Pediatric SNO 2023
TRLS-6

Trial in Progress:
A Phase 1 Open Label, Multi-Center Study to Evaluate the Safety and Tolerability of BXQ-350 in Children with Newly Diagnosed Diffuse Intrinsic Pontine Glioma (DIPG) and Diffuse Midline Glioma (DMG) with H3K27M alteration

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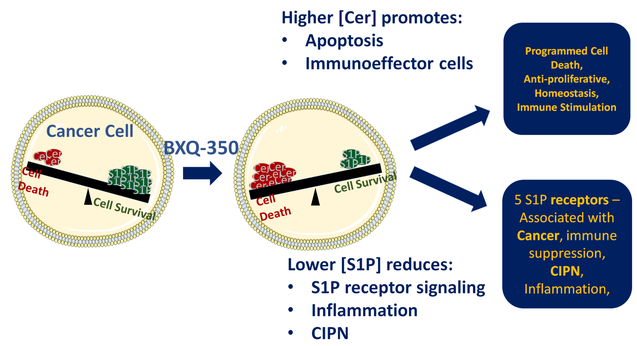
1. Introduction:

- BXQ-350 is a novel biologic agent being investigated in adult and pediatric cancer patients
- BXQ-350 modulates sphingolipid metabolism, increasing ceramide concentration and lowering sphingosine-1-phosphate (S1P) [1]
  - Ceramides are pro-apoptotic, down regulate oncogenic pathways, and stimulate immuno-effector cells
  - S1P promotes proliferation of cancer cells, activates oncogenic pathways, and stimulates immuno-suppressor cells.



- Phase 1 adult and pediatric studies indicate that BXQ-350 is well tolerated with potential single agent activity [2] in several solid tumor types, including GBM and ependymoma
- Ceramides and S1P are key signaling molecules involved in cancer [3] and their role in CNS tumors has been recognized and is investigated as a therapeutic target [4], including DIPG / DMG tumors [5]

2. Study Design (NCT04771897):

Phase 1 dose-escalation safety study in DIPG/DMG patients in combination with radiation at 3 US sites:

- 54 Gy fractionated radiation concurrent with BXQ-350
- Accelerated dose escalation from 2.4 to 3.2 mg/kg
- Disease assessment every 8 weeks
- Dosing up to 12 cycles or unacceptable toxicity or disease progression

Summary

- **BXQ-350 is a novel biologic** and a nanovesicle formulation of Saposin C, an allosteric activator of enzymes involved in sphingolipid metabolism
- BXQ-350 modulates sphingolipid metabolism**, lowers S1P and increases ceramide levels**
- BXQ-350 is **well-tolerated in pediatric and adult cancer patients**
- **BXQ-350 showed signs of single agent activity in multiple tumor types** in adult patients with solid tumors refractory to standard therapies

Other Clinical Studies

BXQ-350 is also being investigated in:

- Phase 1/2 study in combination with SoC in newly diagnosed mCRC patients (NCT05322590)
- PoC and PK/PD study in cancer patients with established CIPN (NCT05291286)

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Acknowledgement: Patients who participated in the trials and their families, clinicians and staff at investigational sites, Bexion's personnel

- Primary objective: Safety & tolerability of BXQ-350 in combination with radiation in children with newly diagnosed DIPG & DMG
- Secondary objectives:
  - ORR as defined by RANO; OS and 1-year OS
  - PK, biomarkers
  - Quality of Life (PROMIS®)

3. Safety / Adverse Events:

- In previous single agent pediatric study (NCT03967093), results showed that BXQ-350 was well-tolerated warranting further clinical investigations
- BXQ-350 in combination with radiation has been thus far well tolerated with infusion reactions being the most frequent SAE observed; managed by pretreatment and slowing infusion rate

4. Enrollment & Patient Status:

Patients	Diagnosis	Age	Gender	Disposition	Best Disease Assessment
1-01*	**DMG**	19	M	PD -8 month	SD
1-02	**DMG**	25	M	PD-12 month	**PR**
2-02	**DMG**	6	F	PD-4 month	SD
2-04	**DMG**	20	M	PD-8 month	SD
1-03	**DIPG**	6	f	PD-11 month	**PR**
2-01	**DIPG**	4	M	SAE / PD-8 m	**PR**
2-03	**DIPG**	5	M	SAE / PD-3 m	SD
3-01	**DIPG**	14	M	PD-6 month	SD

- ***2.4 mg/kg; all other patients @ 3.2 mg/kg;**
- **PD: Progressive Disease; SD: Stable Disease; PR: Partial Response;**
- **SAE: Serious Adverse Event (hypersensitivity infusion reaction)**

- Monitoring patient survival
- Three additional patients to complete enrollment

(1) Bexion Pharmaceuticals, *manuscript in preparation.*
(2) M. Abdelkabi *et al.,* An Open-label Multi Center Phase 1 Safety Study of BXQ-350 in Children and Young Adults with Relapsed Solid Tumors , Including Recurrent Malignant Brain Tumors, *Heliyon 2022 Dec 19;8(12): e12450.*
(3) B. Ogretmen, Sphingolipid metabolism in cancer signaling and therapy, *Nat Rev Cancer 2018, January, 18(1), 33-50.*
(4) a) S. Grassi et al., S1P Receptors and Metabolic Enzymes as Druggable Targets for Brain Diseases, *Front . Pharmacol Review,* Jul 2019, 10, 807; b) S. Mahajan-Thakur *et al.*, S1P Signaling in Glioblastoma Multiforme – A Systematic Review, Int Jour of Mol Sciences, 2017, 18, 2448; c) L. Riboni *et al.*, S1P in the Tumor Microenvironment: A Signaling Hub Regulating Cancer Hallmarks, Cells Review, 2020, 9, 337.
(5) a) L. Dai *et al*., Targeting Sphingosine Kinase against Diffuse Intrinsic Pontine Glioma (DIPG), Journal of Cancer, 2020, vol 11(16), 4683; b) E. Hayden *et al.*, Therapeutic Targets In Diffuse Midline Gliomas – AN Emerging Landscape, *Cancers Review,* 2021, 13, 6251; c) A. Wingerter *et al*., Exploiting Gangliosides for the Therapy of H3K27M Mutant Diffuse Midline Glioma, *Cancers*, 2021, 13, 520; d) C Mount *et al.*, Potent antitumor efficacy of anti-GD2 Car T-cells in H3K27M+ diffuse midline gliomas., *Nat Med* 2018 May, 24(5), 572.