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DelMar Pharmaceuticals Presents Positive Preclinical Data on VAL-083 for Treatment of Non-Small Cell Lung Cancer at the American Association of Cancer Research Annual Meeting

- Data support VAL-083's importance as a potential therapy for non-small cell lung cancer (NSCLC), including drug-resistant NSCLC -

VANCOUVER, British Columbia and MENLO PARK, Calif., April 19, 2015 /PRNewswire/ -- [DelMar Pharmaceuticals, Inc.](#) (OTCQX: DMPI) (DelMar and the Company), a biopharmaceutical company focused on developing and commercializing proven cancer therapies in new orphan drug indications, today announced positive preclinical data on its lead product candidate [VAL-083](#) (dianhydrogalactitol) for treatment of platinum drug-resistant non-small cell lung cancer (NSCLC) and as a potential combination therapy option in newly diagnosed NSCLC patients.

VAL-083 is a 'first-in-class' bi-functional alkylating agent mediating inter-strand DNA crosslinks at N⁷ of guanine. VAL-083 has previously demonstrated activity against lung cancer in preclinical and clinical trials and is approved for treatment of lung cancer in China.

The data was presented in a poster entitled, "*In vitro activity of dianhydrogalactitol alone or with platinum drugs in the treatment of non-small cell lung cancer*," at the [106th Annual Meeting of the American Association for Cancer Research](#) (AACR), being held April 18-22, 2015, in Philadelphia, Pennsylvania.

The purpose of this study was to investigate: 1) the role of p53 status in the activity of VAL-083; 2) VAL-083 activity in comparison to cisplatin and oxaliplatin; and 3) the combination of VAL-083 with cisplatin or oxaliplatin.

"We previously presented data demonstrating that VAL-083 is active against platinum and tyrosine-kinase resistant NSCLC in *in vivo* models of lung cancer," stated Mr. Bacha, DelMar's president and CEO. To further research these observations, DelMar's team worked with leading researchers at MD Anderson cancer center to explore the potential relationship between the activity of the p53 gene and VAL-083's activity in drug-resistant non-small cell lung cancer."

The p53 gene plays a central role in the protection of the human body from cancer and is responsible for initiating the process of programmed cell death, or apoptosis, which directs a

cell to commit suicide if it becomes damaged or cancerous. The p53 pathway is also integral to the activity of many chemotherapy drugs. p53 is frequently mutated in NSCLC and p53 mutations are highly correlated with resistance to chemotherapy and poor patient outcomes in NSCLC.

DelMar's study demonstrated that VAL-083's mechanism is distinct from platinum-based chemotherapy, the current standard of care for NSCLC. VAL-083 retains its high level of anti-cancer activity in p53 mutated NSCLC cell lines compared to cisplatin or oxaliplatin which provides support for the potential of VAL-083 as a viable treatment option for NSCLC patients failing platinum-based therapy.

In addition, the combination of VAL-083 with either cisplatin or oxaliplatin demonstrated superadditivity/synergy against NSCLC cell lines, including those resistant to tyrosine kinase inhibitors. These results support the potential benefit of a VAL-083/platinum combination therapy in newly diagnosed NSCLC patients.

"VAL-083's novel cytotoxic mechanism is distinct from other alkylating agents used in the treatment of cancer and the data from this study show the promise of VAL-083 not only in drug-resistance NSCLC, but also as a standalone agent and potential in combination therapy," added Mr. Bacha. "As a next step, we plan to initiate a clinical study of VAL-083 in relapsed or refractory NSCLC patients to further explore the potential of VAL-083 to become a key component of modern lung cancer therapy."

A summary of the results of the preclinical *in vitro* study of VAL-083 alone or with platinum drugs in the treatment of NSCLC are below and the Company's poster presentation may be found on DelMar's website under <http://www.delmarpharma.com/products/publications/>.

About Lung Cancer

Lung cancer is a leading cause of cancer-related mortality around the world. In general, prognosis for lung cancer patients remains poor, with 5-year relative survival less than 14% among males and less than 18% among females in most countries. Globally, the market for lung cancer treatments may exceed \$7 billion by 2019 according to report published by Transparency Market research.

