DelMar Presents Interim Clinical Data for Brain Cancer Drug VAL-083 at American Association of Cancer Research (AACR) Meeting

DelMar Note

On April 10, 2013, DelMar Pharmaceuticals (OTC BB: DMPI) presented clinical data at the 2013 AACR Annual Meeting from a Phase I/II clinical trial of VAL-083, a first-in-class chemotherapy for the treatment of glioblastoma multiforme (GBM). The new data demonstrates that VAL-083 is safe and well tolerated at the doses tested to date and there was an initial efficacy signal.

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VAL-083 Phase I/II Dose Escalating Study. DelMar initiated a Phase I/II clinical trial of VAL-083 in November 2011. The study is an open label, single-arm, safety, tolerability and pharmacokinetic study of VAL-083 for adult patients with recurrent malignant glioma or secondary brain tumors that have failed both *Temodar*® (temozolomide) and *Avastin*® (bevacizumab), unless contraindicated. The trial protocol calls for administration of VAL-083 on the first 3 out of every 21 days.

The primary endpoint for the Phase I/II trial is to establish the maximum tolerated dose (MTD) of VAL-083. Secondary endpoints include monitoring antitumor activity, progression free survival (PFS), and pharmacokinetics of the treatment. Once the MTD is established, additional patients will be enrolled to begin the Phase II portion of the study and PFS will be monitored as the primary endpoint. 3 of 9 patients in the trial experienced a response, defined as either stable disease (2) or partial response (1), giving an initial indication of efficacy. While these are early results, an initial indication of efficacy before the MTD is reached is a promising sign.

VAL-083 is a bi-functional DNA alkylating agent with a long history of pre-clinical and clinical studies by the National Cancer Institute demonstrating its chemotherapeutic properties. It is currently approved in China for the treatment of chronic myelogenous leukemia and lung cancer.

Ticker	DMPI
Price	$1.85
Market Cap (M)	$57
EV (M)	$49
Shares Outstanding (M)†	30.6
Fully Diluted Shares (M)	56.9
Avg. Daily Vol.	30,204
52-week Range:	$1.25-2.50
Cash (M)	$8.3
Net Cash/Share	$0.26
Debt (M)	$0.26
Short Interest (M)	N/A

†The number of shares outstanding is inclusive of exchangeable shares held by Canadian holders of the pre-IPO private entity.

FY Dec		2010A	2011A	2012A
EPS:	Q1	N/A	N/A	N/A
	Q2	N/A	N/A	N/A
	Q3	N/A	($0.03)A	($0.05)A
	Q4	N/A	N/A	N/A
	FY	N/A	($0.16)A	($0.15)*

*9-months ended 9/30/12

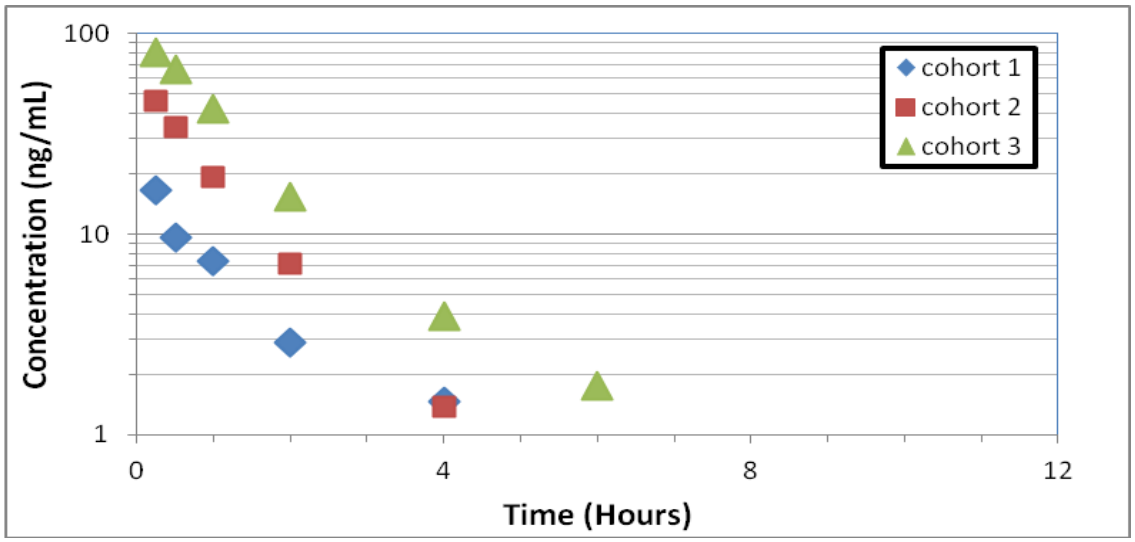
VAL-083 Produced No Serious Adverse Events and Favorable Pharmacokinetics. Interim data was announced from nine patients receiving VAL-083 in the Phase I/II study. The patients were treated in three cohorts, each receiving a different concentration of VAL-083. The trial uses a standard 3 x 3 dose escalation design.[1] As part of this protocol, the first cohort is receiving 1.5 mg/m^2, the second cohort is receiving 3 mg/m^2, and the third cohort is receiving 5 mg/m^2 of VAL-083. Doses are administered on days 1, 2, and 3 of each 21-day cycle. Dose-limiting toxicity was not reached using these doses, and future patients will receive higher doses of VAL-083 until the maximum tolerated dose (MTD) or maximum specified dose is reached. Current patients have received anywhere from one to fifteen cycles of VAL-083 treatment.

