Zacks Small-Cap Research

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Delmar Pharma (DMPI-OTCQB)

DMPI: High doses may enhance success rate of VAL-083 for the treatment of glioblastoma, registrational trial expected to begin in late 2014 or early 2015– Outperform

Current Recommendation	**Outperform**
Prior Recommendation	Neutral
Date of Last Change	11/26/2013
Current Price (09/15/14)	$0.74
Twelve- Month Target Price	**$4.50**

OUTLOOK

DMPI is a clinical/commercial stage drug development company with a focus on oncology. We are impressed with the efficacy data and safety profile of its lead drug candidate VAL-083 for brain cancer.

DMPI recently reported positive VAL-083 Phase I/II clinical data for brain cancer. The company is on track to initiate registration directed trial of VAL-083 for brain cancer in late 2014 or early 2015. Valuation is attractive now. We maintain an Outperform rating on its shares.

SUMMARY DATA

52-Week High	**$2.20**
52-Week Low	**$0.80**
One-Year Return (%)	**N/A**
Beta	**N/A**
Average Daily Volume (sh)	**178,061**
Shares Outstanding (mil)	**36**
Market Capitalization ($mil)	**$26**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**5.7**
Insider Ownership (%)	**38.5**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2013 Estimate	**N/A**
P/E using 2014 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**N/A**
Type of Stock	**N/A**
Industry	**Med-Drugs**
Zacks Rank in Industry	**N/A**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Sep)	Q2 (Dec)	Q3 (Mar)	Q4 (Jun)	Year (Jun)
2014	0.00 A	0.00 A	0.00 A	0.00 A	0.00 A
2015	0.00 E	0.00 E	0.00 E	0.00 E	0.00 E
2016					0.50 E
2017					1.00 E

Earnings per Share
(EPS is operating earnings before non recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	-$0.03 A	-$0.06 A	-$0.05 A	-$0.03 A	-$0.16 A
2015	-$0.05 E	-$0.05 E	-$0.06 E	-$0.06 E	-$0.21 E
2016					-$0.24 E
2017					-$0.26 E

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

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WHAT'S NEW

- **Higher doses will increase the success rate of VAL-083 for the treatment of glioblastoma;**
- **On track to initiate registration directed Phase II trial in late 2014 or early 2015;**
- **New Preclinical data may expand VAL-083 utility for lung cancer;**
- **Balance sheet remained relatively strong;**
- **Valuation attractive, and maintain Outperform rating;**

Higher Doses Will Increase the Chance of Success for VAL-083

On August 19, 2014, DelMar filed a protocol amendment with the FDA to increase the doses of VAL-083 up to 60mg/m^2. The Company already initiated the treatment of patients at 50mg/m^2 in the **Phase I/II** clinical trial for **glioblastoma**.

Dose Escalation Scheme (mg/m^2)		Patients Treated	Cumulative Dose	Status
Original	**Revised**			
1.5	**1.5**	3	9 mg/m2	Completed – No DLT
3.0	**3.0**	4	18 mg/m2	Completed – No DLT
5.0	**5.0**	10	30 mg/m2	Completed – No DLT
10.0	**10.0**	3	60 mg/m2	Completed – No DLT
15.0	**20.0**	3	120 mg/m2	Completed – No DLT
20.0				
25.0	**30.0**	3	180 mg/m2	Completed – No DLT
30.0				
	40.0	3	240 mg/m2	Completed – No DLT
	50.0	3 (planned)	300 mg/m2	enrollment ongoing
	60.0	3 (planned)	360 mg/m2	To be initiated subject to evaluation of 50mg/m^2 dose

DelMar is now delivering higher doses compared to previous glioblastoma clinical trials conducted by the National Cancer Institutes in the United States.

Data to date have demonstrated that VAL-083 is safe and well tolerated at doses up to 40mg/m^2. In addition, one of three patients in the most recent (40mg/m^2) cohort and one of three patients in the previous (30mg/m^2) cohort exhibited stable disease after one or two cycles of treatment with VAL-083. No drug-related serious adverse events or dose limiting toxicities (DLTs) have been detected and a maximum tolerated dose (MTD) has not been reached at doses up to 40 mg/m^2.

The company plans to present detailed results at scientific meetings during the second half of 2014.

With an excellent safety profile, it's our belief that such higher doses may increase the efficacy of VAL-083 for the treatment of glioblastoma and therefore enhance the potential of VAL-083 to impact a patent's tumor and improve patient outcomes. As a result, the use of higher doses will increase the chance of success in commercializing VAL-083 as a new chemotherapy for glioblastoma patients in our view.

Background of the Phase I/II clinical trial

DelMar initiated the **Phase I/II** clinical trial of VAL-083 for the treatment of **refractory glioblastoma multiforme (GBM)** or **progressive secondary brain tumor** in October 2011. The Phase I/II study is an

open-label, single arm dose-escalation study designed to evaluate the safety, tolerability, pharmacokinetics and anti-tumor activity of VAL-083 in patients with histologically confirmed initial diagnosis of primary WHO Grade IV malignant glioma (GBM), now recurrent. Patients with prior low-grade glioma or anaplastic glioma are eligible if histologic assessment demonstrates transformation to GBM. Patients must have been previously treated for GBM with surgery, and/or radiation, if appropriate, and must have failed both Bevacizumab (Avastin) and temozolomide (Temodar), unless either or both are contra-indicated. Patients with brain tumors that have developed due to CNS metastases were eligible for the DelMar clinical trial at early doses.

The primary outcome measures in the dose-modernization portion of the clinical trial will be the determination of maximum tolerated dose (MTD). **Secondary outcome measures** include tumor response in patients and pharmacokinetics.

An initial phase of the study will involve dose escalation cohorts until a maximum tolerated dose (MTD) is established in the context of modern care. Once the modernized dosing regimen has been established, additional patients will be enrolled at the MTD in a registration directed **Phase II** clinical trial. Up to **30 patients** will be enrolled in the Phase I study.

In Aug, 2013, DelMar received a notice of allowance from the FDA that will enable the company to accelerate the dose-escalation of its ongoing **Phase I/II** of VAL-083 in refractory glioblastoma multiforme (GBM) patients.

