Zacks Small-Cap Research

November 17, 2011
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Titan Pharmaceuticals, Inc. (TTNP-OTC)

TTNP: Probuphine NDA Expected Soon, Titan May Seek Priority Review…

Current Recommendation	**Outperform**
Prior Recommendation	N/A
Date of Last Change	06/01/2011
Current Price (11/17/11)	$1.24
Target Price	**$3.00**

UPDATE

In October, Titan announced that it has met with the U.S. FDA for a pre-NDA meeting regarding Probuphine. Based upon this meeting, management believes that its Phase 3 clinical program completed to date is acceptable to the FDA to support a submission of a NDA via the 505(b)(2) pathway and that no additional clinical efficacy or safety studies are required to support the application. Additionally, Titan believes it has clear guidance from the FDA on the requirements for submitting the NDA for consideration to be designated as a Priority Review. This is a significant positive in our view.

We remain optimistic on the story and see the shares as meaningfully under-valued at today's price. Our target is $3.

SUMMARY DATA

52-Week High	**$2.16**
52-Week Low	**$1.10**
One-Year Return (%)	**5.00**
Beta	**10.08**
Average Daily Volume (sh)	**111,868**
Shares Outstanding (mil)	**59**
Market Capitalization ($mil)	**$75**
Short Interest Ratio (days)	**0.25**
Institutional Ownership (%)	**2**
Insider Ownership (%)	**15**
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 2011 Estimate	**N/A**
P/E using 2012 Estimate	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2010	2.4 A	1.3 A	3.6 A	2.7 A	10.1 A
2011	0.9 A	0.7 A	0.5 E	0.5 E	2.6 E
2012					27.7 E
2013					33.3 E

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

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2010	-$0.01 A	-$0.03 A	-$0.01 A	-$0.05 E	-$0.09 E
2011	-$0.08 A	-$0.12 A	-$0.06 E	-$0.06 E	-$0.31 E
2012					$0.23 E
2013					$0.24 E

Zacks Projected EPS Growth Rate - Next 4 Years % **N/A**

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WHAT'S NEW

Financial Update

On November 17, 2011, Titan Pharmaceuticals held a conference call to discuss its third quarter financial results and provide an update on recent developments. Total revenues in the quarter were $1.012 million, and consisted of $0.973 million in royalties on Fanapt sales at Novartis and $0.039 million in grant revenues from the NIH (for Probuphine) and the SBIR (for ProNeura). Operating expenses were in-line with expectations in the quarter at $2.969 million. Net loss in the quarter totaled $0.8 million, or ($0.01) per share, which included a $2.390 million gain in other expenses resulting in the change in the fair value of stock warrant liability. Titan exited the third quarter with $2.8 million in cash and equivalents.

…Worked Deerfield Transaction…

In November 2011, the company entered into another transaction with Deerfield Management whereby Titan will sell the vast majority of its remaining royalty stream on Fanapt in exchange for $5 million in cash and $10 million in debt forgiveness from the previous Deerfield transaction. As a reminder, in March 2011, Titan entered into an agreement with Deerfield Management that provides Titan with $20 million in financing through a five year senior secured credit facility at 8.5% per annum. Besides principal and interest repayment, Titan agreed to pay 2.5% of the global net sales of Fanapt to Deerfield. Titan received between 8% and 10% royalty on sales of Fanapt from Novartis AG. The deal in November 2011 provides for the bulk of the remaining royalties to be paid to Deerfield under the following schedule: 100% below and 40% above a prespecified sales threshold. The sales threshold is as follows for the royalty payments:

	2011	2012	2013	2014	2015	2016	2017
Threshold Sales Level (mil)	All	$70M	$85M	$109.25M	$120.75M	$126.5M	$46M

Titan will still owe Deerfield $10 million in principal and interest repayments following closing of the transaction. The first payment will be due in April 2013, followed by three additional equal payments in April 2014, April 2015, and April 2016. Deerfield continues to own 6 million warrants exercisable at approximately $1.57 per share. If Deerfield were to exercise all 6 million warrants, it would provide $9.4 million (gross) to Titan.

