BXQ-350: A Phase 1b/2 Placebo Controlled, Double Blinded Study on the Efficacy and Safety of BXQ-350 in Combination with mFOLFOX7 and Bevacizumab in Newly Diagnosed Metastatic Colorectal Carcinoma (mCRC)

Background:

Ceramides and sphingosine-1-phosphate (S1P) are key bioactive signaling molecules. Ceramides are proapoptotic and mitigate chemoresistance. Conversely, S1P promotes cancer cell proliferation, activates multiple oncogenic pathways, and stimulates immuno-suppressor cell populations promoting a pro-tumoral microenvironment. Several studies in colorectal cancer patients have shown high levels of ceramides are associated with improved survival, while high S1P levels are associated with a poor prognosis. Hence, modulation of sphingolipid metabolism could be a promising therapeutic approach.

BXQ-350 is a nanovesicle of Saposin C, an allosteric activator of sphingolipid metabolism, that lowers systemic S1P and increases C18 ceramide. BXQ-350 was investigated in a Phase 1 dose-escalation safety study in an cancer patients with advanced solid malignancies (NCT02859857). BXQ-350 was safe and well-tolerated (no DLT, no MTD). Also, 13 patients (~17.8% of evaluable patients) had a clinical benefit up to cycle 6 and beyond (PR, SD). Among patients with PFS > 6 months, there were 4 recurrent CRC patients: 1 patient had a PFS of ~12 months, 2 of ~18 months, and 1 is still on study after 6 years. Furthermore, there were signs that BXQ-350 may alleviate symptoms of CIPN as 4 out of 10 patients with chronic CIPN at time of enrollment experienced an improvement of their symptoms.

Trial design:

BXQ-350 is being investigated in a Phase 1b/2 study in combination with mFOLFOX7 and Bevacizumab in newly diagnosed mCRC patients (NCT05322590) to assess the efficacy and safety of BXQ-350.

Design of the Phase 1b (open label study):

1) A safety dose escalation part to establish the RP2D: patients will initially receive 1.8 mg/kg BXQ-350 in combination with mFOLFOX7 and Bevacizumab. If safe (no MTD), dose of BXQ-350 will be increased to 2.4 mg/kg and 9 additional patients will be entered at this dose level. If safe, then this dose will be the RP2D and 21 additional patients will be enrolled, completing a 30 patient expansion cohort
2) Efficacy will then be evaluated for all patients entered at the RP2D.

Primary objectives of the Phase 1b are to assess safety, identify RP2D, and assess preliminary efficacy of BXQ-350 in this combination. A secondary objective is to determine if BXQ-350 decreases CIPN.

Design of the Phase 2, a double-blinded, placebo-controlled study:

1) Eligible patients (up to 160 patients) will be randomized in a 1:1 fashion to receive either BXQ-350 or placebo with mFOLFOX7 + Bevacizumab.

Primary and secondary objectives include efficacy, safety and CIPN incidence.

Enrollment in the Phase 1b dose escalation portion is completed. After review of the safety results, the DSMB approved enrollment of the expansion cohort, with a planned 30 patients at the Phase 2 dose. Available Phase 1b data will be presented.