The revised dosing regimen was allowed by the FDA following an extensive safety review of patients treated to date. In comparison to the original dose-escalation scheme, the revised plan will enable the trial to reach higher doses and complete the dose-escalation portion of the clinical trial **more quickly** by skipping two interim doses. The revised dosing scheme also permits dosing above 40mg/m^2 if VAL-083 is safe and well-tolerated at that dose.

Accelerating the program will enable DelMar to complete the dose-escalation portion of the Phase I/II clinical trial, attain doses that are more likely to have anti-tumor effects and advance into registration-directed studies for refractory GBM in the timeliest manner possible. The company's goal remains to advance into registration-directed trials in 2014.

A Registration Directed Phase II Trial and a Phase II/III to Begin in 2H2014

Based on the positive interim data, we expect DelMar to initiate a **registration directed Phase II trial** in **refractory GBM** in 2H2014. Based on historical development of other products in GBM, it's possible that DelMar may be able to obtain FDA approval to commercialize VAL-083 to treat patients who have failed other therapies from an open-label Phase II registration-directed clinical trial, which will save significant costs of a large Phase III clinical trial. It's also possible that the FDA may grant fast-track, accelerated approval and/or priority review status to VAL-083, which will enable DelMar to begin filing for commercial approval during the clinical trial process.

Based on historical precedent with the FDA, the **Phase II registration directed trial** are expected to mirror the Avastin approval study in that indication. Under this scenario, the Phase II trial would be:

- Single-arm; open label design;
- Primary endpoints: overall survival;
- N = 80-100 patients;
- Minimum response rate = 20%;
- Enrollment: Patients with recurrent GBM who have failed or are ineligible for both Temodar® and Avastin® (i.e. the same population as in the current trial);

The recent failure of **Avastin** in the front line treatment of GBM has highlighted the need for new therapies in newly diagnosed patients, particularly those with unmethylated MGMT promoter regions who do not respond to standard of care with **temozolomide**.

DelMar would plan to advance modernized dosing regimen into a **Phase II/III trial** in **newly diagnosed patients** with unmethylated MGMT promoter in parallel with the refractory GBM registration trial (i.e. in 1H2014). The Company has begun designing this trial with KOLs.

- Randomized groups: Temodar vs. VAL-083;
- Primary endpoints: overall survival;
- Secondary endpoints: PFS6 & radiographic response;
- N = 500 – 600 patients (with interim endpoint at ~10% enrollment);

Balance Sheet Remained Relatively Strong

As of June 30, 2014, DMPI held $4.8 million in cash and cash equivalents.

In July, 2014, Del Mar was awarded a non-refundable financial contribution of up to CDN$194,000 from the National Research Council of Canada's Industrial Research Assistance Program (NRC-IRAP). This funding represents the fourth contribution that DelMar has received from NRC-IRAP, bringing the total to CDN$327,000 in financial support to date.

The fund will be used to support continued non-clinical research aimed at providing competitive differentiation for VAL-083 as a new medicine in the treatment of glioblastoma and other cancers, including non-small cell lung cancer.

DelMar received gross proceeds of $2.4 million from the exercise of warrants at $0.65 per warrant that closed on June 6 and an additional $0.5 million in gross proceeds from exercise of these warrants under the tender offer which closed on August 8.

Current cash will be sufficient to fund current operations through at least the end of December 2015.

New Pre-clinical Data May Expand VAL-083 Utility

On April 7, 2014, DelMar presented new **preclinical** data of VAL-083 in the treatment of non-small cell lung cancer **(NSCL)** at the 105th Annual Meeting of the American Association for Cancer Research (AACR) in San Diego.

The purpose of this pre-clinical study was to evaluate the activity of VAL-083 in in vivo models of drug-resistant NSCLC in comparison to cisplatin.

In an established murine xenograft model of NSCLC, the activity of VAL-083 was compared to standard platinum-based therapy with cisplatin against human NSCLC cell lines A549 (TKI-sensitive) and H1975 (TKI-resistant). In the study, VAL-083 demonstrated superior efficacy and safety in the treatment of TKI-susceptible (A549) tumors and in TKI-resistant (H1975) tumors.

- Treatment of TKI-sensitive (A549) NSCLC with 3 mg/kg of VAL-083 resulted in tumor growth delay of 26 days compared to untreated controls. Cisplatin (5 mg/kg) resulted in tumor growth delay of just four days. In addition, mean tumor volume on day 68 was significantly reduced in animals treated with 3 mg/kg VAL-083 (p=0.001) compared to untreated control.

- Treatment of TKI-resistant (H1975) NSCLC with 4 mg/kg of VAL-083 resulted in a statistically significant reduction in tumor volume (p = 0.01) versus untreated control after 27 days. In the same model, treatment with 5 mg/kg of cisplatin failed to achieve statistically significant reduction in tumor volume (p = 0.23) versus untreated control after 27 days. Longer-term safety assessments are ongoing in this model.

We think these data suggest that VAL-083 may be a viable treatment option for NSCLC patients failing TKI-therapy, especially where platinum-based therapy has already failed or is predicted to give sub-optimal outcomes.

VAL-083 is approved for treatment of lung cancer in China. These data have immediate implications in the treatment of NSCLC in China. The data also support exploring future clinical development of VAL-083 as a lung cancer therapy in the rest of the world thereby providing DelMar with a potential opportunity to expand its clinical development focus beyond glioblastoma.

Valuation Very Attractive

We maintain our Outperform rating on DelMar shares and reiterate our 12-month price target of $4.50 per share. Our call is based on recent clinical progress the company has made and attractive valuation of the company shares.

DMPI is a clinical and commercial stage biopharmaceutical company focused on the development and commercialization of oncology drugs. The Company's lead drug candidate VAL-083 is currently in a **Phase I/II** trial for the treatment of recurring GBM.

Previous multiple clinical studies conducted by NCI have demonstrated that VAL-083 is safe and efficacious for the treatment of GBM. Interim data from the Company's Phase I/II trial confirmed the efficacy and safety profile of VAL-083 in GBM patients. Based on the data currently available, DMPI intends to initiate a registration directed **Phase II** trial of VAL-083 for **recurring GBM** and a **Phase II/III** trial for **first line GBM** in late 2014 or early 2015. This will be a significant milestone for the Company which will position the Company in a late stage development.