For the purpose of our financial model, we assume global net sales of Fanapt will not eclipse the threshold level before 2017, and thus Titan will receive no net royalty on Fanapt. We now forecast that Titan will exit 2011 with just under $5 million in cash and investments. We find this to be sufficient to fund operations until June 2012. We note management continues to work with Woodside Capital Partners and Keelin Reeds Partners in its search for a commercialization partner on Probuphine. Woodside is focused on identifying potential partners and introducing them to the Probuphine story. Keelin Reeds is focused on the analytics and valuation of the asset.

Pre-NDA Meeting Brings Positive News

On October 26, 2011, Titan announced that it met with the U.S. Food and Drug Administration (FDA) for a Pre-New Drug Application (Pre-NDA) meeting regarding Probuphine, a subcutaneous implant formulation of the marketed drug buprenorphine. Based upon this meeting, Titan believes that its phase 3 clinical program completed to date is acceptable to the FDA to support submission of an NDA via the 505(b)(2) pathway and that no additional clinical efficacy or safety studies are required to support the submission. This was in-line with our thinking.

However, to our surprise, the company also received clear guidance from the FDA on the requirements for submitting an NDA for consideration to be designated as a Priority Review. The FDA grants a Priority Review for products believed to address unmet medical needs. The designation shortens the average amount of time from completed application until approval decision from 10 months to 6 months as defined under the Prescription Drug User Fee Act (PDUFA).

Titan has also received initial comments from the FDA regarding manufacturing and non-clinical information and is in ongoing discussions with the agency to confirm these requirements. The company will confirm the overall regulatory path forward upon receipt of formal meeting minutes from the FDA in the coming weeks and will provide a further update at that time. We expect this update to coincide with the release of the third quarter financials, in mid-November 2011. Our best guess is that management will be in position to file the NDA by the middle of 2012.

…Time To Partner…

Now that Titan has a clear path toward the NDA filing, and potentially an application that the U.S. FDA could consider a Priority Review, we believe management will begin actively pursuing a commercialization partnership. Approval is the ultimate value driver, but we believe that two positive phase 3 trials and a NDA potentially under Priority Review by the second quarter 2012 should provide enough of a road-map with a potential partner to sign a deal in 2012. We think Probuphine, with potential peak sales between $300 and $350 million, could fetch as much as $25 million upfront, with another $20 to $25 million for approval, along with a tiered royalty that pays Titan roughly 20% on U.S. sales. As noted above, management continues to work with Woodside Capital Partners and Keelin Reeds Partners in its search for a commercialization partner on Probuphine. Woodside is focused on identifying potential partners and introducing them to the Probuphine story. Keelin Reeds is focused on the analytics and valuation of the asset. As of November 2011, management reports being engaged with several potential partners that are doing detailed due diligence.

We forecast that Titan exited 2011 with $4.8 million in cash. We project this is enough cash to fund operations into the second quarter 2012. By this time, the NDA should be under review. The goal is to find a commercialization partner on Probuphine to generate non-dilutive cash. However, if management cannot get a deal done before the end of the second quarter 2012, we would expect a dilutive offering enough to bridge fund operations to the PDUFA data. One potential for raising cash outside of a deal is the 6 million warrants outstanding at Deerfield, although we note at the current stock price those warrants remain under-water.

INVESTMENT THESIS

Second Phase 3 On Probuphine Hits!

