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DelMar Presents Clinical Update on VAL-083 From Ongoing First- and Second-Line Trials in Patients with MGMT-unmethylated GBM at The Society for NeuroOncology Annual Meeting

VANCOUVER, British Columbia and MENLO PARK, Calif., Nov. 20, 2018 /PRNewswire/ -- [DelMar Pharmaceuticals, Inc.](#) (NASDAQ: DMPI) ("DelMar" or the "Company"), a biopharmaceutical company focused on the development and commercialization of new cancer therapies, presented scientific updates, including data from two ongoing clinical trials, at the 23rd Annual Meeting and Education Day of the Society for Neuro-Oncology (SNO) held on November 15-18, 2018 in New Orleans, LA.

"In our much-awaited Phase 2 study of VAL-083 in patients with MGMT-unmethylated, Bevacizumab-Naïve Recurrent Glioblastoma Multiforme (rGBM), we are pleased with the accelerated enrollment of this study with the vast majority of subjects already enrolled. What has become amply clear is that in this aggressive tumor type, which can double in size every 6-8 weeks, VAL-083 when used for two or more cycles can stabilize the tumor and slow down its incessant growth," commented Saiid Zarrabian, President and Chief Executive Officer.

"At this time, some subjects are still on drug and others are being followed for survival and we wait to see if this observed stabilization of the tumor favorably impacts median overall survival. The preclinical and clinical efficacy of VAL-083 in MGMT-unmethylated GBM population, along with the 2017 revised NCCN guidelines for MGMT-unmethylated patients which cautions against the use of temozolomide for MGMT-unmethylated GBM patients, creates a therapeutic opportunity not only for newly diagnosed patients, but also in the follow-on maintenance setting currently using temozolomide, all of which signals a path forward for VAL-083," added Mr. Zarrabian.

At the SNO 2018 conference, DelMar provided an update on the company's ongoing Phase 2 clinical study in a poster entitled "*Phase 2 Study of Dianhydrogalactitol (VAL-083) in Patients with MGMT-unmethylated, Bevacizumab-Naïve Recurrent Glioblastoma.*" This study is being conducted in collaboration with The University of Texas MD Anderson Cancer Center (MDACC). This biomarker-driven trial (testing for MGMT methylation status) is designed to enroll up to 48 patients to determine if VAL-083 treatment improves overall survival compared to historical reference control of 7.15 months with lomustine.

- As of October 31, 2018, 44 (of 48) patients have been enrolled
- 41 of those enrolled have received at least 1 cycle of VAL-083
- 7 patients are currently receiving treatment; 22 being followed for survival; 19 deceased thus far
- Study subjects received a median of 2 cycles of therapy
 - 12 patients received only 1 cycle of VAL-083
 - 2 patients received 1 cycle and are ongoing
 - 27 patients completed 2 or more cycles of therapy
- Of the 27 subjects that completed at least 2 cycles of treatment, 9/27 (33.33%) subjects exhibited stable disease (SD) at the end of cycle 2
 - 8/23 initially receiving 40 mg/m² exhibited SD at the end of cycle 2
 - 1/4 initially receiving 30 mg/m² exhibited SD at the end of cycle 2
- The most prevalent side effect with the 40 mg/m²/day dose of VAL-083 was myelosuppression (thrombocytopenia and neutropenia)
- Myelosuppression was also correlated with prolonged (> 5 cycles) prior front-line temozolomide use
 - in such patients a VAL-083 dose reduction to 30 mg/m² was found optimal

The Company also provided an update on its Phase 1/2 clinical study in a poster entitled "*Phase I/II Study of Dianhydrogalactitol (VAL-083) with Radiation Therapy with Newly Diagnosed MGMT-unmethylated Glioblastoma.*" This trial is being conducted at the Sun Yat-sen University Cancer Center (SYSUCC) in Guangzhou, China in collaboration with Guangxi Wuzhou Pharmaceutical Company. The trial is designed to enroll up to 30 patients to determine if first-line therapy with VAL-083 treatment, *in lieu* of first-line temozolomide, improves progression free survival (PFS).

- As per the 2017 National Comprehensive Cancer Network (NCCN) guidelines, this trial sets out with the vision of eradicating the unnecessary use of temozolomide in the approximately 60% of GBM patients, as noted in prior studies, with unmethylated MGMT gene promoter
- The Company reported that 10 patients have been enrolled as of October 31, 2018
- These 10 patients were part of the "3+3" dose escalation cohorts, and were treated with VAL-083 at each different dose on days 1 to 3 of a 21-day cycle along with radiation at 2Gy/day x 5 days for 6 weeks. The same dosing regimen of VAL-083 would be applied during the maintenance stage following six-week chemo-radiation
- In the dose-escalation stage, grade 3+ myelosuppression was observed in 2 of 3 patients treated with VAL-083 at 40 mg/m²/day
- The lower VAL-083 dose of 30 mg/m²/day was hence moved forward into the expansion phase of the trial
- A 20-patient expansion cohort has now commenced enrolling
- The primary endpoint of this trial is progression free survival and secondary endpoints include tumor response, overall survival and pharmacokinetics

In addition, DelMar presented three preclinical updates during the conference:

VAL-083 Inhibits Proliferation of a Panel of Eight Glioblastoma Stems Cell Lines: Downregulation of BDR4 as a Novel Anti-Neoplastic Mechanism

In this poster, the authors discuss their preclinical finding that when glioblastoma stem cell lines are treated with VAL-083 there is a downregulation of the transcription activator bromodomain-containing protein 4 (BRD4).

