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GLOBAL FORMULATION REPORT

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Lilli Zakarija, MBA
Keys to a Robust Combination Product Design Verification & Validation

Roelof Rongen, MS
Encochleated Drug Formulations: Enhancing Efficacy, Minimizing Toxicity

Robert Lins, MD
Early Phase Pharmacodynamic Models for Respiratory Drug Candidates

IN THIS ISSUE

INTERVIEW WITH **DELMAR PHARMACEUTICALS'** CHAIRMAN & CEO JEFFREY BACHA, MBA

Drug Development
EXECUTIVE

Jeffrey Bacha, MBA
Chairman & CEO
DelMar Pharmaceuticals

DelMar Pharmaceuticals: Polishing NCI Diamonds in the Rough With Modern Science

DelMar Pharmaceuticals, Inc. was founded to develop and commercialize new cancer therapies in indications where patients are failing or have become intollerant to modern targeted or biologic treatments. The company's lead drug in development, VAL-083, is currently undergoing clinical trials in the US as a potential treatment for refractory glioblastoma multiforme. VAL-083 has been extensively studied by the US National Cancer Institute and is currently approved for the treatment of chronic myelogenous leukemia and lung cancer in China. Published preclinical 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. Jeffrey Bacha, Chairman & CEO of DelMar Pharmaceuticals, recently spoke with *Drug Development & Delivery* about the company's unique approach to developing VAL-083, the challenges in working within cancer indications associated with low survival, and the importance of strategic collaborations with universities and organizations to further develop its technology.

Q: Can you please provide some background on DelMar Pharmaceuticals for our readers?

A: DelMar was founded by myself and Dennis M. Brown, PhD, in 2010 around a drug candidate identified from prior work conducted by the US National Cancer Institute. VAL-083 had been studied in more than 40 published clinical trials sponsored by NCI. These studies demonstrated promising clinical activity against a number of tumors; however, like several other promising drug candidates of the era, VAL-083 was never commercialized. DelMar's strategy is to leverage that promising historical data with a robust, modern understanding of the drug's mechanism of action to identify opportunities to solve unmet clinical needs in the treatment of cancer today.

Q: How does DelMar's VAL-083 work and why is it so unique?

A: VAL-083 is a type of chemotherapy known as an alkylating agent. Alkylating agents bind to a tumor cell's DNA to interrupt cellular processes and kill the tumor. They are among the oldest types of cancer therapy still in use today. What we have demonstrated through our research in collaboration with institutions, such as MD Anderson Cancer Center and the BC Cancer Agency, is that the way VAL-083 binds to the tumor's DNA is different than other alkylating agents. This suggests – and our data supports – that VAL-083's activity is not subject to the same resistance mechanisms that hinder other treatments. Therefore, we have an opportunity to treat chemo-resistant cancers, and to consider combination therapies with other agents, including other chemotherapies and immunotherapy. Additionally, VAL-083 crosses the blood brain barrier. Most chemotherapies cannot. This provides an opportunity to treat brain tumors, which has been our primary area of clinical focus to date.

Q: How critical is historical data for a developing line of cancer therapies?

A: It is not critical, but it is certainly helpful in accelerating development as well as reducing cost, risk, and time to market.

Q: What are the top clinical indications for VAL-083?

A: Our focus is driven by our modern understanding of VAL-083's unique mechanism juxtaposed against historical clinical data from prior NCI-sponsored clinical trials. The first place this strategy has taken us is glioblastoma multiforme (GBM), which is the most common and aggressive form of brain cancer. Therapeutic options for GBM patients are limited, and patients who fail front-line therapy have a very poor prognosis.
The current standard-of-care in the treatment of GBM is surgery followed by chemotherapy combined with radiation. The challenge is that two-thirds of the patients diagnosed have tumors resistant to the chemotherapies available [mainly a drug called temozolomide (Temodar)]. Fortunately, researchers have developed an understanding of why patients fail Temodar – it is due to the activity of a DNA repair enzyme called MGMT. We have shown that VAL-083 is active independent of MGMT-mediated resistance mechanisms. That fact, combined with historical clinical data demonstrating activity of VAL-083 in the treatment of GBM give us confidence that we have an opportunity to treat patients whose tumors have failed or exhibit features making them unlikely to respond to Temodar. We have recently completed a Phase I/II clinical trial in refractory GBM.
Additional indications of interest – driven by our research into VAL-083's mechanism of action and historical clinical data – include non-small cell lung cancer, ovarian cancer, and childhood brain tumors. The FDA has granted VAL-083 an orphan drug designation for glioma, ovarian, and a type of childhood brain cancer known as medulloblastoma.

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Q: What are the challenges in working within cancer indications commonly associated with low survival expectations?

A: The biggest challenge is that the patients may be so sick that even if your drug works, it may be too late to help them in a meaningful way. To date, our data supports the potential to increase survival in refractory GBM patients who currently have a median survival of 2 to 5 months. We're excited to be able to offer a potential new therapy for these patients, but now that we have confirmed a dosing regimen for advanced clinical trials in refractory GBM, we will also begin exploring opportunities for newly diagnosed patients with a high expression of MGMT (the enzyme responsible for Temodar resistance). Being able to offer an effective therapy to these patients – before they are at the end stage – is where we hope to make the biggest impact in the treatment of GBM.

Q: How has DelMar established collaboration with MD Anderson and the University of British Columbia's Vancouver Prostate Center?

A: DelMar operates largely as a virtual company. Establishing research relationships with leading academic medical centers, such as MD Anderson, the University of British Columbia, the Mayo Clinic, and UCSF, have enabled us to access leading minds in our field and world-class infrastructure while maintaining our expenditures at a manageable level. In some cases, we have long-standing relationships with the researchers, in others, we have approached key investigators based on mutual interest or expertise described in their published research.

Q: What are the next steps for DelMar?

A: We presented top-line data from our refractory GBM trial at the American Association for Cancer Research (AACR) annual meeting and recently held an End of Phase II meeting with the FDA to discuss advancing VAL-083 into a pivotal Phase III clinical trial. We were very pleased with the FDA's feedback, and we look forward to advancing to Phase III as soon as practical. We also plan to expand our clinical focus into newly diagnosed GBM and lung cancer during 2016.
From a corporate perspective, we have taken steps to "up-list" our shares from the OTCQX to a senior US stock exchange – NASDAQ or NYSE – which we believe will position us to access the capital necessary to support late-stage clinical trials, continue to build our business, and unlock liquidity and value for our shareholders. ◆

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