Usher 1F Collaborative Strategic Plan

Landscape Analysis

- Description of the Need: focused on finding an effective treatment for blindness associated with Usher Syndrome type 1F
- What is not currently happening? Why?: While cochlear implants have made it possible for deaf individuals to hear, there is no treatment to restore vision. There has not been a significant investment by big pharma/biotech in gene therapy because the return on investment is low.
- Consequences: (source: *Clinical Ophthalmology – Dovepress, published July 1, 2021*)
    - Cost to individual –increased risk of development of mental health conditions including depression and anxiety (1.6-2.8 times more likely to develop depression). Individuals who want/need to live independently face higher cost of living as they must live in urban setting with reliable public transport. Social isolation.
    - Cost to family – psychosocial problems faced by family members who worry that their child will be teased. Sibling guilt.
    - Cost to society – (Usher Syndrome aggregate: health system, productivity, caregiver, deadweight loss, loss of wellbeing, other) $371 million - $880 million in 2019.
- Who is attempting to address? How? Usher 1F Collaborative funds medical research to find an effective treatment to save or restore the vision of those with Usher Syndrome type 1F. The Collaborative only funds research that has a clear path to the clinic.
- Benefits of a solution: With an effective treatment, the vision loss will be halted and/or restored, changing the trajectory of the lives of those with Usher 1F. Additionally, the gene therapy knowledge can be applied to other inherited retinal diseases so a treatment can be found for those as well.

Disease Description

- What is it? Usher Syndrome is the leading cause of inherited deaf-blindness. Type 1 is the most severe, with individuals born profoundly deaf and vision loss beginning in childhood and progressing through adulthood
- Why does it occur? Usher Syndrome type 1F is a specific genetic mutation of a protein, protocadherin 15 (PCDH15). It is most commonly found among those of Ashkenazi Jewish descent.
- What is currently known/understood?
    - 2001 the Usher 1F gene was discovered
    - 2013 Usher 1F Collaborative formed, resulting in research strides.
    - Animal models (mouse and zebrafish) created leading to gene, drug and stem cell therapy developments
    - RUSH1F launched – natural history study in collaboration with Foundation Fighting Blindness
    - Most promising research in gene therapy, in which we are 3-5 years from a clinical trial
- What is yet to be known/discovered? The Ush1F gene (PCDH15) is too large to fit on one viral vector for gene therapy delivery. Thus, researchers are testing dual vector delivery, in addition to creating a mini gene that can fit on one vector. Additionally, RUSH1F, the natural history study, is

providing valuable information about the progression of the disease that will be critical for clinical trials.

The Market (Patient Population and Families)

- Who needs a solution? Individuals living with Usher 1F are in a race against time as their field of vision progressively deteriorates. The families are also impacted as outlined above.
- Demographics of known market? Usher 1F impacts patients worldwide, and patients are born with the disease. Sixty percent of Usher 1F patients are of Ashkenazi Jewish descent.
- Unidentified markets? Due to the privacy of patients, we rely on individuals to self-identify to Usher 1F Collaborative. We have partnered with the Broad Institute in order to get a better understanding of how many patients worldwide live with Usher 1F.

Value Proposition

- What do you propose to do? Usher 1F Collaborative funds research in order to find an effective treatment for the vision loss associated with Usher Syndrome type 1F. We will do this by funding labs and leveraging research in gene and drug therapies.
- Over what period of time? Usher 1F Collaborative was established in 2013 and since then has invested $8 million in research. At least one gene therapy is 2-4 years from clinical trial.
- Why are you uniquely positioned to do so? Usher 1F Collaborative has brought together top research teams worldwide; families around the world, including the U.S., Australia, Canada, France, Brazil and Israel, affected by this devastating disease; a distinguished board of directors comprised of 11 individuals who cumulatively possess over 100 years of experience in drug research funding and execution, and over 200 years of experience in effective non-profit management; as well as an esteemed scientific advisory board; and generous funders wishing to be part of the cure. Due to the diverse knowledge of its board, Usher 1F Collaborative is unique in its ability to discern valuable research initiatives, and nimble enough to change course when necessary.