy, i.e. change in lung function as measured by percent predicted FEV1, with secondary endpoints assessing pharmacokinetics and other measures. SpliSense is finalizing enrollment for the third cohort, with the goal of sharing a full data set with the CF community. More information in ClinicalTrials.gov

About SPL84

SPL84 is an inhaled antisense oligonucleotide (ASO) designed to correct the splicing defect caused by the 3849+10 Kb C->T mutation in the CFTR gene. By binding to the mutated CFTR RNA, SPL84 enables the production of a functional CFTR protein. In preclinical studies, SPL84 fully restored CFTR activity in gold-standard pharmacological models. SPL84 is delivered via inhalation, on a weekly basis to directly target the lungs, the primary site of CF pathology. SPL84 has been granted Orphan Drug and Fast Track designations by the U.S. Food and Drug Administration (FDA) for the treatment of people with CF carrying the 3849+10 Kb C->T mutation. Fast Track designation is intended to expedite development and review of therapies for serious conditions with unmet medical need. This designation underscores the potential of SPL84 to deliver meaningful clinical benefit.

About SpliSense

SpliSense is a biotechnology company focused on the development of RNA-based treatments for pulmonary diseases. The Company's pioneering ASO platform is designed to target the root cause of pulmonary disease by restoring or reducing protein function. SpliSense is advancing a pipeline of programs addressing pulmonary indications, including muco-obstructive diseases (COPD, asthma, NCFB) and idiopathic pulmonary fibrosis (IPF) on top of CF. For more information, please visit: www.splisense.com

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