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# DelMar Pharmaceuticals Announces New Data Supporting the Unique Anti-cancer Mechanism of VAL-083

## Unique mechanism of action takes advantage of tumor mutations; Findings provide direction for future combination therapies

VANCOUVER, British Columbia and MENLO PARK, Calif., April 19, 2016 /PRNewswire/ -- DelMar Pharmaceuticals, Inc. (OTCQX: DMPI) ("DelMar" and the "Company"), a biopharmaceutical company focused on the development and commercialization of new cancer therapies, today announced that its collaborators from the University of British Columbia's Vancouver Prostate Center presented results of new research related to the anti-cancer mechanism of its lead anti-cancer product candidate, VAL-083 (*dianhydrogalactitol*).

Abstract **#2985**: *"Molecular mechanisms of dianhydrogalactitol (VAL-083) in cancer treatment,"* is being presented during this morning's "New Mechanisms of Anticancer Drug Action" session at the American Association of Cancer Research (AACR) Annual Meeting in New Orleans.

Specifically,

- VAL-083 displayed broad anti-tumor activity against lung and prostate cancer cells;
- VAL-083 treatment causes rapid and durable DNA interstrand crosslinks leading to irreparable DNA double-strand breaks, S/G2 phase cell-cycle arrest and apoptosis in cancer cells; and
- This new understanding of the molecular mechanisms underlying VAL-083's anti-cancer activity offers support for effective combination therapies.

"These data indicate that the DNA-damaging cross-links resulting from VAL-083 treatment occur rapidly and, once formed, are not easily repaired by the cell," noted Dr. Dennis Brown, DelMar's Chief Scientific Officer.

"Typically, a normal cell employs check-point control and DNA repair mechanisms to identify

and remove DNA cross-links and double strand breaks such as those resulting from treatment with VAL-083. However, cancer cells, by their very nature tend to have mutations or deficiencies in these mechanisms that may allow VAL-083 mediated cross-links to persist resulting in irreparable and lethal damage to the tumor cell."

Jeffrey Bacha, DelMar's chairman & CEO continued, "These findings are very exciting and continue to support our belief that VAL-083's anti-cancer mechanism is unique. Understanding where in the cell cycle VAL-083 elicits its cancer-lethal activity provides guidance in considering combination therapies. This knowledge combined with our own and historical clinical data demonstrating activity against a number of tumors truly establishes a broad stage for the future clinical development of VAL-083."

**About the Research:**

VAL-083 (dianhydrogalactitol) is a bi-functional alkylating agent causing N7-guanine alkylation and inter-strand DNA crosslinks. VAL-083's cytotoxic activity is independent of MGMT-expression in various cancer cells and cancer stem cells, suggesting a mechanism that is distinct from that of other alkylating agents. Preclinical and clinical trial data suggest that VAL-083 may have effects in treating various cancers, including lung, brain, cervical, ovarian tumors, and leukemia. However, the detailed molecular mechanisms mediating VAL-083 sensitivity or resistance in cancer have been unclear.

This research was undertaken to investigate the signaling events responsible for VAL-083's robust activity against cancer.

Crystal violet proliferation assays were performed to assess VAL-083 sensitivity in a variety of cancer cell lines. Propidium iodide (PI) staining and immunofluorescent analyses were used to evaluate cell cycle phases. Western blots were employed to investigate DNA damage response induced by VAL-083 treatment.

Pulse (1 hour) treatment with VAL-083 activated DNA damage signaling pathway as demonstrated by expression of phospho-ATM (S1981), phospho-Chk2 (T68), phospho-RPA32 (S33) and ɣH2A.X which persisted for 24 - 48 hours after removal of VAL-083 from the medium. Specifically, VAL-083 treatment led to long-lasting cell cycle arrest at S/G2 phase of the cell cycle. Additionally, DNA double-strand break signals such as increased levels of ɣH2A.X continued to accumulate at 72 hours following treatment of cancer cells with VAL-083, demonstrating irreparable damage to the tumor cell.

**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 FDA'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 (Avastin™) and a range of salvage therapies 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).

Interim data from the ongoing Phase I/II clinical trial were presented today at the American Association of Cancer Research Annual Meeting (abstract #CT074). Results to date support the potential of a 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. DelMar plans to discuss a proposed Phase III protocol with the FDA in the coming months.

Further details can be found at http://www.delmarpharma.com/scientific-publications.html.

**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 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+. Investor Relations Counsel: Amato & Partners LLC.

***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.*

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To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/delmar-pharmaceuticals-announces-new-data-supporting-the-unique-anti-cancer-mechanism-of-val-083-300253664.html

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