DelMar Pharmaceuticals Updates Ongoing Phase I/II Refractory GBM Clinical Trial with VAL-083 at American Association Cancer Research (AACR) Annual Meeting

Results to date support the potential of VAL-083 as a new treatment paradigm for GBM patients who have failed or are unlikely to respond to currently available treatments


In summary, DelMar presented that:

- A well-tolerated VAL-083 dosing regimen of 40 mg/m²/daily every 3 days in a 21 day cycle has been selected for advancement into a Phase III refractory GBM study;
- The Phase III study design and initiation shall be determined in consultation with the USDFA during a meeting planned for the first half of 2016;
- The majority of GBM patients enrolled in DelMar's Phase I/II clinical trial have tumors exhibiting features correlated with resistance to currently available therapies, aggressive disease and poor patient outcomes; and
- This clinical trial is ongoing with expected median survival of eight to nine months following bevacizumab failure. Results to date support the potential of VAL-083 to offer a clinically meaningful survival benefit and a promising new treatment option for GBM patients who have failed or are unlikely to respond to currently available
chemotherapeutic regimens.

"We are pleased with the continued progress and promise of VAL-083 as a potential new treatment for GBM," said Jeffrey Bacha, DelMar's chairman & CEO. "We look forward to discussing our plans for advancement into registration-directed Phase III clinical trials with the USFDA in the coming months."

Abstract #CT074, *Phase I/II study of VAL-083 in patients with recurrent glioblastoma* was presented as a late-breaking abstract during the "Phase II/III Clinical Trials in Progress" session.

DelMar's Phase I/II protocol was designed to establish a safe dosing regimen for VAL-083 in refractory GBM patients before advancing the agent to larger and more advanced clinical studies. Enrolled patients must have recurrent GBM and have failed both temozolomide (Temodar™) and bevacizumab (Avastin™) unless one or both are contraindicated.

In studies of VAL-083 conducted by the National Cancer Institute (NCI) in the 1970s and 1980s, a variety of dose regimens were used to treat a range of cancers, including GBM. The most common regimen was 25-30 mg/m^2/day for 5 days, with re-treatment every 5 weeks.

DelMar's dosing regimen uses a cycle of treatment consisting of intravenous VAL-083 administered on days 1, 2 and 3 of a 3-week cycle. The three-day dose regimen was developed to be more patient-friendly than a five-day sequence and to take advantage of a shorter platelet nadir and recovery period observed in the literature.

**Tumor Response and Outcomes**

GBM patients were not re-resected prior to treatment with VAL-083 and therefore had a growing recurrent GBM tumor at the time of enrollment. Patients were monitored for tumor response by MRI.

Consistent with un-resected refractory GBM, median progression free survival (PFS) was short at 1.2 months (range: 0.2 – 20.1 months). Five GBM patients treated with VAL-083 were reported to have stable disease as their best response following treatment; the remainder reported progressive disease.

Ad-hoc subgroup analysis of the Phase 1 dose-escalation data indicated a dose response trend. Increase survival was observed at 6, 9 and 12 months following initiation of treatment in a high dose (30 and 40mg/m^2) sub-group vs. a low dose (≤5mg/m^2) sub-group.

GBM patients failing bevacizumab have a poor prognosis with expected survival under five months. To date, more than half of patients receiving an assumed therapeutic dose of VAL-083 (≥20mg/m^2) have survived more than six months following bevacizumab failure; more than 40% have survived for nine months or are currently alive and more than 20% have survived for twelve months or are currently alive with median survival expected to be determined at between eight and nine months following bevacizumab failure.
The study is ongoing and analysis of patient outcomes is continuing.

**MGMT & IDH1**

High expression of DNA repair protein O\(^6\)-methylguanin-DNA-methyltransferase and wild-type form of the enzyme isocitrate dehydrogenase (IDH1) have been correlated with poor outcomes in GBM. The methylation status of the MGMT promoter was characterized by PCR and/or ELISA for nineteen GBM patients enrolled in DelMar’s trial; IDH1 status was reported in eleven patients; both MGMT and IDH1 status were reported in four patients.

Of patients tested, 84% exhibited high MGMT and 90% were wild-type IDH1. All patients whose samples were tested for both markers were MGMT unmethylated by PCR and wild-type IDH1, a genotype that is correlated with particularly poor prognosis.

These data indicate that the majority of patients enrolled in DelMar’s clinical trial have GBM tumors that exhibit features correlated with resistance to currently available therapies, aggressive disease and poor patient outcomes.

**Pharmacokinetics**

Pharmacokinetic (PK) analyses showed dose-dependent linear systemic exposure with a short (1-2h) plasma terminal half-life; average Cmax at 40 mg/m\(^2\)/day was 781 ng/mL (5.3µM). The observed PK profile is comparable to published literature. Prior NCI-sponsored studies demonstrated that VAL-083 readily crosses the blood brain barrier and has a long (>20 hour) half-life in the central nervous system.

Based on observed and previously published pharmacokinetics, DelMar believes that therapeutic doses equal to or above 20 mg/m\(^2\) daily on days 1, 2 and 3 of a 21 day cycle should deliver sufficient levels of VAL-083 to brain tumors to achieve a therapeutic benefit.

**Safety & Tolerability**

In the DelMar Phase I dose escalation regimen, no serious adverse events (SAEs) related to VAL-083 were encountered at doses up to 40 mg/m\(^2\)/day.

