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2019 OUTSMARTING OSTEOSARCOMA AWARD

(in partnership with MIB Agents)

New Immune-mediated Therapies for Lung Osteosarcoma

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Osteosarcoma (OS) is a highly aggressive malignant primary bone cancer with a high propensity for lung metastasis. OS frequently originates from primitive mesenchymal bone-forming cells in the long bones during periods of rapid bone growth. Consequently, OS represents the most prevalent bone cancers affecting children and adolescent and young adults (AYA), with ~400-600 cases a year and accounts roughly half of all new cases of OS diagnosed in the United States. Despite aggressive combination chemotherapy and surgery, the outcome for metastatic OS remains dismal, and the overall survival in children and AYA patients with metastatic OS has not improved significantly over the past 3 decades. A high proportion of OS patients develop metastatic disease at distant sites either at the time of diagnosis or after initiation of multimodal therapy including combination chemotherapy and surgery. The lung accounts for >80% of all OS metastatic sites. Unfortunately, almost all of the patients who develop surgically unresectable pulmonary metastatic OS (pOS) invariably succumb to this devastating disease. Therefore, pOS represent a disease with urgent unmet needs. Dr. Huang's research aims to achieve meaningful, immunotherapy clinical trial-enabling pre-clinical studies in 3 areas: 1) Perform in vivo treatment efficacy validation and complete safety and toxicity profiling studies using BG34-200 in 2 other pOS mouse models to establish generalizability of this approach as well as to gather data for IND filing with the FDA. 2) Gather in vivo efficacy data of treating pre-clinical pOS model using TGFbR1 inhibitor, Vactosertib, with either immune checkpoint blockade or NK cell therapy. These results will inform the creation of another clinical trial design, submission for PRMC approval and IND filing with the FDA in the next 8-12 months; and 3) Investigate anti-tumor efficacy and immune reactivation in pOS by treating pre clinical pOS models with CA IX-specific inhibitor VD11-4-4 in the next 12 months in order to provide strong scientific rationale for future 3rd OS clinical trial. Our

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ongoing multi-pronged approach to finding novel therapeutic options for pOS is based on strong scientific rationales, demonstrated efficacy data, and unique opportunities to leverage existing ready-to-go pharmacologic agents and engaging industry partners. Coupled these factors with institutional knowledge in immuno-oncology translational research pipeline and infrastructure at Angie Fowler AYA Cancer Institute and Case Comprehensive Cancer Center, we are uniquely poised to quickly evaluate and offer these therapies for pediatric and AYA OS patients in the very near future.breakthrough for patients with UHR neuroblastoma by shifting it from a fatal diagnosis to one that is both identifiable and treatable.