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DelMar Pharmaceuticals Presents Positive Data on the Benefit of VAL-083 in Combination with Platinum-Based Chemotherapy for Non-Small Cell Lung Cancer (NSCLC)

- VAL-083 retains activity in chemo-resistant NSCLC tumor types -

- VAL-083 demonstrates a super-additive effect in NSCLC when used in combination with platinum-based chemotherapeutic agents -

VANCOUVER, British Columbia and MENLO PARK, Calif., Nov. 6, 2015 /PRNewswire/ -- DelMar Pharmaceuticals, Inc. (OTCQX: DMPI) ("DelMar" and the "Company"), a biopharmaceutical company focused on the development and commercialization of new cancer therapies, today presented data on the benefit of VAL-083 (*dianhydrogalactitol*) in combination with platinum-based chemotherapy regimens in the treatment of non-small cell lung cancer (NSCLC).

"We have recently shown that VAL-083's mechanism is distinct from platinum-based chemotherapy, the current standard of care for NSCLC, and is active against platinum and TKI-resistant NSCLC in both *in vitro* and *in vivo* models of lung cancer," stated Jeffrey Bacha, DelMar's president and CEO. "The data presented today further demonstrate the non-overlapping mode of action between the platinum drugs and VAL-083 and the potential for treatment synergy in combination with therapeutic regimens."

The Company presented results from a collaborative study on the potential of VAL-083 in NSCLC in a poster entitled, "*Dianhydrogalactitol (VAL-083) enhances activity of platinum drugs in non-small cell lung cancer*," at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, hosted by American Association for Cancer Research, the National Cancer Institute, and the European Organisation for Research and Treatment of Cancer. The study was conducted in conjunction with research teams at MD

Anderson Cancer Center, Shanghai Chest Hospital, and the BC Cancer Agency.

NSCLC is generally treated with surgery followed by chemotherapy with either tyrosine kinase inhibitors (TKIs) or platinum-based regimens, but long term prognosis is poor. VAL-083 is a "first-in-class" bi-functional alkylating agent with proven activity against NSCLC in preclinical and clinical studies that meditates inter-strand DNA crosslinks at N7 of guanine.

VAL-083 demonstrated clinical activity as a single agent and in combination therapy in prior clinical trials sponsored by the US National Cancer Institutes (NCI) and has been approved by the Chinese Food and Drug Administration (CFDA) for the treatment of lung cancer. Use of VAL-083 in China has been limited by a lack of modern data and preference for targeted therapies, such as TKIs, in the modern era.

The results of the study presented at AACR-NCI-EORTC support VAL-083 as a viable treatment option for NSCLC patients who fail to respond to standard-of-care platinum-based therapy or TKI therapy, and also support potential therapeutic benefit of a VAL-083 along with platinum combination regimens in newly diagnosed patients:

- VAL-083 demonstrated cytotoxic activity in all tested NSCLC cell lines, including TKI-resistant cell lines;
- VAL-083 demonstrated super-additivity/synergy against NSCLC cell lines H460, A549 and H1975 when combined with either cisplatin or oxaliplatin, *in vitro*;
- VAL-083 is less dependent on p53 for its activity than both cisplatin and oxaliplatin, and appears to have a distinct mode of action in comparison to platinum-based chemotherapy; and
- The combination of VAL-083 with cisplatin significantly decreased tumor growth and increased median survival time in a xenograft A549 in vivo model of NSCLC.

"These data are aligned with our strategy to leverage VAL-083's established clinical activity with modern biologic research to target specific, underserved markets where resistance to current standard-of-care is correlated with poor patient outcomes. This tactic establishes a personalized-medicine approach based on a potent and broadly-active chemotherapy to address significant unmet medical needs in the modern treatment of cancer," Mr. Bacha added.

SUMMARY

The purpose of the *in vitro* portion of this study was to investigate: 1) the role of p53 status in VAL-083 activity; 2) VAL-083 cytotoxicity in a panel of NSCLC cell lines; and 3) the combination of VAL-083 with cisplatin or oxaliplatin in NSCLC cells.

Additionally, the combination of VAL-083 with cisplatin in NSCLC was also studied *in vivo*. Dependence on p53 status was investigated in isogenic HCT-116p53-/- and HCT-116p53+/+ models. VAL-083, cisplatin and oxaliplatin cytotoxicity was tested in a panel of nine (9) human NSCLC cell lines: four (4) wt, four (4) mutant and one (1) null for p53. The combination potential for VAL-083 with cisplatin or oxaliplatin was investigated in three (3) human NSCLC cell lines, H460 (p53wt), A549 (p53wt) and H1975 (p53mut), by determining super-additivity and synergy using the criteria of combination index (CI)<1.