In July 2011, Titan Pharma announced positive results from its phase 3 trial, PRO-806, evaluating Probuphine in treating patients with opioid dependence. PRO-806 was the second, confirmatory, phase 3 program evaluating Probuphine vs. placebo for safety and efficacy. The phase 3 clinical trial was a randomized, placebo and active-controlled, multi-center study conducted at 20 sites in the U.S. that treated 287 patients, aged 18 to 60 years across three dosing arms: Probuphine (114 patients), the approved and widely-used sublingual formulation of buprenorphine, Suboxone, (119 patients) and placebo implants (54 patients). Patients were treated for up to 24 weeks and the Probuphine and placebo dosing arms were double-blinded, while the Suboxone arm was open-label.

The trial had two primary analyses:

1) Cumulative Distribution Function of the percentages of opioid-negative urines (CDF-ONU) over the 24-week treatment period ➔ Results were statistical significance at $p<0.0001$ vs. placebo, and were consistent with the previously reported phase 3 data (from PRO-805), and published in JAMA, October 2010.

   In fact, in August 2011, management provided some additional color on the CDF-ONU endpoint, breaking down the 24-week period into two sections, weeks 1-16 and weeks 17-24. The statistical significance for weeks 1-16 was $p<0.0001$, whereas for weeks 17-24 it was $p=0.0002$.

2) Cumulative Distribution Function of the percentages of opioid-negative urines incorporating patient self-reported opioid use over the 24-week treatment period ➔ Results were statistical significance at $p<0.0001$ vs. placebo.

Probuphine demonstrated statistical and clinical superiority over placebo for the 24-week treatment period in the mean percentages of urine samples negative for illicit opioids, 36% vs. 14% ($p<0.0001$). Probuphine treatment resulted in significant improvement in clinician-rated global severity of opioid dependence ($p=0.0003$) and clinician-rated global improvement in opioid dependence ($p=0.0002$) vs. placebo at the end of the 24-week treatment period.

Probuphine also met a key trial secondary objective by demonstrating non-inferiority to Suboxone (12-16 mg) over the 24-week treatment period. There was no statistically significant difference between Probuphine and Suboxone on the clinician-rated global severity ($p=0.7831$) and clinician-rated global improvement ($p=0.9881$). We remind investors that Suboxone is used by over 500,000 patients in the U.S. each year, with annualized sales over $1 billion. Worldwide, Suboxone is a $1.2 billion drug.

Pro-806	Probuphine (n=114)	Suboxone (12-16mg) (n=119)	Placebo (n=54)
Negative Urine Samples	36%	35%	14%
Trial Retention	64%	64%	26%

The trial further demonstrated that Probuphine was well tolerated, with an overall safety profile similar to that seen in previous studies. We present the most common adverse events below:

Headache	13.2%	16.0%	9.3%
Up Resp. Tract Infection	8.8%	9.2%	7.4%
Depression	8.8%	2.5%	3.7%
Insomnia	7.9%	13.4%	14.8%
Sore Throat	7.0%	3.4%	1.9%
Nausea	6.1%	6.7%	1.9%
Vomiting	6.1%	4.2%	1.9%

Titan presented these results at a plenary session at the 13th annual meeting of the International Society of Addiction Medicine (ISAM) in Oslo, Norway in September 2011.

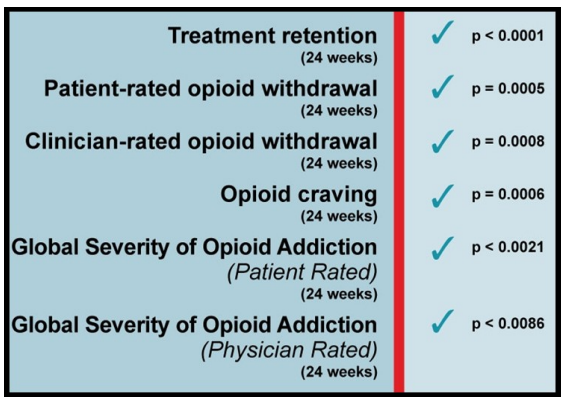
We remind investors that Titan is still conducting an open-label, 6-month re-treatment trail, PRO-811, for patients that completed PRO-806. As of November 2011, management noted that over 80% of the eligible patients have elected to enroll in the study. Data is expected from PRO-811 later this year or in early 2012.

