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DelMar Presents New Mechanism of Action Data for its Lead Agent VAL-083 in Temozolomide-Resistant Glioblastoma Multiforme (GBM) at the World Federation of Neuro-Oncology Societies (WFNOS)

VANCOUVER, British Columbia and MENLO PARK, Calif., May 8, 2017 /PRNewswire/ - DelMar Pharmaceuticals (Nasdaq: DMPI) ("DelMar" and the "Company"), a biopharmaceutical company focused on developing new cancer therapies, today announced new mechanism of action (MOA) data for its anti-cancer product candidate, VAL-083 (*dianhydrogalactitol*), a "first-in-class" small-molecule DNA-targeting agent in temozolomide (Temodar™)-resistant GBM, at the World Federation of Neuro-Oncology Societies (WFNOS).

The Company presented two posters at the Quadrennial session of the WFNOS Conference in Zurich, Switzerland.

The titles and summaries of the posters are as follows:

Abstract 1: Distinct mechanism of action of dianhydrogalactitol (VAL-083) overcomes chemoresistance in glioblastoma. Zhai et al, 2017.

It has been previously demonstrated, both preclinically and in the clinic, that VAL-083 is active in temozolomide-resistant GBM. Glioblastoma cells are known to become refractory to treatment because they are able to repair the DNA damage caused by temozolomide using the MGMT* enzyme and the MMR** family of enzymes. While temozolomide is inactive in GBM cells where MGMT is functional, it has already been demonstrated that the activity of VAL-083 is unaffected by the MGMT status of a cell and hence VAL-083 remains active, even when temozolomide has failed.

The authors now show that VAL-083 is not only able to circumvent the MGMT pathway but is also able to override the secondary temozolomide resistance mechanism seen in GBM—MMR DNA repair. In cancer cell-lines VAL-083 is able to induce DNA damage and resultant cell apoptosis even when MMR enzymes (MLH-1 and MSH-2) are made constitutively active.

Taken together, these data provide preclinical evidence, and support the clinical rationale, that VAL-083 should be studied as a front-line therapy for GBM patients in whom active MGMT and MMR pathways will result in chemoresistance to temozolomide.

These results also add to the growing evidence that temozolomide may only be a viable front-line treatment in the 1/3 of GBM patients for whom biomarker data reveal inactive MGMT and MMR enzymes. VAL-083, whose activity is independent of, and agnostic to, the MGMT and MMR activity, may in fact be a superior alternative.

Abstract 2: Clinical trials of VAL-083 in patients with chemoresistant glioblastoma. Bacha et al, 2017.

In this poster the authors review historic clinical trials of VAL-083 run by the National Cancer Institute and the modern dose-finding trials conducted by DelMar (ASCO 2016) to provide the rationale for the ongoing and new clinical development of VAL-083 in GBM. This topic was also the recent subject of a contributed editorial by CEO Jeff Bacha and CSO Dennis Brown for Life Science Leader, entitled [Cancer Breakthroughs: A Look to the Past Can be a Look to the Future.](#)

DelMar has announced plans to investigate VAL-083 in Phase 2 and Phase 3 clinical trials in recurrent and newly diagnosed GBM. A pivotal randomized, controlled Phase 3 **S**tudy in **T**emozolomide-**A**vastin **R**ecurrent GBM ("**STAR-3**") will evaluate the overall survival of VAL-083 versus salvage chemotherapy for GBM patients who have previously failed both temozolomide and bevacizumab (Avastin™) and for whom there exists no approved treatment option. Should VAL-083 show a survival benefit in this moribund, recalcitrant population, it could revolutionize the GBM treatment landscape. A Phase 2 study of VAL-083 at MD Anderson Cancer Center is currently enrolling second-line GBM patients who have failed front-line temozolomide and test positive for MGMT. Finally, a Phase 2 trial enrolling MGMT-expressing front-line GBM patients to be treated with VAL-083 *in lieu* of temozolomide has the potential to introduce biomarker testing into the GBM treatment paradigm to determine which patients will receive temozolomide and VAL-083, respectively, based on their MGMT expression status.

*MGMT= O₆-Methyl Guanine DNA-Methyl Transferase **MMR=mismatch repair

About VAL-083

VAL-083 is a "first-in-class," small-molecule chemotherapeutic that demonstrated clinical activity against a range of cancers including GBM in historical clinical trials sponsored by the U.S. National Cancer Institutes (NCI). DelMar has demonstrated that VAL-083's anti-tumor activity against GBM is unaffected by the expression of MGMT and MMR *in vitro*. Further details can be found at <http://www.delmarpharma.com/scientific-publications.html>.

