Dihydrgalactitol (VAL-083) is a bi-functional DNA targeting agent with a distinct mechanism-of-action differentiating it from other chemotherapeutic agents used in the treatment of GBM and other CNS tumors. VAL-083 targets N7 of guanine and has demonstrated MGMT-independent cyotoxicity in multiple GBM cell lines, cancer stem cells and is able to overcome temozolomide-resistance in vitro, demonstrating a distinct mechanism of action.

**CONCLUSIONS & NEXT STEPS**

- VAL-083 is a “first-in-class” DNA targeting agent with demonstrated activity against GBM in historical-NCI sponsored clinical trials.
- VAL-083’s unique cytotoxic mechanism maintains activity against GBM cell lines and cancer stem cells independent of MGMT methylation status in vitro.
- A dosing regimen of 40 mg/m²/day VAL-083 administered on days 1,2,3 of a 21-day cycle was well-tolerated and data supports the potential to offer a clinically meaningful survival benefit in bevacizumab failed GBM patients.

Taken together, these data support the potential of VAL-083 to offer a new treatment option for GBM patients whose tumors exhibit features correlated with resistance to currently available therapies.

**Three additional clinical trials with VAL-083 are planned or enrolling**

1. **Phase 3 Study in Temozolomide-Avatin Recurrent GBM (“STAR-3”):** A pivotal randomized, controlled trial of VAL-083 in patients with recurrent GBM who have failed temozolomide/radiation therapy and bevacizumab.

2. **Open label, single-arm, biomarker-driven Phase 2 trial in MGMT unmethylated, bevacizumab-naive, recurrent GBM is currently enrolling at MD Anderson Cancer Center** (clinicaltrials.gov identifier: NCT02717962)

3. **Open label, single-arm, biomarker-driven, Phase 2 trial of VAL-083 and radiation therapy in newly diagnosed MGMT-Unmethylated GBM** (clinicaltrials.gov identifier: NCT03050763)