…Confirms Previous Positive Data With First Phase 3 Trial…

Titan successfully completed the first phase 3 study (Study Pro-805) and presented the data at U.S. and international scientific meetings held during 2008 and 2009. Pro-805 enrolled a total of 163 subjects (2-1 randomization) from 18 clinical sites all in the U.S. participated in the program.

In this study, Probuphine showed a clinically and statistically significant difference over placebo in illicit opioid use as measured by urine testing performed three times per week, for the entire duration of the 6 month treatment (p=0.0117). As agreed with the FDA, the statistical analysis was an evaluation of the Cumulative Distribution Function of the percent opioid negative urines (CDF-ONU) analyzed using the Wilcoxon Rank Sum Test conducted twice, specifically, the primary endpoint compared the CDF-ONU of percent negative urines for weeks 1-16 (p=0.0361) and the key secondary endpoint compared the CDF-ONU of the percent negative urine samples for weeks 17-24 (p=0.0004).

We note that approximately 66% of the Probuphine patients completed the study vs. only 31% on the placebo. There is often a mixed bag of reasons why patients discontinue, from lack of response to such a great response that patients opted out of the return visits prior to the trials completion. We think it is important to note, however, that there were no treatment failures in the test group, vs. approximately 31% on the placebo. We believe this evaluation demonstrates the effectiveness of Probuphine compared to placebo for the entire treatment period, as well as emphasizes that patients who are compliant to treatment with Probuphine show even better results (compared to placebo) over time.



Additional secondary analysis demonstrated things like, comparison of the mean percent negative urines, retention in treatment, patient and clinician opioid withdrawal, opioid craving, and patient and clinician rated improvement and disease severity all showed highly statistically significant differences in favor of Probuphine.

We believe this emphasizes the clear effectiveness of the product, and should help drive sales in the real-world setting. Safety parameters including adverse events, vital signs, and clinical laboratory testing demonstrated that Probuphine was generally well tolerated in this patient population. Data from this study has been published in the Journal of American Medical Association (JAMA) in October 2010.

Following completion of the Pro-805 program, patients were eligible to enroll into a six-month, open-label, multi-center retreatment trial, dubbed Pro-807. This trial was completed in the second quarter 2009. We note that 70% of the eligible test subjects from Pro-805 elected to participate in the open-label safety extension. Approximately 74% of these patients completed the 6 month follow-up. Results show that Probuphine was safe and well-tolerated. During Pro-805 and Pro-807, implant insertion and removal procedures were safe and well-tolerated. Results from these studies have been presented at the American Society of Addiction Medicine (ASAM), the California Society of Addiction Medicine (CSAM), and the American College of Neuropsychopharmacology (ACNP) meeting all in 2009.

…Pre-NDA Meeting Outlines Path Forward – With Potential Priority Review…

On October 26, 2011, Titan announced that it met with the U.S. Food and Drug Administration (FDA) for a Pre-New Drug Application (Pre-NDA) meeting regarding Probuphine, a subcutaneous implant formulation of the marketed drug buprenorphine. Based upon this meeting, Titan believes that its phase 3 clinical program completed to date is acceptable to the FDA to support submission of an NDA via the 505(b)(2) pathway and that no additional clinical efficacy or safety studies are required to support the submission. This was in-line with our thinking.