VAL-083 has received an orphan drug designation in Europe for the treatment of malignant gliomas and the U.S. FDA Office of Orphan Products has granted an orphan designation to VAL-083 for the treatment of glioma, medulloblastoma and ovarian cancer. Based on historic clinical trials run by the NCI, the modern Phase 1/2 dose finding trial run by DelMar in GBM (ASCO 2016), and recent guidance from the FDA, the Company has embarked on Phase 2 or 3 trials for VAL-083 across recurrent and newly diagnosed GBM. DelMar has announced plans to advance VAL-083 into a pivotal randomized multi-center Phase 3 clinical trial for the treatment of bevacizumab-failed GBM, a Phase 2 trial (with MD Anderson Cancer Center) in first recurrence GBM patients prior to bevacizumab therapy, and into a separate international Phase 2 trial for newly diagnosed MGMT-unmethylated GBM. DelMar believes that data from its clinical trials, if successful, will form the basis of a new treatment paradigm for the vast

majority of GBM patients whose tumors exhibit features that make them unlikely to respond to currently available therapies.

About Glioblastoma Multiforme (GBM)

GBM is the most common and aggressive primary brain cancer. Current standard of care includes surgery, radiation and treatment with temozolomide (TMZ), however nearly all tumors recur and the prognosis for recurrent GBM is dismal. Most GBM tumors have unmethylated promoter status for MGMT. Second-line treatment with anti-angiogenic agent bevacizumab has not improved overall survival (OS) and 5-year survival is less than 3%. VAL-083 (*dianhydrogalactitol*) is a first-in-class bi-functional DNA-targeting agent that induces interstrand DNA cross-links at the N7-position of guanine leading to DNA double-strand breaks and cell death in GBM cell lines and GBM cancer stem cells, independent of MGMT or MMR status *in vitro*. VAL-083 readily crosses the blood-brain barrier and accumulates in brain tumor tissue. Our recent Phase 1/2 clinical trial in recurrent GBM patients failing both TMZ and bevacizumab, suggested that VAL-083 offers clinically meaningful survival benefits for patients with recurrent GBM and pinpointed a new dosing regimen (40 mg/m²/d on days 1,2,3 of a 21-day cycle) which was well-tolerated and was selected for study in subsequent GBM trials. These trials include, i) an ongoing single-arm, biomarker driven, Phase 2 study to determine if VAL-083 treatment of MGMT-unmethylated adult GBM patients at first recurrence/progression, prior to bevacizumab improves overall survival, compared to historical control with lomustine (clinicaltrials.gov identifier: NCT02717962). ii) A pivotal Phase 3 study in recurrent GBM after failing both TMZ and bevacizumab. The control arm will consist of a limited number of salvage chemotherapies currently used in bevacizumab-failed GBM. If successful, this study will serve as the basis for a New Drug Application (NDA) submission for VAL-083. iii) A single arm, biomarker driven, Phase 2 study to confirm the tolerability and efficacy of VAL-083 in combination with radiotherapy in newly diagnosed MGMT-unmethylated GBM patients whose tumors are known to express high MGMT levels. The results of these studies may support a new treatment paradigm in chemotherapeutic regimens for the treatment of GBM.

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. DelMar's VAL-083 is currently undergoing clinical trials in the U.S. as a potential new therapy for GBM. VAL-083 has been extensively studied by the U.S. National Cancer Institutes, 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 <http://delmarpharma.com/>; or contact DelMar Pharmaceuticals Investor Relations: ir@delmarpharma.com / (604) 629-5989. Connect with the Company on [Twitter](#), [LinkedIn](#), [Facebook](#), and [Google+](#).

Safe Harbor Statement

Any statements contained in this press release that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities

Litigation Reform Act of 1995. Any forward-looking statements contained herein are based on current expectations, but are subject to a number of risks and uncertainties. The factors that could cause actual future results to differ materially from current expectations include, but are not limited to, risks and uncertainties relating to the Company's ability to develop, market and sell products based on its technology; the expected benefits and efficacy of the Company's products and technology; the availability of substantial additional funding for the Company to continue its operations and to conduct research and development, clinical studies and future product commercialization; and, the Company's business, research, product development, regulatory approval, marketing and distribution plans and strategies. These and other factors are identified and described in more detail in our filings with the SEC, including, our current reports on Form 8-K.



To view the original version on PR Newswire, visit <http://www.prnewswire.com/news-releases/delmar-presents-new-mechanism-of-action-data-for-its-lead-agent-val-083-in-temozolomide-resistant-glioblastoma-multiforme-gbm-at-the-world-federation-of-neuro-oncology-societies-wfnos-300452896.html>

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