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August 22, 2023

Dear Swim Across America Friends:

This year has been a good one in our fight against osteosarcoma. As is the case periodically, our current Swim Across America Stacey Leondis Fellow, Yifei Wang, MD will be replaced, as he is moving onto a new role performing a clinical Orthopedic Spine Fellowship in Boston. We are now in the process of recruiting an individual to serve as sixth Stacey Leondis Fellow, and we anticipate that Dr. Wang's fellowship will serve as a next step in his future return to clinical oncology. Dr Wang leaves the laboratory having accomplished much of our goals of developing new treatments for their clinical translation to patients with osteosarcoma.

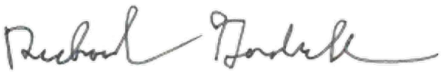
Dr. Wang's work has identified drugs that exist that could be repurposed for treating osteosarcoma as well as proteins that may be targeted that do not have drugs yet developed. In prior letters and conversations, we have mentioned we are very excited about one protein target – B7H3 also known as CD276, which already has drugs and cell therapy approaches made to target it. Laboratory research demonstrated the activity of multiple antibody-drug conjugates targeting this protein in preclinical models of osteosarcoma. Laboratory studies continue investigating how to combine these drugs with both the existing treatments for osteosarcoma as well as together with other novel agents. Finally, and most importantly, these drugs have moved into phase 2 clinical trials, testing their safety and effectiveness, in patients with osteosarcoma.

While at one time we would have never envisioned developing drugs specifically for osteosarcoma; however, new approaches such as creating antibody-drug conjugates allows this to be feasible, mixing and matching existing components as well as reducing both the cost and complexity of their development. Indeed, for rare diseases, such as osteosarcoma, this is paradigm shifting, allowing an optimization never before possible. For one of the identified targets, cell adhesion molecule 1 (CADM1), a novel antibody-drug conjugate was created and tested in preclinical models. This critical proof-of-principle testing demonstrated that this novel, CADM1 antibody-drug conjugate is dramatically effective at limiting osteosarcoma growth. Work is ongoing developing this tool compound into a drug which can be given to patients with osteosarcoma as well as exploring additional targets for novel treatments.

We are immensely grateful for all of the support we have received from Swim Across America. For the past fourteen years, the support for our research efforts has been provided in the form of a Research Fellowship named in honor of Stacey Leondis. The ongoing and longstanding trust by the Leondis Family

and their circle of family and friends have sustained our efforts through these many years, with us collectively believing the long-stalled progress in improving outcomes of this dreaded disease could be ended. We would never be at the point of where we are today without the immense dedication and support of the Leondis Family and friends, and we sincerely hope the approaches we are taking today are the light at the end of the tunnel.

Sincerely,



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