VAL-083 has been approved in China for leukemia and lung cancer and DMPI has acquired its commercial rights in China market. Delmar is seeking to enter into a marketing partnership that could generate upfront fees, milestones and royalty revenue for DMPI, which is a de-risking event for the Company.

VAL-083 is a first-in-class alkylating agent with a different mechanism of action from that of **Temodar**, current market leader for GBM. The unique MOA of VAL-083 overcomes the resistance problem for Temodar.

Currently, DMPI shares are trading at around $0.8 per share, which values the Company at about $29 million in market cap based on 36 million outstanding shares. This is a deep discount compared to its peers. We noticed that most small biotech companies of development stage are valued from $50 million to $1 billion depending on how advanced the pipeline is and which indications the company is targeting. DMPI's lead drug candidate VAL-083 is in a Phase I/II clinical trial and will enter a registration directed Phase II trial in late 2014 or early 2015.

We estimate VAL-083 could be approved by the FDA in calendar 2017 for recurring GBM. The broad application of VAL-083, including first line, second line and third line treatment of GBM, and other cancers, means a great market potential for VAL-083, which could be a blockbuster for DelMar. We estimate DMPI will be profitable in fiscal 2019 with an EPS of $0.06 based on product sales of $35 million. EPS will grow to $0.35 in fiscal 2020 based on total product sales of $70 million.

Based on our financial model and the Company's fundamentals, we have a price target of $4.50 per share for DMPI. We think a P/E ratio of 38x is appropriate for DMPI considering its growth in the next few years. Based on this P/E multiple, we come up with our price target of $4.50 per share using 25% discount for 5 years. Our price target values DMPI at $162 million in market cap, which we think is still conservative compared to its peers.

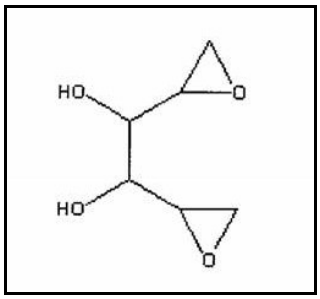
But risk is high at this point for DMPI. Although VAL-083 has been approved in China for marketing, its indications are leukemia and lung cancer, different from the current indication of GBM under development in the US. The bar on both clinical and regulatory hurdle in the US is higher. We remind investors that risks associated with drug development are high, especially for early stage drug candidates. VAL-083 is only in Phase I clinical trial, and both clinical and regulatory hurdles are significant at this point.

Another concern we have is that DMPI has a limited pipeline. Right now, VAL-083 is the Company's only clinical-stage candidate. While DelMar has early-stage second-generation analogues from the VAL-083 chemistry platform and has access to additional clinical-stage product candidates through its relationship with Valent Technologies LLC, no other clinical stage candidates currently in the DelMar portfolio. If VAL-083 fails, the value of the Company will be negatively impacted significantly.

Background Information

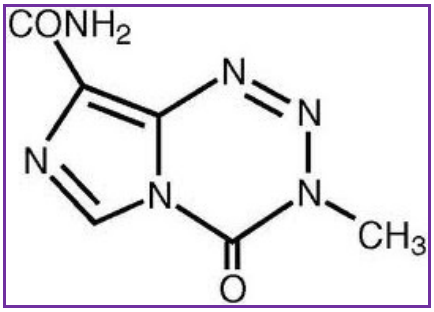
GBM: First Target Market for VAL-083

VAL-083 represents a "first-in-class" small-molecule chemotherapeutic, which means that the molecular structure of VAL-083 is not an analogue or derivative of other small molecule chemotherapeutics approved for the treatment of cancer.



VAL-083 has been assessed in multiple NCI-sponsored clinical studies in various cancers including lung, brain, cervical, ovarian tumors and leukemia. **The results for brain cancer were most compelling**. VAL-083 has been assessed as chemotherapy in the treatment of **newly diagnosed** and **recurrent brain tumors**. In general, tumor regression in brain cancer was achieved following therapy in greater than 40% of patients treated and stabilization was achieved in an additional 20% - 30%. In published clinical studies, VAL-083 has previously been shown to have a statistically significant impact on median survival in high grade glioma brain tumors when combined with radiation vs. radiation alone.

Temozolomide (Temodar, TMZ) is a front-line therapy for the treatment of GBM, however, it is often ineffective due to drug inactivation by O^6-methylguanine-DNA methyltransferase **(MGMT).**