Non-small cell lung cancer is the most common type of lung cancer, accounting for 85% of all lung cancer cases in the United States and approximately 90% of lung cancer cases diagnosed in China. NSCLC is usually treated with surgery followed by treatment with either tyrosine kinase inhibitors (TKIs) or platinum-based chemotherapy regimens. TKI resistance has emerged as a significant unmet medical need, and long-term prognosis with platinum-based therapies is poor.

The role of p53 status in the activity of VAL-083

VAL-083 dependence on p53 status was investigated in isogenic models with or without p53 knockout. Loss of p53 increased resistance to cisplatin and oxaliplatin by three- and six-fold, respectively, whereas the increase in resistance to VAL-083 was less than two-fold. This suggests a mechanism of VAL-083 that is less dependent on wild-type p53 for its activity than both cisplatin and oxaliplatin and appears to have a distinct mode of action.

VAL-083 cytotoxicity activity in comparison to cisplatin and oxaliplatin

The cytotoxic activity of VAL-083 was tested in a panel of nine human NSCLC cell lines, of

which four were wild-type (wt) p53, four were mutant p53 and one was null for p53, and VAL-083 demonstrated cytotoxic activity in all tested NSCLC cell lines. As single agents, VAL-083, cisplatin and oxaliplatin displayed cytotoxic activity in all nine NSCLC cell lines to varying degrees, with H460 being the most sensitive to the three agents ($IC_{50} < 0.5 \mu M$). The IC_{50} in the other cell lines ranged from 0.9 to 6.1 μM , 0.5 to 2.2 μM and 0.6 to 2.6 μM for VAL-083, cisplatin and oxaliplatin, respectively, and there was no overt difference in drug sensitivity between the wt and mutant/null p53 group. This suggests that either wt p53 is not activated and/or other genetic alterations attenuate cytotoxic activities. If the agents have similar mode of action, then combinations may only demonstrate cytotoxic additivity.

Combination of VAL-083 with cisplatin or oxaliplatin

The potential for VAL-083 in combination with either cisplatin or oxaliplatin was investigated in human H460, A549 and H1975 NSCLC models by determining superadditivity and assessing synergy using the criteria of combination index (CI) of < 1 , obtained by following the Compusyn constant-dose ratio protocol. Cytotoxicity in all cases was monitored on day five with the MTT assay. VAL-083 demonstrated significant superadditivity (p less than or equal to 0.05) and/or synergism ($CI < 1$) against these NSCLC cell lines in combination with either cisplatin or oxaliplatin.

Significantly, this cytotoxic effect of VAL-083 in combination with either platinum drug was observed in both TKI-resistant (H1975) and TKI-sensitive (H460 and A549) NSCLC cells. These results suggest non-overlapping mechanism of action between the platinum drugs and VAL-083, and support the potential for synergistic benefit for a combination of VAL-083 and platinum-based therapies. This strongly favors non-overlapping mechanism of action between the platinum drugs and VAL-083.

About VAL-083

[VAL-083](#) is a "first-in-class", small-molecule chemotherapeutic. In more than 40 Phase 1 and 2 clinical studies sponsored by the National Cancer Institute, VAL-083 demonstrated 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 appears to be 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 I/II clinical trial for patients with refractory glioblastoma multiforme.

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 further information, please visit <http://delmarpharma.com/>; or contact DelMar Pharmaceuticals Investor Relations: ir@delmarpharma.com / (604) 629-5989 follow us on Twitter [@DelMarPharma](https://twitter.com/DelMarPharma) or [Facebook.com/delmarpharma](https://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.

To view the original version on PR Newswire, visit <http://www.prnewswire.com/news-releases/delmar-pharmaceuticals-presents-positive-preclinical-data-on-val-083-for-treatment-of-non-small-cell-lung-cancer-at-the-american-association-of-cancer-research-annual-meeting-300068212.html>

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