Pharmacokinetic analysis indicates a dose-dependent increase in plasma levels of VAL-083 as shown in **Figure 1**. The drug was effectively eliminated from patients with a half-life in the plasma of 1-2 hours. Historical data for VAL-083 suggests that the half-life in cerebrospinal fluid is about 20 hours.[2] Selective retention in the cerebrospinal fluid and rapid clearing from the plasma means that VAL-083 has relatively high CNS exposure with limited side effect potential in the rest of the body. VAL-083 appears to be safe so far, as no drug-related serious adverse events were reported. The MTD has not yet been achieved with these three cohorts, and additional patients will be recruited to identify an effective and safe treatment regimen for Phase II studies. We expect the MTD to be established later this year and for Phase II recruitment to begin shortly thereafter.

[1] www.clinicaltrials.gov/ct2/show/NCT01478178

[2] Echkardt, S. et al., 1977. Uptake of labeled dianhydrogalactitol into human gliomas and nervous tissue. *Cancer Treatment Reports*, 61, pp841-847.

Figure 1: Dose-dependent Increase in VAL-083 Plasma Concentration



Source: Shih, K.C. et al., 2013.[3]

We expect that DelMar will continue to present interim data from this trial at upcoming conferences including, possibly, the American Society for Clinical Oncology (ASCO) conference in early June and the Society for Neuro-Oncology (SNO) conference in November. If patient enrollment continues at the current pace, we would not be surprised to see DelMar find the MTD for VAL-083 in time for the SNO meeting.

One-Third of Patients Experienced Either Stable Disease or Partial Response. Evaluation of the tumor response in patients is the secondary endpoint for the Phase I portion of the VAL-083 clinical trial. So while measuring efficacy is not the primary purpose of this trial, there is an opportunity to gauge an initial efficacy signal. DelMar presented data demonstrating that 3 of 9 patients either experienced stable disease or a partial response as shown in **Figure 2**. Of the three patients experiencing a tumor response, one has been continuing to receive VAL-083 therapy with a durable response lasting more than one year, compared with an average life expectancy for refractory GBM of just a few weeks in many cases. The overall response rate of 33.3% observed early in the study is promising. It is also promising considering that the administered doses are low compared to historical safety trials where patients received doses exceeding 100 mg/m^2 and responses on the order of 40% were achieved at doses of 25 mg/m^2. It is possible that with additional rounds of treatment, especially at higher dosing levels, further responses may be recorded.

[3] Shih, K.C., et al., 2013. Phase I/II study of VAL-083 in patients with recurrent malignant glioma or secondary brain tumor. American Association for Cancer Research, 2013 Annual Meeting. Abstract #4672.

