



Compochiaro et al., "Adenoviral Vector-Delivered Pigment Epithelium-Derived Factor for Neovascular Age-Related Macular Degeneration: Results of a Phase I Study," February 2006

AdPEDF—Therapeutic Protein for Ocular Diseases A Differentiated, First-in-Class, Clinical Stage Treatment/Cure with Broad Applications

Strong Human Safety Database—Compelling Activity Data

AdPEDF is a product candidate designed to deliver sustained levels of the human Pigment Epithelium-Derived Factor (PEDF) protein in the eye. PEDF is the eye's key natural regulator of normal blood vessel growth and neuronal function and has been demonstrated to have dual potent antiangiogenic and neuroprotective properties. Several laboratories have shown that PEDF protein levels in eyes of patients with wet AMD (the leading cause of blindness in people over 50 years of age) are significantly lower than in normal eyes.

Broad Activity - PEDF, due to its dual activity has demonstrated potential to treat additional ocular diseases, including diabetic retinopathy (5.3 million patients US), diabetic macula edema (2.5 million patients), dry AMD (13.5 million patients US), glaucoma (67 million patients), and retinitis pigmentosa.

Unmet Need and Product Differentiation – Existing wet AMD therapies only temporarily slow down vision loss, resulting in continued treatment dissatisfaction. Frequency of administration is also a significant problem. AdPEDF has a unique mechanism of action which has the potential to differentiate the product through (i) the ability to halt or reverse the natural progression of the underlying disease (ii) synergistic activity with existing therapy, and (iii) a significantly reduced dosing paradigm.

Wet AMD Product	Antiangiogenic		Regression of Lesions	Anti-permeability	Neuro-protective	Delivery
	VEGF	FGF& Other				
AdPEDF (GenVec)	✓	✓	✓	✓	✓	Local
Visudyne® (QLT/Novartis)				✓		Systemic/Laser
Macugen™ (Eyeteck/Pfizer)	✓			✓		Local
Retaane™ (Alcon)		✓				Periocular
Lucentis™ (Genentech/Novartis)	✓			✓		Local
Squalamine (Genaera)	✓	✓	✓			Systemic
VEGF Trap (Regeneron/Aventis)	✓			✓		Systemic
Cand 5 (Acuity Pharmaceuticals)	✓			✓		Systemic

Safety and Activity - AdPEDF is a Phase I/II product that has consistently demonstrated efficacy when tested in multiple animal models of ocular neovascularization/abnormal anti-angiogenesis. In wet AMD specifically, AdPEDF has been demonstrated to rapidly elevate the intraocular PEDF protein levels in the eye, to inhibit new blood vessel growth, and cause abnormal blood vessels to regress, while protecting the photoreceptors, the vision sensing cells of the eye.

The product has now been studied in two clinical trials. In the first trial, it was shown to be safe and well tolerated in severe wet AMD patients. Of the 28 patients tested with advanced disease, the majority (~70%) had stable or improved visual acuity at 3 weeks and 12 weeks after a single administration of AdPEDF, suggesting the need for a less frequent dosing regimen. Some patients also had improved retinal appearance despite the advanced stage of disease in patients studied. Data from the second trial, in less severe disease, is being collected.