

November 14, 2014



# DelMar Pharmaceuticals Presents Preclinical Data Supporting VAL-083 as a Potential New Treatment in Glioblastoma at the Society of Neuro-Oncology Annual Meeting

## VAL-083 Anti-tumor Activity Is Consistently Superior to Temozolomide in Preclinical Models of Glioblastoma

VANCOUVER, British Columbia, MENLO PARK, Calif., and MIAMI, Nov. 14, 2014 /PRNewswire/ -- [DelMar Pharmaceuticals, Inc.](#) (OTCQB: DMPI) ("DelMar" and "DelMar Pharma") today announced the presentation of an abstract entitled, *In vivo efficacy of VAL-083 in the treatment of MGMT-positive glioblastoma multiforme (GBM)*.

"The purpose of this study is to evaluate the activity of VAL-083 in comparison to temozolomide in preclinical models of glioblastoma multiforme," said Jeffrey Bacha, president and CEO of DelMar Pharmaceuticals, Inc. "We saw in comparative *in vitro* studies, VAL-083 was not only cytotoxically active against temozolomide-resistant cell lines with high MGMT levels, it was also substantially more potent than temozolomide against cell lines expressing low levels of MGMT, that are known to be susceptible to temozolomide."

The cytotoxic mechanism of VAL-083 is understood to be via interstrand bi-functional cross-links at the N<sup>7</sup> position of guanine leading to double-strand DNA breaks and apoptosis. This mechanism is distinct from temozolomide, the current standard of care in glioblastoma, which primarily acts by mono-functional methylation at the O<sup>6</sup> position of guanine. The anti-cancer mechanism of temozolomide is known to be repaired by the enzyme O<sup>6</sup> methylguanine methyltransferase (MGMT), which causes chemotherapy resistance.

"More than two-thirds of glioblastoma patients will fail Temodar because of chemotherapy resistance. DelMar's research demonstrates that the anti-cancer activity of VAL-083 is independent of MGMT, which is known to reverse the anti-cancer activity of temozolomide. Taken together, these results suggest that VAL-083 may be a promising therapeutic option for patients with high expression of MGMT, who fail or are unlikely to respond to standard temozolomide therapy," concluded Mr. Bacha.

### ***In Vitro Study Results***

In SF188 (pediatric GBM) and U251 (adult GBM) cell lines, which are characterized by low expression of MGMT, the concentration of temozolomide required to inhibit tumor cell growth

by 50% (IC50) was approximately 50uM whereas the IC50 for VAL-083 in the same cell lines was approximately 2.5 – 5 uM, doses that should be readily achievable in patients.

Temozolomide was ineffective at doses in up to 100 uM against the T98G cell line (adult GBM), which is known to exhibit high expression of MGMT, while the IC50 of VAL-083 was maintained at 2.5 uM.

VAL-083 furthermore inhibited the growth of brain tumor initiating cells (BTICs) (BT74, GBM4 and GBM8) by 80-100% in neurosphere growth assays, with minimal effect on normal human neural stem cells. Temozolomide was ineffective against these BTICs, which are thought to give rise to relapse as they are often resistant to chemotherapy.

### ***In Vivo Study Results***

To examine the comparative effects of VAL-083 and temozolomide, we established a mouse model of glioblastoma with female Rag2 mice bearing intracranial human GBM xenograft tumors of U251MG (temozolomide-sensitive) or BT74 (temozolomide-resistant) origin in collaboration with researchers at the British Columbia Cancer Agency. The research was funded in-part by a non-repayable financial contribution from the National Research Council of Canada Industrial Research Assistance Program (NRC-IRAP).

On day 0,  $7.5 \times 10^4$  cells were implanted intracranially. On day 18, treatment with temozolomide or VAL-083 was initiated. Disease progression is evaluated by overall survival, clinical observations and body weight measurements. Animals were treated with a dose of 30 mg/kg of temozolomide; we explored three different doses of VAL-083 ranging from 3 mg/kg to 5 mg/kg.

As expected, animals bearing U251 (temozolomide-sensitive) tumors were sensitive to both temozolomide and VAL-083. Treatment with either compound resulted in a statistically significant survival benefit. Studies with BT74 (temozolomide-resistant) tumors are ongoing.

DelMar will present two additional abstracts this evening, Friday November 14, 7:30pm EST, during the Evening Scientific Session.

**Title: VAL-083 is a novel N<sup>7</sup> alkylating agent that inhibits the growth of glioma stem and non-stem cultures, including temozolomide-resistant lines**

[Link to DelMar \*in vitro\* abstract ET-18](#)

**Title: Phase I/II study of dianhydrogalactitol (VAL-083) in patients with recurrent malignant glioblastoma multiforme (GBM)**

[Link to DelMar clinical abstract AT-53](#)

Copies of the DelMar presentations will be available on the company's website at: <http://www.delmarpharma.com/products/publications/>

### **About VAL-083**

VAL-083 (*dianhydrogalactitol*) is a first-in-class, small-molecule chemotherapeutic with a unique mechanism of action. In more than 40 Phase 1 and 2 clinical studies sponsored by

the National Cancer Institute, VAL-083 has shown safety and efficacy in treating a number of cancers including lung, brain, cervical, ovarian tumors and leukemia. VAL-083 is approved in China for the treatment of chronic myelogenous leukemia and lung cancer and has received orphan drug designation in Europe and the U.S. for the treatment of gliomas. As a potential treatment for glioblastoma, VAL-083's mechanism of action is unaffected by the expression of MGMT, a DNA repair enzyme that causes chemotherapy resistance to front-line treatment with Temodar® (temozolomide). DelMar is currently studying VAL-083 in a Phase 1/2 clinical trial for patients with refractory glioblastoma multiforme.

### **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 the Society for Neuro-Oncology (SNO) annual meeting**

The Society for Neuro-Oncology is a multidisciplinary organization dedicated to promoting advances in neuro-oncology through research and education. It is the premier North American organization for clinicians, basic scientists, nurses and other health care professionals whose focus is central nervous system tumors in children and adults. The 19th Annual Scientific Meeting and Education Day will be held November 13-16, 2014, at the Loews Hotel South Beach in Miami.

### **About DelMar Pharmaceuticals, Inc.**

DelMar Pharmaceuticals, Inc. was founded to develop and commercialize proven cancer therapies in new orphan drug 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 U.S. National Cancer Institute, and is currently approved for the treatment of chronic myelogenous leukemia (CML) 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 more information, please visit [www.delmarpharma.com](http://www.delmarpharma.com) or follow us on Twitter [@delmarpharma](https://twitter.com/delmarpharma) or [Facebook.com/delmarpharma](https://www.facebook.com/delmarpharma).

### ***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. We do not undertake to update these forward-looking statements made by us.*

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