SAPHTx: Injectable Hydrogel for Treating Neovascular Ocular Diseases

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Technology: Age-related macular degeneration (AMD) and diabetic retinopathy (DR) are leading causes of blindness in the world. Debilitating vision loss causes a significant socio-economic burden on afflicted geriatric, diabetic, at-risk youth, and under-represented populations. Proliferation of maladaptive blood vessels (angiogenesis) on the retina characterize these posterior segment neovascular diseases of the eye. Current treatments focus on inhibitors of angiogenesis (monoclonal antibodies or small molecule therapeutics). These treatments are expensive and require monthly intraocular dosing, resulting in patient discomfort and poor compliance. The proposed solution is a cost-effective, long lasting, and injectable hydrogel called **SAPHTx** (**Figure 1**). This hydrogel is composed exclusively of naturally occurring amino acids engineered to include an anti-angiogenic domain from the human plasminogen Kringle 5 (Kr5). We have further engineered the hydrogel to slowly dissociate over a 6-month period for long-term disease management. This will drastically reduce injection frequency, provide long-term attenuation of angiogenesis, improve patient compliance, and reduce the likelihood of side effects, such as endophthalmitis. Through interviews with advisors and key opinion leaders in ophthalmology, we have elected to pursue an initial target market of patients suffering from wet AMD. Depending on results of Phase II and Phase III trials, we will strategically expand to DR.

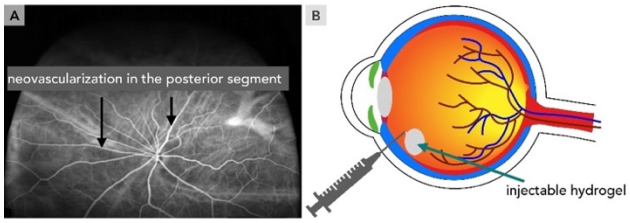

Figure 1. Neovascular disease in the eye and schematic of proposed solution. (A) Aberrant vascularization on the retina as a result of wet-AMD and DR is the leading cause of blindness for older individuals. (B) **SAPHTx** aims to treat excessive angiogenesis and reduce dosing frequency to semi-annually.

Market: AMD is a leading cause for vision loss in Americans aged 60 and above, and it is categorized into two types: dry and wet. Dry AMD occurs when light-sensitive cells in the macula break down, causing a gradual loss of central vision. Conversely, wet AMD occurs when abnormal blood vessels, which tend to be leaky, grow in the choroid layer underneath the macula, damaging the retina and degrading vision. In addition to age, the risk for AMD is increased for people who smoke, are overweight, or have a family history of AMD. More than 7 million AMD patients exist across 7 major markets: US, UK, Spain, France, Italy, Germany, and Japan. The total market for AMD in these countries is estimated to be greater than $5 billion and is expected to reach $11.5 billion by 2026 with an 8.9% compound annual growth rate (CAGR). Key players in the market include Lucentis®, Eylea®, Avastin®, Visudyne®, and others in clinical trials (e.g. Novartis' brolucizumab and Allergan's abicipar). The current standard of care is monthly intraocular injections of inhibitors of vascular endothelial growth factor (VEGF), which are costly (~$36,000-50,000 per year), cause patient discomfort, and increased risk of endophthalmitis. Alternative invasive laser procedures to ablate vessels are not preferred due to scarring, disease recurrence, invasiveness, and significantly higher inpatient costs.

Commercialization Strategy:

STEP 1. Market Research:

(i) Initial **SAPHTx** GMP manufacturing, (ii) establishing preclinical efficacy in a rabbit model prior to large non-human primate studies, iii) customer discovery and development of a business model canvas through NSF I-Corps program, and (iv) reaching out to pharmaceutical companies for potential partnerships.

STEP 2. Towards Investigational New Drug (IND):

Funding required to achieve a successful IND filing is estimated at $3-4 million. These funds will be required for remaining CMC and ADMET studies. These have been established in consultation with AmbioPharm, Inc. (CMC) and Absorption Systems, Inc. (CRO). This will aid in GMP manufacture feasibility, mechanism of action, and animal efficacy.

STEP 3. Clinical Trials:

We have spoken to 3 clinical CROs for guidance. Based on initial quotes we expect a 15-20 patient Phase I ($3- 5 million) and 50-100 patient Phase II ($8-10 million). Primary outcomes for Phase I would be safety in a dose escalation study in a patient population with wet AMD. Improvement in visual acuity and optical coherence tomography (OCT) measured retinal angiogenesis will be evaluated with dosing ranging from 0.4, 4, and 40 mg/mL in 100 μL intraocular boluses. An optimized dosing schedule will be used in a Phase II non-inferiority study compared to standard-of-care aflibercept. Phase II endpoints will be improvement vs. standard of care as measured by visual acuity measure and OCT. Dosing of the peptide will be provided at a frequency recommended by the ophthalmologist at symptomatic/physiologic endpoints identical to aflibercept. Clinical trials are expected to require a total of $11-15 million to complete based on quotes from clinical CROs.

We have begun consultation with investors, clinicians, and pharmaceutical companies on this technology platform for possible exits. The recommended course of action is a possible Phase I/II exit with a licensing deal with a pharmaceutical partner for initiation and completion of Phase III clinical trials (>$50M).