

2.0 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 progressively leads to serious lung disease and death. Attempts are being made to replace the missing gene function using special gene carriers, or vectors, which carry corrected genes into cells. Targeted Genetics Corporation has developed a 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 90 patients without serious side effects.

Targeted Genetics Corporation recently completed a study of cystic fibrosis in which 20 study subjects received tgAAVCF via inhalation (inhale and exhale through a mouthpiece, with a nasal clip used to ensure that vector is not exhaled through the nose), and 17 subjects received placebo (inactive study drug) once every 30 days for three doses. In this study, subjects who received tgAAVCF had no more side effects than those who received placebo, but their lung function seemed to improve slightly. In order to confirm this trend in improvement, Targeted Genetics Corporation plans to do another study with more study subjects. In this trial, 100 subjects 12 years of age and older with CF and mild lung disease will be randomly assigned (like the flip of a coin) to either tgAAVCF or placebo every 30 days via inhalation for two doses. Subjects will have breathing tests to measure how well their lungs work every two weeks during the study. The study will be overseen by a panel of experts who will recommend that the study be stopped if safety issues arise.