A PHASE 1/2 STUDY OF BDC-3042, A NOVEL DECTIN-2 AGONISTIC ANTIBODY, IN PATIENTS WITH ADVANCED CANCERS

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Background Tumor-associated macrophages (TAMs) are a major component of the immune infiltrate in most cancers and play a key role in establishing the immunosuppressive tumor microenvironment (TME) that enables tumor progression. However, TAMs are phenotypically plastic and have the potential to be reprogrammed into immunostimulatory cells that enhance innate and adaptive anti-tumor immunity. BDC-3042 is a novel agonistic antibody targeting an immune-activating receptor expressed on TAMs known as Dectin-2 (CLEC6A). Dectin-2 is a C-type lectin receptor best known for its role in pathogen recognition and induction of protective immune responses against fungi and other microbes. We have previously demonstrated that Dectin-2 agonism stimulates pro-inflammatory cytokine secretion and antigen presentation by TAMs, resulting in robust CD8+ T cell-mediated anti-tumor immunity in syngeneic mouse models. Differential gene expression of Dectin-2 has been found in a wide range of solid tumor-associated macrophages compared to non-malignant tissues. Nonclinical studies with BDC-3042 have demonstrated its potential to reprogram TAMs and elicit anti-tumor activity as a novel immunotherapeutic approach for diverse human cancers. A phase 1/2, four-part, first-in-human, dose-escalation and dose-expansion study of BDC-3042 as a single agent and in combination with pembrolizumab in subjects with advanced malignancies has been initiated.

Methods This dose-escalation and dose-expansion study is enrolling approximately 185 subjects with advanced malignancies, including triple-negative breast cancer, renal cell carcinoma, colon cancer, head and neck cancer, non-small cell lung cancer, and ovarian cancer. Primary objectives of the dose-escalation phase are to define safety and tolerability and to determine the recommended phase 2 dose (RP2D) of BDC-3042 as a monotherapy (Part 1) and in combination with pembrolizumab (Part 2). Part 2 is planned to start once single agent BDC-3042 safety data are available. Part 1 will be the dose escalation. The dose-expansion phase of the study will evaluate preliminary anti-tumor activity of BDC-3042 monotherapy (Part 3) and in combination with pembrolizumab (Part 4). Secondary objectives will evaluate pharmacokinetic parameters and pharmacodynamic biomarkers in tumor tissue and in peripheral blood associated with drug exposure. Exploratory analyses will also be conducted to assess BDC-3042’s ability to reprogram TAMs and identify biomarkers associated with BDC-3042 biological activity with and without pembrolizumab. This study is being conducted in the US and is currently recruiting patients.

REFERENCES