Increasing frequency of and higher grade hematologic toxicities were observed at doses above 40 mg/m\(^2\)/day. Consistent with the published literature, the observed dose limiting toxicity for VAL-083 is primarily thrombocytopenia. Observed platelet nadir occurred at approximately day 18, and recovery was rapid and spontaneous following treatment.

Based on Phase 1 observations, fourteen additional patients were enrolled in a Phase 2 expansion cohort at 40mg/m\(^2\).

Consistent with Phase 1, the dose of VAL-083 40 mg/m\(^2\) on days 1, 2 and 3 of a 21 day cycle was generally well tolerated in Phase 2. At this dose, one subject previously treated with CCNU reported Grade 4 thrombocytopenia (low platelets). As a result of this observation, the protocol inclusion criterion for platelet count was increased from 100,000/µL to 150,000/µL for patients receiving prior nitrosoureas within 12 weeks preceding enrollment. No other dose limiting toxicities were observed at this dose.
**Next Steps**

DelMar plans to discuss a proposed registration-directed Phase III protocol and data from its current Phase I/II clinical trial with the USFDA in the coming months with a goal of advancing VAL-083 into registration-directed clinical trials for GBM patients who have failed temozolomide and bevacizumab. Subject to discussions with USFDA and the Company's advisors, along with sufficient financial resources, DelMar hopes to initiate a registration-directed Phase III clinical trial with VAL-083 in refractory GBM within the next six to nine months.

In addition to the proposed Phase III clinical trial, DelMar plans to conduct two additional Phase II studies in separate GBM populations:

- In collaboration with the University of Texas MD Anderson Cancer Center, DelMar plans to conduct a randomized Phase II clinical trial of VAL-083 versus CCNU in bevacizumab-naïve MGMT-unmethylated GBM patients at first recurrence/progression to confirm the tolerability of DelMar's dosing regimen and assess outcomes in recurrent bevacizumab-naïve GBM patients whose tumors are known to express high levels of MGMT (clinicaltrials.gov identifier: NCT02717962); and
- In collaboration with Sun Yat-Sen University and Guangxi Wuzhou Pharmaceutical (Group) Co., Ltd, DelMar plans to conduct a single arm Phase 2 clinical trial to confirm the tolerability of DelMar's dosing regimen in combination with radiotherapy (XRT) and to explore the activity of VAL-083 in newly diagnosed MGMT-unmethylated GBM patients whose tumors are known to express high levels of MGMT.

"We believe that the results of these planned studies, if favorable, will position VAL-083 to create a paradigm shift for the majority of GBM for patients whose tumors exhibit molecular features that make them unlikely to respond to currently available chemotherapies," stated Mr. Bacha.

**About VAL-083**

VAL-083 is a "first-in-class," small-molecule chemotherapeutic. In more than 40 Phase I and II clinical studies sponsored by the U.S. National Cancer Institute, VAL-083 demonstrated clinical activity against a range of cancers including lung, brain, cervical, ovarian tumors and leukemia both as a single-agent and in combination with other treatments. VAL-083 is approved in China for the treatment of chronic myelogenous leukemia (CML) and lung cancer, and has received orphan drug designation in Europe and the U.S. for the treatment of malignant gliomas. DelMar recently announced that the USFDA's Office of Orphan Products had also granted an orphan designation to VAL-083 for the treatment of medulloblastoma.

DelMar has demonstrated that VAL-083's anti-tumor activity is unaffected by the expression of MGMT, a DNA repair enzyme that is implicated in chemotherapy resistance and poor outcomes in GBM patients following standard front-line treatment with Temodar® (temozolomide).

DelMar has been conducting a Phase I/II clinical trial in GBM patients whose tumors have
progressed following standard treatment with temozolomide, radiotherapy, bevacizumab and a range of salvage therapies. The trial is being conducted at five clinical centers in the United States: Mayo Clinic (Rochester, MN); UCSF (San Francisco, CA) and three centers associated with the Sarah Cannon Cancer Research Institute (Nashville, TN, Sarasota, FL and Denver, CO) (clinicaltrials.gov identifier: NCT01478178). DelMar announced the completion of enrollment in a Phase II expansion cohort in September, 2015.

About Glioblastoma Multiforme (GBM)
Glioblastoma multiforme (GBM) is the most common and most malignant form of brain cancer. Approximately 15,000 people are diagnosed with GBM each year in the U.S., with similar incidence in Europe. Standard of care is surgery, followed by either radiation therapy, or radiation therapy combined with temozolomide. Approximately 60 percent of GBM patients treated with temozolomide experience tumor progression within one year. More than half of glioblastoma patients will fail the currently approved therapies and face a very poor prognosis.

About DelMar Pharmaceuticals, Inc.
DelMar Pharmaceuticals, Inc. was founded to develop and commercialize new cancer therapies in indications where patients are failing or have become intolerable to modern targeted or biologic treatments. The Company's lead drug in development, VAL-083, is currently undergoing clinical trials in the U.S. as a potential treatment for refractory glioblastoma multiforme. VAL-083 has been extensively studied by the U.S. National Cancer Institute, and is currently approved for the treatment of chronic myelogenous leukemia and lung cancer in China. Published pre-clinical and clinical data suggest that VAL-083 may be active against a range of tumor types via a novel mechanism of action that could provide improved treatment options for patients.

For further information, please visit www.delmarpharma.com; or contact DelMar Pharmaceuticals Investor Relations: ir@delmarpharma.com / (604) 629-5989. Connect with the Company on Twitter, LinkedIn, Facebook, and Google+.

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