VAL-083 showed cytotoxic activity against all NSCLC cell lines in a human NSCLC panel, including TKI-resistant cell lines

VAL-083, cisplatin and oxaliplatin were tested in a panel of nine (9) human NSCLC cell lines, of which four (4) were wild-type p53 (H460, A549, H838, H226), four (4) were mutant p53 (H1975, SkLU1, H2122, H157) and one (1) was null for p53 (H1299). VAL-083 was active against all tested NSCLC cell lines, including TKI-resistant cell lines H1975, H460, and H1299, and VAL-083 activity was independent of p53 status.

VAL-083 mechanism is less dependent on p53

The dependence on p53 status was investigated in isogenic models with (HCT-116$^{p53-/-}$) or without (HCT-116$^{p53+/+}$) p53 knockout. Loss of p53 increased resistance to cisplatin and oxaliplatin by 3- and 6-fold, respectively, whereas the increase in resistance to VAL-083 was <2-fold. This suggests a mechanism of VAL-083 that is less dependent on wild-type p53.

VAL-083 displays synergy in combination with cisplatin or oxaliplatin in NSCLC cells H460, A549 and H1975, *in vitro*

The combination of VAL-083 with either cisplatin or oxaliplatin in three human NSCLC cell lines demonstrated significant super-additivity ($p \leq 0.06$) and/or synergism ($CI < 1$) for both combinations, *in vitro.* Significantly, this cytotoxic effect of VAL-083 in combination with either platinum drug was observed in both TKI-resistant (H1975 and H460) and TKI-sensitive (A549) NSCLC cells, irrespective of their p53 status. 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 in the treatment of lung cancer, including TKI-resistant NSCLC.

VAL-083/cisplatin combination increase median survival time in A549 NSCLC model, *in vivo*

Rag2 mice bearing A549 xenograft tumors were treated with vehicle, 2 mg/kg cisplatin alone, or cisplatin in combination with VAL-083 (2, 2.5, or 3 mg/kg). VAL-083 in combination with cisplatin significantly and dose-dependently decreased tumor growth in the animals and increased median survival time compared to both cisplatin treatment alone and to untreated control.

Mr. Bacha added, "We continue to build a significant portfolio of data demonstrating the activity of VAL-083 against a range of tumors, independent of their p53 status. These data taken together with the historical clinical activity support the potential of VAL-083 in NSCLC. An important next step will be to initiate new clinical studies to validate the clinical activity of VAL-083 in patients with relapsed or refractory NSCLC who currently have a lack of treatment options and poor prognosis."

"Interestingly, recent literature also correlate p53 mutations with high expression of MGMT and poor outcomes in the treatment of glioblastoma multiforme (GBM). Therefore, this latest research likewise supports the potential of our ongoing clinical research with VAL-083 as a potential new therapy in the treatment of refractory GBM," concluded Mr. Bacha.

The poster highlighting the potential of VAL-083 in NSCLC may be found on DelMar's website under http://www.delmarpharma.com/scientific-publications.html.

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 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 recently announced the completion of enrollment in a Phase II clinical trial of VAL-083 in refractory GBM. Patients have been enrolled 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).

In the Phase I dose-escalation portion of the study, VAL-083 was well tolerated at doses up to 40mg/m^2 using a regimen of daily x 3 every 21 days. Adverse events were typically mild to moderate; no treatment-related serious adverse events reported at doses up to 40 mg/m^2. Dose limiting toxicity (DLT) defined by thrombocytopenia (low platelet counts) was observed in two of six (33%) of patients at 50 mg/m^2. Generally, DLT-related symptoms resolved rapidly and spontaneously without concomitant treatment, although one patient who presented with hemorrhoids received a platelet transfusion as a precautionary measure.

Sub-group analysis of data from the Phase I dose-escalation portion of the study suggested a dose-dependent and clinically meaningful survival benefit following treatment with VAL-083 in GBM patients whose tumors had progressed following standard treatment with temozolomide, radiotherapy, bevacizumab and a range of salvage therapies.

Patients in a low dose (≤5mg/m^2) sub-group had a median survival of approximately five (5) months versus median survival of approximately nine (9) months for patients in the therapeutic dose (30mg/m^2 & 40mg/m^2) sub-group following initiation of VAL-083 treatment. DelMar reported increased survival at 6, 9 and 12 months following initiation of treatment with VAL-083 in the therapeutic dose sub-group compared to the low dose sub-group.

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 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+. 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-presents-positive-data-on-the-benefit-of-val-083-in-combination-with-platinum-based-chemotherapy-for-non-small-cell-lung-cancer-nsclc-300173886.html

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