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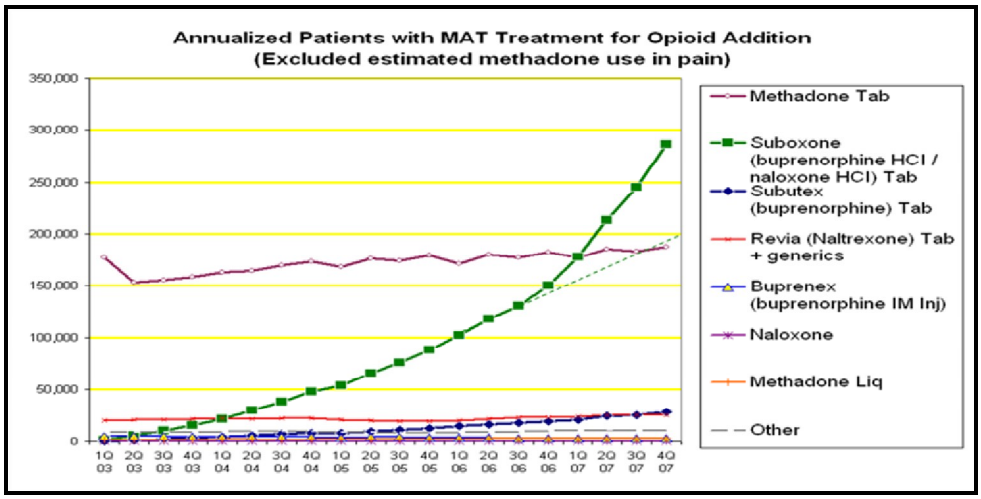
…Large Market Opportunity…

Sublingual buprenorphine sales are just over $1 billion in the U.S., with another $250 million outside the U.S.



Probuphine has several key advantages over Suboxone. On Titan's second quarter update call, management hosted two of the lead investigators in the PRO-806 phase 3 study. They were Dr. Walter Ling, M.D., Professor of Psychiatry and Director, Integrated Substance Abuse Programs at the David Geffen School of Medicine at UCLA and Dr. Richard N. Rosenthal, M.D., Chairman of Psychiatry at St. Luke's-Roosevelt Hospital Center, a teaching hospital of Columbia University, past president of the American Academy of Addiction Psychiatry. Both doctors expressed their enthusiasm for Probuphine and why they believe it will see meaningful commercial uptake.

We do not see the implant procedure as greatly limiting uptake for Probuphine. Management full acknowledges that there will be some patients adverse to an implantable drug, but we suspect that it will be only a small percent of the patients seeking treatment. In our view, and the views of Dr. Ling and Dr. Rosenthal, Probuphine improves compliance greatly over the once daily oral medication, as well as eliminates the risk for diversion or misuse.

It eliminates the need for monthly visits to the clinic or the need for the physician to actively monitor the patient to make sure dosing is on schedule. Once Probuphine is implanted, the drug goes to work unencumbered for six months. Dr. Rosenthal called Probuphine, "The right drug with the right delivery system."

Opioid addiction is a major health and social issue, especially in the U.S. An estimated 5+ million people worldwide, nearly 4 million of which are in the U.S., are abusing or addicted to opioids. In the U.S. alone, opioid abuse has increased 140% from 1992 to 2003. It's a $10+ billion burden to the U.S. healthcare market.

The World Health Organization estimates that between 4.6 and 5.2 million individuals in the U.S. and Europe use illicit opioids such as heroin, and more than 2.0 million individuals in the U.S. alone are addicted to prescription opioid medications. It is estimated that more than 1.0 million people in the U.S. and Europe currently receive pharmacological treatment for opioid addiction. A six month prescription of Suboxone costs roughly $2000, with patients averaging duration between 8 and 10 months. At a similar price of $2000 per implant, if Probuphine can capture 10% market share, the drug is a $300+ million opportunity for Titan.

- Estimated 5 million individuals addicted to opioids…
  - 25% seeking treatment (Suboxone does 500,000+ Rx per year)…
    - 10% try Probuphine (six month implant)…
      - Probuphine costs $2500 per implant…
        - 5 million * 25% * 10% * $2500 per implant ~ $300 million

VALUATION & RECOMMENDATION

Stock Looks Under-Valued

We see Titan shares as meaningfully under-valued today. Our scenario for Probuphine assumes a new drug application (NDA) during the first half of 2012, approval in late 2012, with a launch in early 2013. We expect a U.S. deal around the time of the NDA filing, which should bring upfront cash in the area of $25 million, a similar approval milestone in late 2012, backend milestone totaling $100 million, and a ~20% royalty on sales.

