

## Single Dose Escalation Study to Evaluate Safety of Nasal Administration of CFTR001 Gene Transfer Vector to Subjects with Cystic Fibrosis

### NON-TECHNICAL ABSTRACT

Cystic Fibrosis (CF) is a serious, inherited disease that primarily results in lung disease. Lack of function of a protein called Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) protein is responsible for this disease. People with CF can be treated with a variety of drugs to improve their quality of life, but the disease still results in premature death. Doctors feel that transferring a fully functional CFTR gene into the airway cells of people with CF will “correct” the cause of the disease. This study is a first step in determining if a new gene transfer system may offer a potential treatment. Unlike most previous gene transfer clinical trials, this trial uses a gene transfer system that is not based upon a virus. This trial uses a non-viral vector system that compacts DNA into very small particles and is expected to provide benefits over gene transfer systems previously tested in humans. The first step of the initial proposed clinical test of this gene transfer system is to deliver CFTR DNA to the cells lining the nose of patients with cystic fibrosis. The primary goal of the study is to investigate the safety and tolerability of administering these DNA complexes to the cells lining the nose. The cells of the nose are very similar to those that would need to be treated in the lung to “correct” the disease. Particular attention will be paid in this clinical study to possible side effects of the gene transfer system. The secondary goal of the study is to determine whether this mode of gene transfer is able to deliver the normal CFTR gene to the cells lining the nose. This will be determined by various tests that will be performed to measure the extent of CFTR DNA delivery. Only adult patients with cystic fibrosis will be enrolled in this study after certain screening tests are performed to determine their suitability for the study. Those who qualify and agree to be part of the study will be treated with a single dose of DNA complex (1/2 teaspoonful) in one nostril and placebo fluid (1/2 teaspoonful) in the other nostril. Neither the investigators nor the patients will know which nostril received which treatment. Subjects will be followed by serial physical examinations and by a variety of tests measuring safety parameters as well as gene transfer parameters. These tests will be performed for at least 15 days after dosing, or until all tests return to the subject’s original values, whichever comes last. The initial dose will be 0.080 mg DNA. If no significant toxicity is observed, subsequent subjects may have the dosage amount increased according to the protocol. Doses will escalate by increments until the maximum dose of 8 mg is reached. The trial will be concluded when the highest dose planned has been administered, or when mild or moderate adverse events have occurred in at least three subjects at a lower dose level (this dose then becomes the maximum tolerated dose). If this study shows the DNA complexes delivering the CFTR gene to be safe, future studies will explore the use of this potential therapy in the lungs.