National Brain Tumor Society

April 18, 2024

Dear CIRM Application Review Subcommittee:

We write in support of Grant # **TRAN1-16065** (Funding Cycle: 24.1), Title: A Novel Gene Therapy to Target Glioblastoma via Custom-Engineered Adenovirus-Associated Viral Vectors

Glioblastoma is perhaps the most aggressive, treatment resistant, and complex cancer. More than ten thousand Americans and approximately one thousand Californians are expected to succumb each year to this disease. Less than seven percent of all patients who are diagnosed with glioblastoma are expected to live five years and sadly the average survival time is approximately eight months from time of diagnosis. Despite several compelling reasons to invest public and private dollars in glioblastoma research there continues to be a major research funding gap that needs to be closed in order to realize ready-to-go opportunities (like the Tran proposal) to make a profound difference. These reasons include:

- severity of the disease,
- the fact that any of us might be diagnosed at any time,
- that unlike other cancers,glioblastoma can steal one's sense of self
- progress against this cancer will yield new leads for other cancer and neurodegenerative disease research
- Glioblastoma is genomically well characterized offering opportunities to identify druggable targets and molecular subgroups for treatment development

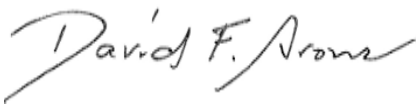
The reasons for lack of funding and hence lack of progress are well known. Among them are:

- The diversity of cancer cells known as the heterogeneity problem
- Difficulty to deliver treatments across the blood brain barrier
- Finding the right shutdown switches to slow and kill the cancer

Dr. Tran's proposal uniquely and exquisitely addresses these top barriers. Instead of taking a whack a mole approach to the heterogeneity problem, he proposes to use powerful new artificial intelligence tools to confront heterogeneity head on. The proposed work can break new ground by identifying master regulators that, if proven out, could be the right switches to flip to slow and kill the cancer. And importantly, his plan calls for a smart chemistry plan to ensure blood brain barrier penetration and a critically important dose optimization plan to ensure that the laboratory concept can actually become a viable therapeutic approach in adults with glioblastoma.

Patients want solutions. In the era of open source journals, patients are now more cognizant of the fact that testing drugs without addressing the top common barriers listed above probably won't lead to any change. Dr. Tran proposes to bring forward a very much needed novel approach to glioblastoma. We encourage CIRM to support this work.

Sincerely,



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