

## M-1 – (2) Non-Technical Abstract

Age-Related Macular Degeneration (AMD) is, together with Diabetic Retinopathy, the most common cause of vision loss among adults in the US and other developed countries. In the US, at least 1.7 million people have impaired vision due to AMD. Every year, more than 165,000 people contract AMD and 16,000 go blind from it,<sup>1</sup> predominantly from a rapidly progressing form of the disease called “wet” AMD. In wet AMD, severe vision loss is caused by abnormal blood vessel growth in or around the retina and subsequent vessel leakage. In functional terms, people with wet AMD are unable to read, recognize faces or drive, and the disease often leads to legal blindness. The onset of severe visual changes in wet AMD can occur suddenly. More than 400,000 Americans are currently affected by this form of the disease, and the incidence is rising rapidly due to the aging of the population.<sup>2</sup> Therefore, the serious consequences of this disease along with the limited treatment options and their effectiveness make this a very good candidate for a gene transfer treatment approach.

This vector is a modified adenovirus vector that has been designed so that it is very unlikely to reproduce and cause viral disease. The vector is designed to contain and transport the gene for human pigment epithelium-derived factor (PEDF) into relevant cells in the eye. PEDF is one of the most potent known inhibitors of blood vessel growth found in humans. As the eye creates a natural barrier between itself and surrounding tissues, it is unlikely that Ad<sub>GV</sub>PEDF.11D would affect tissues other than the eye. Administration of Ad<sub>GV</sub>PEDF.11D directly into the eye provides a convenient means of delivering PEDF to the cells of the eye and is likely to result in a longer duration of effect as compared to administration of PEDF as a protein alone.

In three mouse models of diseases like AMD, significant inhibition (up to 85%) of new blood vessel growth was demonstrated with doses of Ad<sub>GV</sub>PEDF ranging from  $1 \times 10^8$  to  $1 \times 10^9$  pu. In safety studies performed in monkeys, these doses were well tolerated with no toxicity observed at a dose of  $1 \times 10^8$  pu and only minimal and reversible inflammatory responses at  $1 \times 10^9$  pu. Higher doses showed more severe inflammatory responses.

The proposed clinical investigation is an initial study of the safety of gradually increasing doses of Ad<sub>GV</sub>PEDF.11D injected into the eye. In addition, we will look for any potential effect this compound has on vision and other eye examinations. Study subjects will be age 50 or over and have severe wet AMD in at least one eye.

1. Department of Health and Human Services, National Eye Institute, Age-Related Macular Degeneration. Status of Research, Harold Varmus, March 1997.
2. Seddon JM. Epidemiology of age-related macular degeneration. In: *Retina*, 3<sup>rd</sup> Ed, Vol 2, pp. 1039-1050. Edited by SJ Ryan. Singapore: Mosby. 2001.