SONTAG INNOVATION FUND

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April 24, 2024

Dear CIRM Application Review Subcommittee:

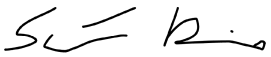
This Sontag Innovation Fund (SIF) is writing in support of Grant # **TRAN1-16065** (Funding Cycle: 24.1), *A Novel Gene Therapy to Target Glioblastoma via Custom-Engineered Adenovirus-Associated Viral Vectors.* SIF is an independent venture philanthropy formed in 2021 as a subsidiary of the Sontag Foundation, which is one of the largest private funders of brain cancer research in North America, providing over $70 million dollars since its inception in 2002. Its signature Distinguished Scientist Award has supported 66 researchers at 39 major academic institutions. The Sontag Foundation is also the founding sponsor of the Brain Tumor Network, a non-profit provider of personalized brain tumor patient navigation services.

Glioblastoma (GBM) afflicts around 15,000 Americans each year with a dismal five-year survival rate under seven percent which has remained virtually unchanged for decades. Unfortunately, a major gap in funding basic and translational GBM programs remains. In combination with a lack of funding, several barriers exist that make development of new treatments for GBM difficult including the blood-brain barrier, tumor heterogeneity, redundant signaling pathways, a lack of "easy" targets and the tumor microenvironment.

The proposal by Dr. Tran has identified a core hub of master regulators across GBM to circumvent tumor heterogeneity and redundant signaling pathways. This approach contrasts with the typical, one example of which are drug repurposing efforts that focus on "easy" targets with therapies developed for a non-brain indication. Further, delivery via an AAV designed to specifically target GBM to reprogram tumor cells has been used to obtain impressive preliminary cure rates in PDX models. Importantly, this grant is focused on technology development via GMP work, delivery via Convection Enhanced Delivery (CED), pilot pharmacology, and initial pilot safety and efficacy studies for this novel approach. As CIRM is aware this is critical as the technology stage combined with the GBM indication of this program makes it incredibly difficult to obtain funding which could accelerate a scientific solution for this terrible disease.

Funding for this work could also lead to further breakthroughs for other brain cancer indications if successful, which may even extend further to other oncology applications and beyond**. Innovative proposals like Dr. Tran's that try something novel and unique are critical, and collectively will lead to the breakthroughs we need to treat GBM.** SIF strongly encourages CIRM to support this research and would follow the results in earnest.

Sincerely,



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