

## **DESCRIPTION OF PROPOSED RESEARCH IN NON-TECHNICAL LANGUAGE**

Cystic fibrosis (CF), the most common inherited disease in North America, is caused by problems in a gene known as “CFTR”. Normal functioning of this gene is required for the movement of water and salt across airway cells. Persons with this disease have abnormal mucous in their lungs which builds up over time and leads gradually, over many years, to serious lung disease. Attempts are being made to replace the missing gene function using special gene carriers, or vectors, which carry corrected genes into cells. The types of vectors tested in patients so far have a temporary effect and therefore may not be ideal for treating CF lung disease. Targeted Genetics Corporation has developed a different type of vector, called tgAAVCF, which is based on a virus, AAV. Many people have been infected by the naturally occurring type of AAV without realizing it, as AAV does not cause disease. AAV is able to maintain its DNA for long periods of time in the cells that it enters. This vector may slow or stop lung destruction seen in cystic fibrosis patients. Tests of AAV vectors carrying the CFTR gene have shown it to be biologically active in cells in the test tube and in animals. This vector has been given to 60 patients without serious side effects.

One of the many complications of CF is ongoing lung infection, inflammation and destruction. The study described herein proposes to administer tgAAVCF in repeat administrations (3 doses), to the lungs of patients with CF. Measurements will be taken to determine whether the vector is present and active in the lung. Cystic fibrosis patients, greater than 12 years of age, will be administered either active drug or placebo, via inhalation (inhale and exhale through a mouthpiece, with a nasal clip used to ensure that vector is not exhaled through the nose). Bronchoscopies will be performed on the first two cohorts only; age restriction on these two cohorts is  $\geq 15$  years of age, to measure vector activity in the lung. Results from this trial will be used to design endpoints for future studies.