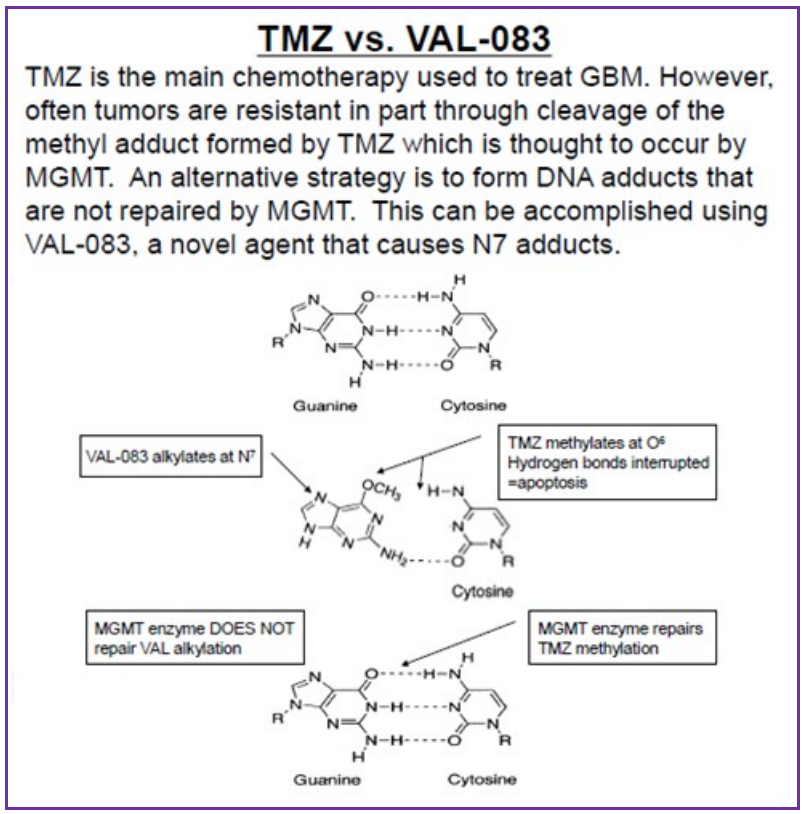


The mechanism of action of VAL-083 is understood to be a **bi-functional alkylating agent**. Alkylating agents are a commonly used class of chemotherapy drugs. They work by binding to DNA and interfering with normal DNA replication processes within the cancer cell, which prevents the cell from making the proteins needed to grow and survive. After exposure to alkylating agents, the cancer cell becomes dysfunctional and dies. There are a number of alkylating agents on the market that are used by physicians to treat different types of cancer.

Based on published research, the functional groups associated with the mechanism of action of VAL-083 are understood to be **functionally different** from commonly used alkylating agents, including **Temodar.** VAL-083 has previously demonstrated activity in cell-lines that are resistant to other types of chemotherapy. No evidence of cross-resistance has been reported in published clinical studies. Based on the presumed alkylating functionality of VAL-083, published literature suggests that DNA repair mechanisms associated with the leading brain cancer therapies, including **Temodar** and **nitrosourea** resistance may not confer resistance to VAL-083. Therefore, VAL-083 may be effective in treating tumors that have failed or become resistant to other chemotherapies.

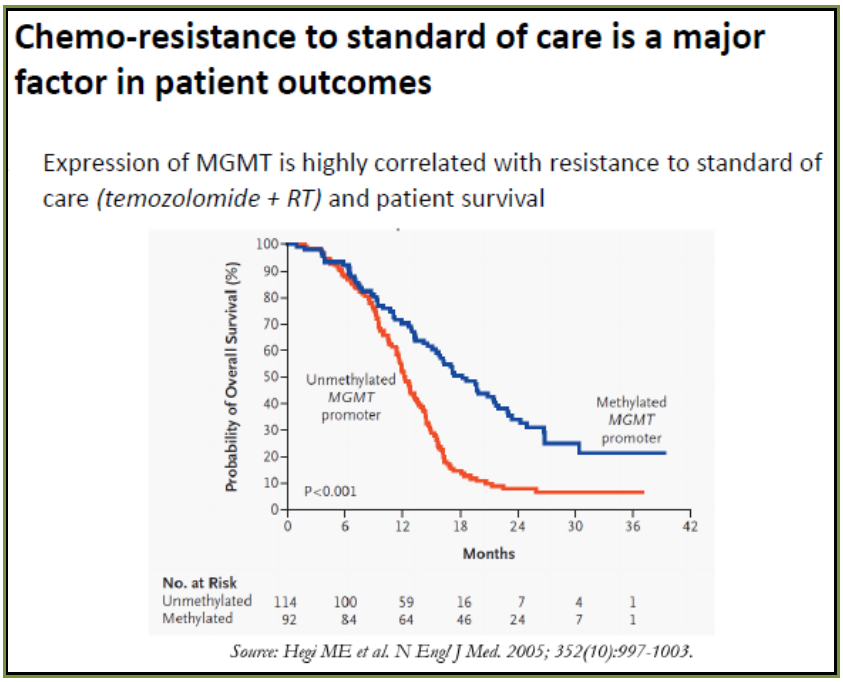
VAL-083 is a novel alkylating agent that creates N^7 cross-links on DNA. The ultimate effect of VAL-083 is to inhibit DNA replication, which will consequently result in cell apoptosis. The alkylation site of VAL-083 is different from those led by other alkylating chemotherapeutic agents, such as temozolomide (TMZ), which creates O^6 methylation on DNA.

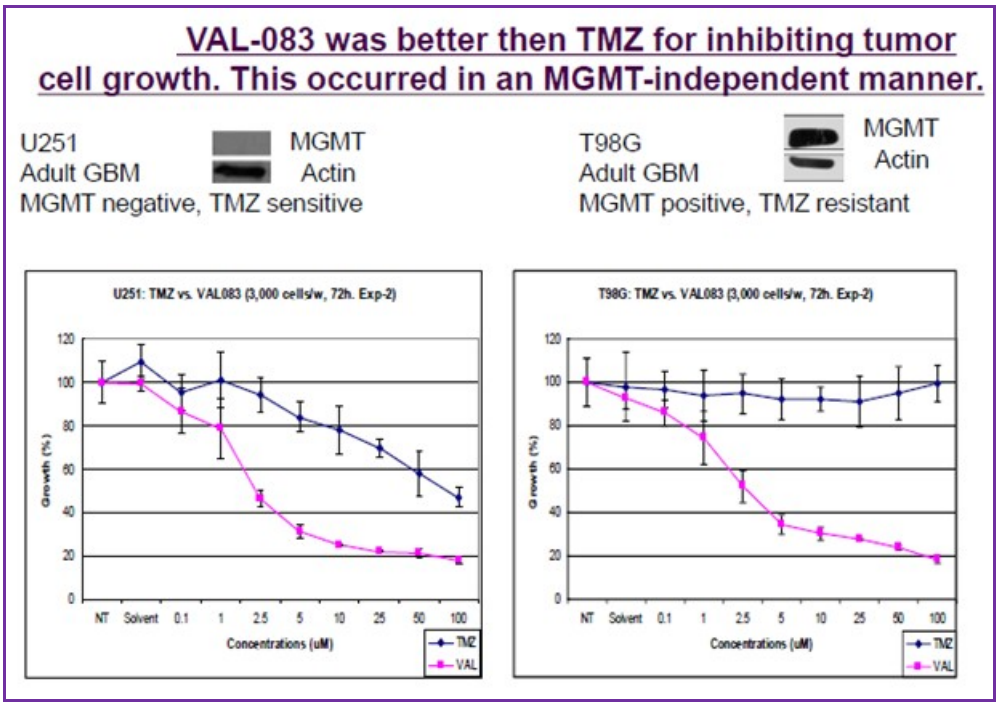
TMZ causes a DNA lesion by creating O^6 methylation on DNA. The drug, however, often becomes ineffective due to DNA repair by MGMT in tumor cells.



