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

**Background:**

Sphingolipids are a class of bioactive signaling molecules implicated in multiple cellular processes and molecular pathways. Amongst these, ceramides and sphingosine-1-phosphate (S1P) are emerging as critical sphingolipids as several studies involving 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 novel and promising therapeutic approach.

BXQ-350 is a nanovesicle of Saposin C, an allosteric activator of sphingolipid metabolism. Clinical and preclinical studies have shown that BXQ-350lowers systemic S1P and increases C18 ceramide.

BXQ-350 was investigated in a Phase 1 dose-escalation safety study in an all-comer cancer patients with advanced solid malignancies ([NCT02859857](https://clinicaltrials.gov/show/NCT02859857)). Results showed that 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 (PR, SD). 8 patients (~11% of evaluable patients) had PFS> 6 months, with 2 patients still on study six years after enrollment. Among patients with PFS > 6 months, there were 4 recurrent CRC patients (1PR, 3SD): 1 patient had a PFS of ~12 months, 2 of ~18 months, and 1 is still on study after 6 years. Furthermore, there were preliminary signs that BXQ-350 may alleviate symptoms of chemotherapy induced peripheral neuropathy (CIPN) as 4 out of 10 patients with chronic CIPN at time of enrollment anecdotally expressed an improvement of their symptoms.

**Trial design**:

BXQ-350 is currently 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 in this combination.

The design of the Phase 1b is as follows (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. If safe, then this dose will be the RP2D.
2. An expansion cohort enrolling 30 patients will then be conducted at the RP2D.

The 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 addition of BXQ-350 reduces CIPN based on total oxaliplatin dose, results from CIPN20 questionnaire, and biomarkers analysis.

 The design of the Phase 2 is as follows (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 (at the RP2D established at Stage 1) or placebo with mFOLFOX7

Primary and secondary objectives of the Phase 2 include efficacy, safety and CIPN incidence.

As of December 2023, enrollment in cohort 1 of Phase 1b is completed. After review of the safety data, the DSM approved enrollment of the expansion cohort with the planned 30 patients. Available data will be presented.