Chromatin remodeling through histone acetylation is a key step in the regulation of the gene expression in both normal and tumor cells. Members of the bromodomain family of proteins, such as BRD4, interact with acetylated histones to assemble chromatin complexes and transcription activators at specific gene promoter sites, including tumor oncogenes. Selective downregulation of bromodomain proteins such as BRD4 by agents such as VAL-083 can therefore inhibit the interaction of BRD4 with acetylated histones at promoter sites, resulting in a reduction of downstream signaling events. Thus, it is possible that VAL-083 may elicit its DNA-damaging action, at least in part, by interrupting chromatin remodeling in cancer cells.

Dianhydrogalactitol (VAL-083) has the Potential to Overcome Major Challenges in the Treatment of Diffuse Intrinsic Pontine Glioma (DIPG)

In this poster, the authors discuss the potential for VAL-083 either as a single-agent, or as part of combination therapy regimens, for the treatment of diffuse intrinsic pontine glioma (DIPG). DIPG is a difficult-to treat, inoperable, rare pediatric brain tumor with very poor prognosis and a dismal survival outlook. In this poster the authors report that VAL-083 is active as a single-agent and synergistic with AZD1775, a Wee1 inhibitor, against DIPG cell lines with varying genetic profile.

Dianhydrogalactitol (VAL-083) Reduces Glioblastoma Tumor Growth In Vivo Upon Bevacizumab-induced Hypoxia

Treatment of GBM with second-line bevacizumab after progression on first-line temozolomide is the standard-of-care for this disease. However, bevacizumab has not only failed to show an improved benefit in these patients, but has also been found to induce intratumor hypoxia, which is then implicated in increased chemoresistance. Preclinically, it has been previously demonstrated that bevacizumab hypoxia upregulates GLUT-1/GLUT-3 glucose transporters. In such a milieu, VAL-083, due to its simple structure, has a unique advantage of enhanced intra-tumoral transport and uptake. The authors seek confirmation of this *in-vitro* observation in a GBM xenograft model. The data shows that in such mouse models the GBM tumor shrinkage is best when bevacizumab and VAL-083 are administered together compared to when either agent is used as monotherapy.

DelMar's poster presentations can be viewed on the company's website at <http://www.delmarpharma.com/scientific-publications.html>

About VAL-083

VAL-083 (dianhydrogalactitol) is a "first-in-class," bifunctional DNA-targeting agent that introduces interstrand DNA cross-links at the N7-position of guanine leading to DNA double-strand breaks and cancer cell death. VAL-083 has demonstrated clinical activity against a range of cancers including GBM and ovarian cancer in historical clinical trials sponsored by the U.S. National Cancer Institute (NCI). DelMar has demonstrated that

VAL-083's anti-tumor activity is unaffected by common mechanisms of chemoresistance, including MGMT, in cancer cell models and animal studies. Further details regarding these studies can be found at:

<http://www.delmarpharma.com/scientific-publications.html>.

VAL-083 has been granted orphan drug designations by the U.S. FDA Office of Orphan Products for the treatment of glioma, medulloblastoma and ovarian cancer, and in Europe for the treatment of malignant gliomas. VAL-083 has been granted fast-track status for the treatment of recurrent GBM by the US FDA.

About DelMar Pharmaceuticals, Inc.

DelMar is focused on the development and commercialization of new therapies for cancer patients who have limited or no treatment options. By focusing on understanding tumor biology and mechanisms of treatment resistance, the Company identifies biomarkers to personalize new therapies in indications where patients are failing, or are unable to tolerate, standard-of-care treatments.

The Company's current pipeline is based around VAL-083, a "first-in-class," small-molecule chemotherapeutic with a novel mechanism of action that has demonstrated clinical activity against a range of cancers including central nervous system, ovarian and other solid tumors (e.g. NSCLC, bladder cancer, head & neck) in U.S. clinical trials sponsored by the National Cancer Institute (NCI). Based on DelMar's internal research programs, and these prior NCI-sponsored clinical studies, the Company is conducting clinical trials to support the development and commercialization of VAL-083 to solve significant unmet medical needs.

VAL-083 is being studied in two collaborator-supported, biomarker-driven, Phase 2 clinical trials for MGMT-unmethylated GBM. Overcoming MGMT-mediated resistance represents a significant unmet medical need in the treatment of GBM. In addition, DelMar has announced the allowance of a separate IND for VAL-083 as a potential treatment for platinum-resistant ovarian cancer.

Further information on DelMar's clinical trials can be found on clinicaltrials.gov:
<https://www.clinicaltrials.gov/ct2/results?cond=&term=val-083&cntry1=&state1=&recrs>

For additional information, please visit <http://delmarpharma.com/>; or contact DelMar Pharmaceuticals Investor Relations: ir@delmarpharma.com / (604) 629-5989.

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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 the Company's filings with the SEC, including, the Company's Annual Report on Form 10-K for the year ended June 30, 2018, the Company's Quarterly Reports on Form 10-Q, and the Company's Current Reports on Form 8-K.



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