DelMar has presented new research at peer-reviewed scientific meetings demonstrating that VAL-083 is active in some patients, patient-derived tumor cell lines and cancer stem cells that are resistant to other chemotherapies. Of particular importance is resistance to Temodar ® due to activity of the repair enzyme known as **MGMT**, which results in resistance to front-line therapy in many GBM patients. At

AACR in 2012, DelMar presented data demonstrating that VAL-083 is active independent of MGMT resistance in laboratory studies.





VAL-083 readily crosses the blood brain barrier where it maintains a long half-life in comparison to the plasma. Published preclinical and clinical research demonstrates that VAL-083 is selective for brain tumor tissue.

VAL-083 has been granted **Orphan Drug Status** by both the FDA and European Medicines Agency (EMEA) for the treatment of glioma. As an orphan drug for glioma, VAL-083 will enjoy market exclusivity for seven years in the US and ten years in the EU following market approval.

Historical Pre-Clinical and Clinical Data of VAL-083 for GBM

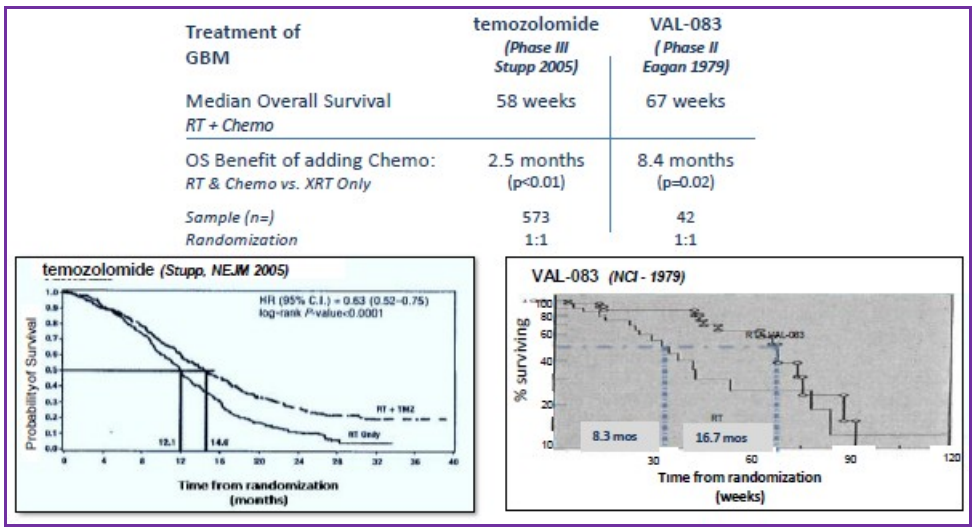
VAL-083 was originally discovered in the 1960's.

Previous preclinical studies showed that VAL-083 had cytotoxic activity in a wide range of cell lines, including sarcomas, melanomas, GBM, and lung cancer. VAL-083 was also found active in cyclophosphamide, nitrosourea (BCNU) and phenylanine mustard resistance cell lines. No evidence of cross-resistance has been reported in published clinical studies.

VAL-083 also inhibited the growth of cancer stem cells by 80-100% in neurosphere self-renewal assays. Conversely, there was minimal effect on normal human neural stem cells. VAL-083 has better *in vitro* efficacy than TMZ against brain tumor cells, can overcome resistance associated with MGMT, and targets brain tumor CSCs demonstrating that it has the potential to surpass the standard-of-care.

VAL-083 has been assessed in multiple **NCI-sponsored clinical studies** in various cancers including lung, brain, cervical, ovarian tumors and leukemia. However, further research was not pursued in the United States due to an increased focus by the NCI on targeted therapies during the era.

Among the clinical studies conducted by the NCI, results for **glioblastoma** are of particular interest, because those results were compelling compared to Temodar, current standard of care. Overall, VAL-083 has demonstrated objective response rates of 44% and a median survival of up to 67 weeks in glioblastoma clinical studies and has proven to be synergistic with radiation and other chemotherapies.



In separate historical clinical trials, **combination** of VAL-083 and radiation therapy showed a median survival benefit comparable or superior to that of Temodar plus radiation. Other chemotherapeutics, such as Lomustine (CCNU), Carmustine (BCNU) and Nimustine (ACNU), are less frequently used for the treatment of glioblastoma due to no apparent survival benefits. Lomustine is an akylating nitrosourea compound, and Carmustine is a mustard gas-related β-chloro-nitrosourea agent. Nimustine is also a nitrosourea alkylating agent. In 2009, Roche's Avastin was approved by the FDA for the treatment of recurring GBM based on its 20% response rate. Avastin showed no survival benefit in recurrent GBM. Data presented at ASCO 2013 confirmed that Avastin therapy in newly diagnosed GBM patients demonstrated no survival benefit in the front-line setting.

Chemotherapy	Comparative Therapy Survival		Median Survival Benefit vs. XRT
	Radiation	Radiation + Chemotherapy	
Temodar™	12.1 months	58 weeks (14.6 months)	2.5 months
VAL-083	8.3 months	67 weeks (16.7 months)	8.0 months

Reported Radiation + Chemo Survival w/ other chemotherapeutic agents in GBM

Carmustine™ (BCNU)	40-50 weeks
Lormustine™ (CCNU)	52 weeks
Nimustine™ (ACNU)	35 weeks
Avastin™	No reported benefit to survival

VAL-083 also showed a favorable safety profile. The main dose-limiting toxicity related to the administration of VAL-083 in previous NCI-sponsored clinical studies was **myelosuppression**. Bone marrow suppression is a common side effect of chemotherapy. There is no evidence of lung, liver or kidney toxicity even with prolonged treatment by VAL-083. Commercial data from the Chinese market where the drug has been approved for more than 15 years supports the safety findings of the NCI studies.

Please remember the dose-limiting toxicity of VAL-083 was established prior to the development of medicines now available to manage myelosuppression. Various types of medications and other forms of therapy are now available for management of myelosuppressive side effects. This offers the potential of increasing the dose of VAL-083 in the modern patient population thereby providing a potential opportunity to improve the drug's already established efficacy profile.

