BDB001, A TOLL-LIKE RECEPTOR 7 AND 8 (TLR7/8) AGONIST, CAN BE SAFELY ADMINISTERED INTRAVENOUSLY IN COMBINATION WITH ATEZOLIZUMAB AND SHOWS CLINICAL RESPONSES IN ADVANCED SOLID TUMORS

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Background BDB001 is an intravenously administered TLR 7/8 dual agonist immune modulator capable of reprogramming dendritic cells to produce antitumor activities. BDB001 monotherapy has demonstrated favorable tolerability and robust systemic immune activation leading to durable clinical responses in a Phase I trial. Here, we report on the safety and efficacy of BDB001 in combination with atezolizumab in a Phase I dose escalation/expansion trial in advanced solid tumors (NCT04196530).

Methods BDB001-102 is a Phase 1, open label, dose escalation/expansion trial of BDB001 (IV, Q1W) in combination with an anti-PD-L1 antibody, atezolizumab (IV, Q3W), in patients with advanced solid tumors. The primary endpoint was safety and tolerability. Secondary endpoints included efficacy, pharmacokinetics and pharmacodynamic profiling of immune activation.

Results Forty-one subjects with 17 different tumor types were enrolled across 4 dose levels. Fifty-nine percent were female, median age was 67 years (range, 32–80), median number of prior therapies was 3 (range, 0–8), and 63% of tumors had progressed on prior anti-PD-(L)1 therapy. Overall, BDB001 in combination with atezolizumab was well tolerated and 13 (31.7%) subjects did not experience any treatment related adverse events (TRAEs). No dose-limiting toxicities were observed. Common TRAEs were transient Grade 1 or 2 fatigue (31.7%), fever (26.8%) and chills/rigor (26.8%). Only 3 (7.3%) subjects experienced Grade 3 TRAEs of fatigue and nausea. There were no Grade 4 or 5 TRAEs and no new safety concerns. Pharmacodynamic evaluation of plasma cytokine levels showed robust increases in interferon gamma and interferon inducible protein-10 (IP-10) at BDB001 Dose Level 4. IP-10 induction was associated with clinical responses. Preliminary efficacy evaluation of the 19 subjects at Dose Level 4 showed durable and deep clinical responses in 3 (16%) subjects, 2 with urothelial carcinoma and 1 with anti-PD-1 mAb refractory NSCLC. All responders remain on treatment, with a duration of response ranging from 7.1+ to 34.1+ weeks. Ten (53%) subjects had stable disease (DCR 68%), 3 of whom had a reduction in tumor burden and were on treatment for over 18 weeks (up to 56 weeks).

Conclusions Intravenous BDB001 in combination with atezolizumab is well tolerated. Deep and durable clinical responses were observed in PD-1 refractory and naive patients, supported by robust systemic immune activation. BDB001 in combination with atezolizumab is a promising therapeutic option for patients with advanced solid tumors. A phase 2 trial (NCT03915678) of BDB001 in combination with atezolizumab and radiotherapy is currently enrolling patients.

Ethics Approval This study was approved by the institutional review boards at the five participating institutions. All subjects signed informed consent before enrolling in the clinical trial.