Figure 2: Tumor Response of Patients Treated with VAL-083

Patient	Tumor Type	Prior Therapy	Rounds of Treatment	Tumor Response
1	GBM	Radiation *Temodar*; *Avastin*	2	Progressive Disease (PD)
2	GBM	Radiation *Temodar*; *Avastin*	15	Partial Response (PR)
3	GBM	Radiation *Temodar*; *Avastin*	2	PD
4	GBM	Radiation *Temodar*; *Avastin*	2	PD
5	GBM	Radiation *Temodar*; *Avastin*	4	Stable Disease (SD)
6	Small Cell Lung Cancer Metastasis	Radiation	2	Stable Disease
7	Small Cell Lung Cancer Metastasis	Radiation	2	PD
8	Melanoma Metastasis	Radiation	2	PD
9	GBM	Radiation *Temodar*; *Avastin*	1	PD

Source: Shih, K.C. et al., 2013.[4] & LifeSci Advisors.

Characterizing Patient Responses to MGMT Status. MGMT is a DNA repair enzyme that can inhibit the ability of the front-line treatment *Temodar* to induce cell death in tumor cells of patients with GBM. Studies have demonstrated that methylation of the MGMT promoter is associated with both a lack of MGMT expression and resistance to *Temodar* treatment. VAL-083 induces cell death in tumors via a mechanism that is independent of MGMT expression, making VAL-083 a potential treatment for *Temodar* resistant tumors that express MGMT.

Pre-clinical research presented at the 2012 American Association for Cancer Research directly addressed the effect of VAL-083 on cells expressing MGMT.[5] The study demonstrated that both temozolomide and VAL-083 can induce cell death in cells that do not express MGMT, but only VAL-083 induces death in MGMT-expressing cells. Therefore, VAL-083 may be an effective therapy for patients who express MGMT but do not respond to *Temodar* treatment. This raises the possibility of using the MGMT status of patients in the selection criteria for future trials.

[4] Shih, K.C., et al., 2013. Phase I/II study of VAL-083 in patients with recurrent malignant glioma or secondary brain tumor. American Association for Cancer Research, 2013 Annual Meeting. Abstract #4672.
[5] Hu, K., et al., 2012. VAL083, a novel N7 alkylating agent, surpasses temozolomide activity and inhibits cancer stem cells providing a new potential treatment option for glioblastoma multiforme. American Association for Cancer Research, 2012 Annual Meeting. Abstract #811.

Glioblastoma Multiforme Market. GBM is a common form of malignant brain tumor, which is highly aggressive and associated with poor prognosis in patients. The median survival time post-diagnosis for patients is only 12-14 months. GBM is a cancer of the glial cells, which are non-neuronal cells that give rise to myelin and also perform supportive and protective functions for neurons.

Standard treatment for GBM begins with surgical resection followed by radiation and chemotherapy. However, only 50% of patients treated with current first and second-line chemotherapeutics experience tumor regression or stability within one year. First-line chemotherapy is *Temodar*, an alkylating agent designed to interrupt DNA replication and subsequently induce cell death. Only 40% of patients who receive *Temodar* experience tumor reduction one year after treatment. Despite the low success rate, sales of *Temodar* have been remained steady at ~$1 billion per year for the last three years. Patients not responding to *Temodar* are often prescribed the anti-angiogenesis drug *Avastin*. Only about 20% of patients taking *Avastin* experience tumor reduction after one year. Due to the failure of *Temodar* and *Avastin* to treat GBM, a large unmet need remains for patients both in the third-line setting and in general. VAL-083 represents a strong candidate to fill that role. We have estimated that the market for a third-line treatment may be worth $200 million.

Possibilities for Additional Indications. Expansion to additional indications such as chronic myelogenous leukemia is possible both within the United States and across the world. DelMar has already enrolled patients with secondary brain tumors in the current Phase I/II trial with VAL-083. One patient with small cell lung cancer metastasis experienced a tumor response after two dosing rounds of treatment. Further clinical trials may unveil additional patient populations within the brain cancer category that may benefit from VAL-083.

Upcoming Expected Milestones

- 2H 2013 – Expected completion of Phase I of the Phase I/II trial of VAL-083 in GBM.
- 1H 2014 – Potential expansion of VAL-083 Phase II trial to a registration study.

About DelMar: More information on DelMar Pharmaceuticals can be found in our Initiation of Coverage Report at http://lifesciadvisors.com/clients/delmar/.

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