Toxicity Comparison

	Temodar	BCNU	VAL-083
Severe toxicity reported (>2%)	Hematologic*, nausea, vomiting, fatigue, asthenia, neuropathy	Hematologic*, pulmonary, nausea, vomiting, encephalopathy, renal	Hematologic*
*DLT			
NADR	21-28 days	21-35 days	18-21 days
Recovery	Within 14 days	42-56 days	Within 7-8 days

As reported by BC Cancer Agency monograph (2010) literature (1970s) & China commercial experience

Huge Market Potential for VAL-083

Glioblastoma multiforme (GBM), also called glioblastoma, is the most common and most aggressive type of primary brain tumor and accounts for approximately 50% to 60% of all primary brain tumors.

According to National Cancer Institute (NCI) data, the peak incidence occurs between the ages of 45 and 70 years. In the United States, the age-adjusted brain tumor incidence rate was 6.5 per 100,000 men and women per year. The age-adjusted death rate was 4.3 per 100,000 men and women per year. It is estimated that 23,130 men and women (12,770 men and 10,360 women) will be diagnosed with and 14,080 men and women will die of **cancer of the brain and other nervous system** in 2013 in the US. Worldwide, approximately 238,000 new cases of brain and other CNS tumors were diagnosed in the year 2008, with an estimated mortality of 128,000.

Glioblastomas are among the most aggressively malignant human neoplasms. The median survival time from the time of diagnosis without any treatment is usually less than 1 year. Despite multimodality treatment consisting of open craniotomy with surgical resection of as much of the tumor as possible, followed by radiotherapy, chemoradiotherapy, Avastin, and symptomatic care with corticosteroids, median survival is about 14 months. The overall 5-year survival is less than 10% with the standard of care today. Increasing age (> 60 years of age) carries a worse prognostic risk. Death is usually due to cerebral edema or increased intracranial pressure.

Glioblastoma remains one of the most difficult tumors to treat due to several complicating factors:

- The tumor cells are very resistant to conventional therapies;
- The brain is susceptible to damage due to conventional therapy;
- The brain has a very limited capacity to repair itself;
- Many drugs cannot cross the blood-brain barrier to act on the tumor;
- Resistance develops over time for some drugs including Temodar;
- Many drugs do not target cancer stem cells (CSC) which are responsible for relapse of glioblastoma;

Surgery is the first stage of treatment of glioblastoma. It is used to take a section for a pathological diagnosis, to relieve some of the symptoms of a large mass pressing against the brain, to remove the tumor mass prior to treatment with radiotherapy and chemotherapy, and to attempt to prolong survival.

After surgery, **radiotherapy** in combination with Chemotherapy is the mainstay of treatment for glioblastoma. A pivotal clinical trial carried out in the early 1970s showed that GBM patients who received radiation had a median survival more than double those who did not receive radiation therapy. Subsequent clinical research has attempted to build on the backbone of surgery followed by radiation. A combination of radiotherapy and chemotherapy has generally exhibited a benefit in comparison to radiotherapy alone.

Chemotherapy (including targeted therapy) is a third method to treat glioblastoma. Although the addition of chemotherapy to radiation improves survival in many cancer types, this is not the case for most cases of glioblastoma. Most studies showed little or no benefit from the addition of chemotherapy to radiation for glioblastoma patients. However, currently, two chemotherapeutic agents (including one targeted therapy) approved by the FDA are frequently used for the treatment of glioblastoma in combination with radiation therapy. They are **Temodar** (temozolomide) from Merck/Schering Plough for newly diagnosed GBM and **Avastin** from Roche for recurred GBM. Temodar in combination with radiotherapy demonstrated a survival benefit vs. radiotherapy alone while Avastin following temodar failure demonstrated an ability to slow tumor progression in approximately 1 in 5 patients, although there was no overall survival benefit.

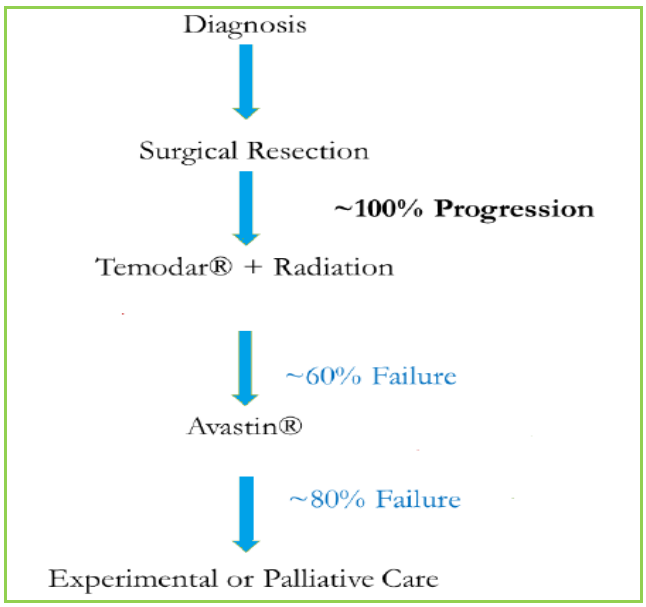
A large clinical trial of 573 newly diagnosed GBM patients randomized to standard radiation versus radiation plus temozolomide chemotherapy showed that the group receiving temozolomide survived a median of 14.6 months as opposed to 12.1 months for the group receiving radiation alone. This treatment regime is currently considered standard of care for glioblastoma and has a 26% survival at two years. Temozolomide is a front-line therapy for the treatment of GBM, however, it is often ineffective due to drug inactivation by O^6-methylguanine-DNA methyltransferase **(MGMT).**

The US FDA recently approved **Avastin** (bevacizumab) to treat patients with **recurred glioblastoma** (but not newly diagnosed GBM) after standard therapy based on the results of 2 studies that showed Avastin reduced tumor size in some glioblastoma patients. In the first study, the efficacy of Avastin was demonstrated by an objective response rate of 25.9%. Median duration of response was 4.2 months. In the second study, the efficacy of Avastin was supported by an objective response rate of 19.6%. Median duration of response was 3.9 months.

