**BXQ-350: A Novel Biologic that Modulates Sphingolipid Metabolism and Shows Potential Therapeutic Applications in Cancer, CIPN, and Viral Diseases**

Gilles Tapolsky, Charlie Cruze, Richard Curry III, Robin Furnish, Michael Gazda, Tim Stephens, Nikhil Wilkins, Ray Takigiku

Dysregulated sphingolipid metabolism is associated with many pathologies including cancer, pain, autoimmune and inflammatory diseases, viral infections, chemotherapy induced peripheral neuropathy (CIPN).  
  
BXQ-350 is a nanovesicle formulation of Saposin C, an allosteric activator of enzymes involved in sphingolipid metabolism. BXQ-350 has been characterized preclinically in cancer, CIPN, and viral models. Currently, BXQ-350 is being investigated in clinical trials in adult and pediatric cancer patients.    
  
Preclinical results show that BXQ-350 possesses activity against multiple viruses including encephalitis viruses. Also, BXQ-350 mitigates the neurotoxic effects of chemotherapy. Results of lipidomic analysis of cellular extracts or tissue samples showed a similar trend: an increase in ceramides, especially C18 ceramide, and a decrease in S1P.   
  
Clinically, BXQ-350 was investigated in a Phase 1 dose-escalation safety study in adult cancer patients with advanced solid malignancies to determine its safety profile and clinical activity as monotherapy. Eight patients (~11% of evaluable patients) had a progression free survival (PFS) > 6 months, including patients with malignant brain tumors. Two patients are still on study six years after enrollment, including a glioblastoma multiforme patient. Analysis of plasma samples revealed changes in sphingolipids similar to what was observed preclinically: an increase in circulating C18 levels and a decrease in S1P levels post BXQ-350. In addition, several patients with established CIPN at the time of enrollment reported an improvement of their symptoms after receiving BXQ-350.   
  
Results demonstrate that BXQ-350 positively impacts sphingolipid metabolism across multiple therapeutic areas, crosses the blood brain barrier, and achieves clinically meaningful concentrations in the CNS. Preclinical, clinical results will be discussed, and current development plans will be presented.