BXQ-350 May Protect from the Direct Toxicity of Chemotherapeutic Agents Associated with Chemotherapy Induced Peripheral Neuropathy (CIPN)

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Background:
Chemotherapy Induced Peripheral Neuropathy (CIPN) is a debilitating side effect associated with many antineoplastic chemotherapeutic agents including cytotoxic and targeted agents. It significantly impacts cancer patients' quality of life during treatment, potentially impacting clinical benefit. The pathology of CIPN is complex and still not completely understood. Altered neuronal sphingolipid metabolism has been linked to neuropathic pain and elevated plasma levels of sphingosine-1-phosphate (S1P) have also been associated with patients receiving chemotherapy and developing CIPN.

Method:
BXQ-350 is a nanovesicle of Saposin C, an allosteric activator of sphingolipid metabolism, that lowers systemic S1P. BXQ-350 was investigated in an adult Phase 1 dose-escalation safety study in heavily pretreated all-comer cancer patients with advanced solid malignancies (NCT02859857). The cytoprotective properties of BXQ-350 against multiple agents known to induce CIPN were investigated *in vitro* in neuronal PC12 cells and BXQ-350's CIPN mitigation properties were investigated *in vivo* in a CIPN preclinical model.

Results:
Several patients with chronic CIPN at time of enrollment in the Phase 1 study reported an improvement of their neuropathic symptoms after receiving BXQ-350. Results from preclinical experiments revealed that BXQ-350 protected cells from oxaliplatin, paclitaxel, bortezomib or MMAE neurotoxicity. BXQ-350 was subsequently investigated in a murine oxaliplatin-induced CIPN preclinical model, showing a dose-dependent reduction of mechanical allodynia correlating with decreasing systemic S1P levels.

Conclusions:
Preclinical results demonstrated that BXQ-350 was highly effective at protecting neuronal cells from antineoplastic agents known to induce CIPN and prevent CIPN in a preclinical model. These results appeared to support the clinical observation that BXQ-350 alleviated CIPN symptoms in several patients soon after receiving BXQ-350. Additional clinical and pre-clinical studies are on-going.