Other less frequently used chemotherapeutics for the treatment of glioblastoma include Bristol Myers Squibb's **Carmustine** injection, and CeeNu capsules (**Lomustine)**, and Eisai's **Carmustine wafer**.

	Median Survival		
Chemotherapy	Radiation alone	Radiation + Chemo	Median Survival Benefit vs XRT
Temodar	12.1 months	14.6 months (56 weeks)	2.5 months
Avastin		N/A	N/A
Lomustine		52 weeks	N/A
Carmustine		40-50 weeks	N/A
Semustine		35 weeks	N/A

Temodar in combination with radiation is the **front-line therapy** for GBM following surgery. However, approximately 60% of GBM patients treated with Temodar experience tumor progression within one year. As a second line treatment of GBM in patients failing Temodar, Avastin only demonstrated 20%-26% response rate in clinical studies. Therefore, approximately 48% of patients who are diagnosed with GBM will fail both front-line therapy and Avastin.

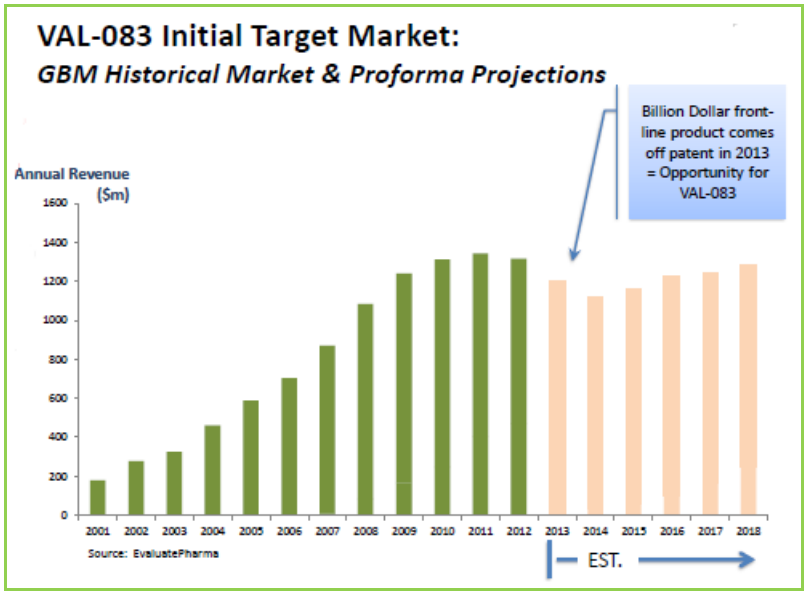


Recently at ASCO 2013, Roche reported that **Avastin** failed to prolong survival when added to chemo-radiation therapy for **newly diagnosed glioblastoma**. Those who received Avastin in the late-stage study of 637 previously untreated patients also experienced more side effects, such as low platelet counts, blood clots and elevated blood pressure.

Clearly, there is an unmet medical need for the treatment of glioblastoma. All these have highlighted the need for new therapies in both newly diagnosed and recurring GBM patients.

The glioblastoma market is a multibillion dollar business. Worldwide sales of **Temodar** reached $1 billion

in 2009. The patent of Temodar will expire in August 2013. **VAL-083** has a differentiated mechanism of action for the treatment of glioblastoma, which will help VAL-083 capture a significant share of the glioblastoma market when it reaches the market. Also, unlike Temodar which only targets newly diagnosed patients and Avastin which only targets recurring patients, VAL-083 targets **both newly diagnosed** and **recurring glioblastoma** patients, which will help drive revenue growth more dramatically if approved.



The market potential is even greater if we consider that VAL-083 can also target other cancer indications, such as lung cancer, breast cancer, ovarian cancer and leukemia. If DelMar only develops VAL-083 for lung cancer and GBM to be conservative, the potential market size for those two indications is huge.

