Phase II Study of VAL-083 in Patients with Recurrent Malignant Glioblastoma Multiforme

Kent C. Shih1, Manish Patel1,4, Jeffrey Bacha2, Dennis Brown3, William J. Garner4, Anne Steino1, Richard Schwartz3, Sarah Kaneal1, Mike LD, Lorena Lopez5, and Howard A. Burns3, III

1Tennessee Oncology, Nashville, USA; 2Florida Cancer Specialists & Research Institute, Florida, USA; 3DelMar Pharmaceuticals, Inc., Vancouver, Canada and California, USA; 4*Sarah Cannon Research Institute, Nashville, USA

**Abstract # CT404: Median survival for patients with recurrent glioblastoma multiforme (GBM) is less than 6 months. Front-line systemic therapy is temozolomide, but chemo-resistance due to O6-methylguanine-DNA methyltransferase (MGMT) activity has implicated in poor outcomes. VAL-083 is a structurally unique small molecule alkylating agent that synergizes with and accumulates in brain tumor tissue. Previous human clinical studies by several investigators have suggested that VAL-083 has anti-tumor activity against a broad range of tumor types including GBM. In preclinical in vitro studies, VAL-083 demonstrated activity in a wide range of cancer cell lines, including pediatric and adult GBM cell lines and GBM cancer stem cells. Notably, VAL-083 overcomes chemo-resistance to MGMT in vitro. In light of extensive safety data from several clinical trials and promising efficacy signals in CNS tumors, DelMar initiated a new clinical study to determine the safety, tolerability, pharmacokinetics, anti-tumor activity in patients with recurrent GBM.

**Conclusions:**
- Treatment of recurrent GBM remains a significant unmet medical need.
- VAL-083 demonstrated promising clinical activity against newly diagnosed and recurrent GBM in historical NCI-sponsored clinical trials.
- VAL-083 has potent MGMT-independent cytotoxic activity against GBM cell lines in vitro.
- Pharmacokinetic analyses show dose-dependent increase in exposure with a short plasma 1/2 life half-life and a Cmax of <256ng/ml (1.8μM) at 20mg/kg (see Table 3).
- VAL-083 therapy is well tolerated to date: no drug-related serious AEs have been detected.
- MTD has not been reached after completion of cohort 5 (20 mg/m²); enrollment and analysis of cohort 6 is ongoing.

**REFERENCES:**

**Figures:**
- Figure 1: Correlation of MGMT promoter methylation with overall survival for patients with GBM
- Figure 2: VAL-083 activity against GBM cell lines SF188, U251, and T98G (Dr. Dunn, S.E.; Eagan R.T., MT)