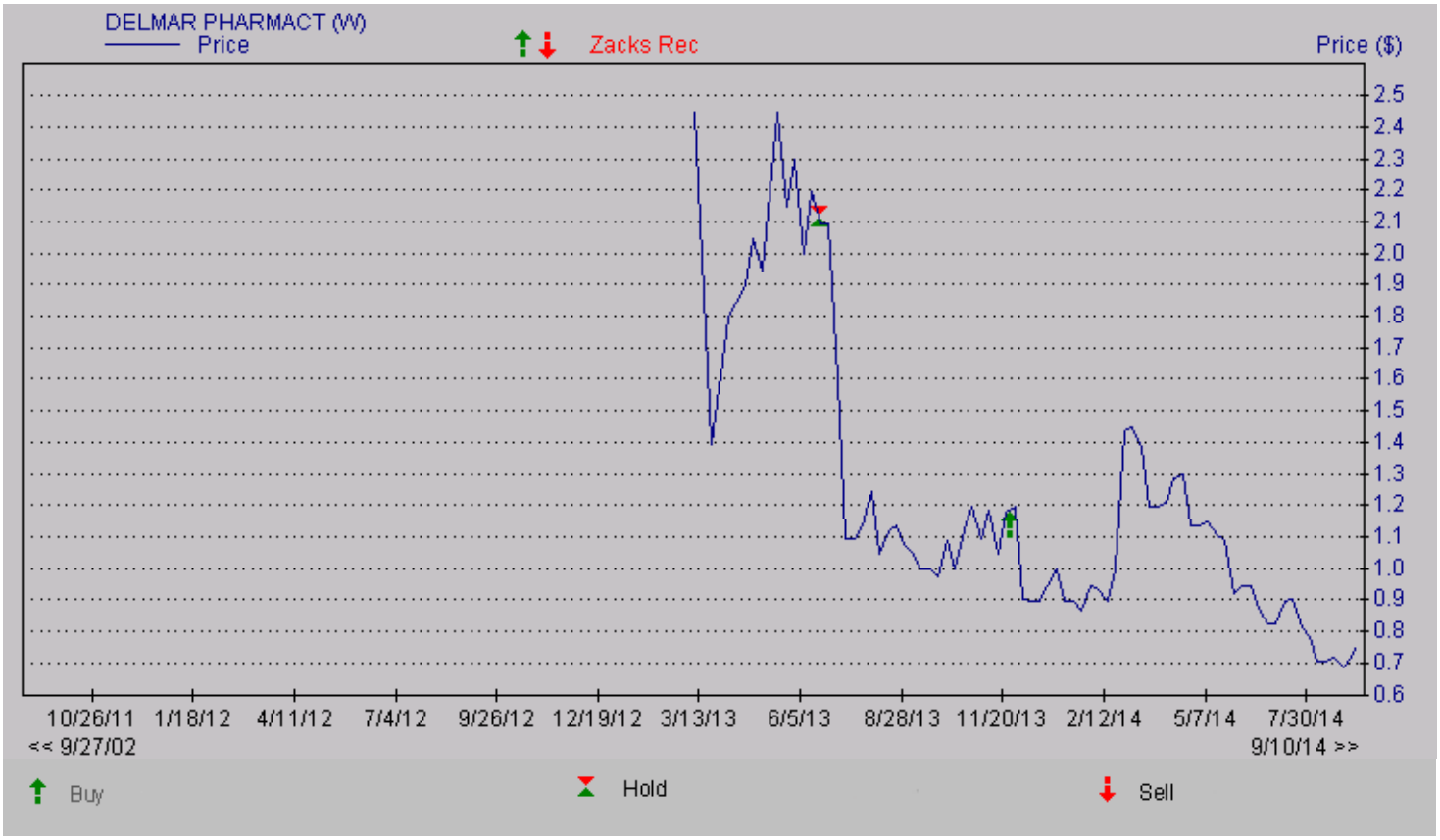
PROJECTED INCOME STATEMENT

	Sept	Dec	Mar	June	FY14	Sept	Dec	Mar	June	FY15	2016	2017	2018	2019	2020
$ in millions except per share data	Q1	Q2	Q3	Q4	FY	Q1	Q2	Q3	Q4	FY	FYE	FYE	FYE	FYE	FYE
Milestone	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Royalty	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.50	$1.00	$2.00	$2.50	$3.50
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	*100.0%*	*100.0%*	*25.0%*	*40.0%*
Product Sales	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$7.50	$35.00	$70.00
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-	-	*366.7%*	*100.0%*
Total Revenues	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.50**	**$1.00**	**$9.50**	**$37.50**	**$73.50**
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	*100.0%*	*850.0%*	*294.7%*	*96.0%*
CoGS	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.75	$3.50	$7.00
Gross Income	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.50**	**$1.00**	**$8.75**	**$34.00**	**$66.50**
Gross Margin	-	-	-	-	-	-	-	-			*100.0%*	*100.0%*	*92.1%*	*90.7%*	*90.5%*
R&D	$0.56	$0.57	$0.62	$0.37	$2.12	$0.60	$0.80	$1.00	$1.20	$3.60	$5.00	$7.00	$7.50	$9.00	$12.00
% R&D	-	-	-	-	-	-	-	-	-	-	*1000.0%*	*700.0%*	*78.9%*	*24.0%*	*16.3%*
SG&A	$0.74	$0.64	$0.97	$0.79	$3.13	$0.85	$0.95	$1.05	$1.10	$3.95	$6.00	$7.50	$15.00	$20.00	$25.00
% SG&A	-	-	-	-	-	-	-	-	-	-	*1200.0%*	*750.0%*	*157.9%*	*53.3%*	*34.0%*
Others	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
% Other	-	-	-	-	-	-	-	-	-	-	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Operating Income	**($1.3)**	**($1.2)**	**($1.6)**	**($1.2)**	**($5.3)**	**($1.5)**	**($1.8)**	**($2.1)**	**($2.3)**	**($7.6)**	**($10.5)**	**($13.5)**	**($13.8)**	**$5.0**	**$29.5**
Operating Margin	-	-	-	-	-	-	-	-	-	-	-	-	-	*13.3%*	*40.1%*
Other Income (Net)	$8.1	$0.3	($1.6)	$0.0	$6.9	($0.2)	($0.2)	($0.2)	($0.2)	($0.8)	($0.8)	($0.8)	($0.8)	($0.8)	($0.8)
Pre-Tax Income	**$6.8**	**($0.9)**	**($3.2)**	**($1.1)**	**$1.6**	**($1.7)**	**($2.0)**	**($2.3)**	**($2.5)**	**($8.4)**	**($11.3)**	**($14.3)**	**($14.6)**	**$4.2**	**$28.7**
Net Taxes (benefit)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$5.0
Tax Rate	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*17.4%*
Reported Net Income	**$6.8**	**($0.9)**	**($3.2)**	**($1.1)**	**$1.6**	**($1.7)**	**($2.0)**	**($2.3)**	**($2.5)**	**($8.4)**	**($11.3)**	**($14.3)**	**($14.6)**	**$4.2**	**$23.7**
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Net Margin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Weighted avg. Shares Out	*41.7*	*21.7*	*31.7*	*32.5*	*31.9*	*36.0*	*38.0*	*40.0*	*45.0*	*39.8*	*48.0*	*55.0*	*60.00*	*65.00*	*70.00*
Reported EPS	**$0.16**	**($0.04)**	**($0.10)**	**($0.03)**	**$0.05**	**($0.05)**	**($0.05)**	**($0.06)**	**($0.06)**	**($0.21)**	**($0.24)**	**($0.26)**	**($0.24)**	**$0.06**	**$0.34**
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
One time charge	($8.09)	($0.34)	$1.61	$0.00	($6.82)	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$1.00
Non GAAP Net Income	**($1.3)**	**($1.2)**	**($1.6)**	**($1.1)**	**($5.2)**	**($1.7)**	**($2.0)**	**($2.3)**	**($2.5)**	**($8.4)**	**($11.3)**	**($14.3)**	**($14.6)**	**$4.2**	**$24.7**
Non GAAP EPS	**($0.03)**	**($0.06)**	**($0.05)**	**($0.03)**	**($0.16)**	**($0.05)**	**($0.05)**	**($0.06)**	**($0.06)**	**($0.21)**	**($0.24)**	**($0.26)**	**($0.24)**	**$0.06**	**$0.35**

Source: company filings and Zacks estimates

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