Under this scenario, we see the net present value (NPV) of Titan's cash from a deal, risk-adjusted backend milestones, and royalties on sales worth $200 million, or around $3.00 per share. We are using a more aggressive 18% discount rate for these cash flows. This is similar to the company's cost of capital based on recent financings.

Upcoming Events

EVENTS TO WATCH	TIMING
Data presentation at NIDA International Forum	June 2011
Top-line data from phase 3 (confirmatory) Pro-806 trial	July 2011
Additional Data from phase 3 Pro-806 trial	August 2011
Data presentation at International Society of Addiction Medicine	September 2011
Meet with U.S. FDA for pre-NDA meeting	October-2011
Data from open-label Pro-811 safety re-treatment study	Q4-2011
Data presentation on Pro-806	Q4-2011
Sign commercialization partnership on Probuphine	Anytime
Data presentation at American Academy of Addiction Psychiatry	December 2011
File U.S. NDA on Probuphine	1H-2012
U.S. FDA NDA acceptance	1H-2012
U.S. FDA PDUFA on Probuphine (w/ Priority Review)	Q4-2012
Launch Probuphine in the U.S.	Q1-2013

Source: Zacks Small-Cap Research, Inc.

PROJECTED FINANCIALS

Titan Pharmaceuticals, Inc.
Income Statement

	2009 A	2010 E	Q1 A	Q2 A	Q3 A	Q4 E	2011 E	2012 E	2013 E	2014 E
Probuphine Royalty	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$5.9**	**$18.1**
YOY Growth	-	-	-	-	-	-	-	-	-	*206.0%*
Fanapt Sales (at Novartis)	*$0*	*$31*	*$9*	*$7*	*$12*	*$13.0*	*$41.2*	*$70.0*	*$85.0*	*$110.0*
YOY Growth	-	-	*-56.5%*	*900.0%*	*148.2%*	*154.9%*	*31.1%*	*70.1%*	*21.4%*	*29.4%*
Fanapt Royalty	**$0**	**$2.5**	**$0.7**	**$0.6**	**$1.0**	**$0**	**$2.3**	**$0**	**$0**	**$0**
YOY Growth	-	-	*-56.7%*	*994.5%*	*145.7%*	*-100.0%*	*-8.8%*	-	-	-
Licensing & Grant Revenue	**$0.1**	**$7.6**	**$0.2**	**$0.1**	**$0.0**	**$0.1**	**$0.5**	**$25.0**	**$25.0**	**$0**
Total Revenues	**$0.1**	**$10.1**	**$0.9**	**$0.7**	**$1.0**	**$0.1**	**$2.8**	**$25.0**	**$30.9**	**$18.1**
YOY Growth	-	-	-	-	-	-	*-72.7%*	*807.4%*	*23.7%*	*-41.4%*
CoGS	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	*100%*	*100.0%*	-	-	-	-	*100.0%*	*#DIV/0!*	*100.0%*	*100.0%*
R&D	$2.5	$12.9	$3.7	$3.9	$2.2	$2.5	$12.4	$8.0	$10.0	$10.0
% R&D	-	*127.4%*	-	-	-	-	*450.6%*	*32.0%*	*32.3%*	*55.2%*
SG&A	$3.4	$3.3	$0.8	$0.9	$0.7	$0.9	$3.4	$3.6	$4.0	$4.0
% SG&A	-	*32.3%*	-	-	-	-	*122.7%*	*14.4%*	*12.9%*	*22.1%*
Operating Income	($5.8)	($6.0)	($3.6)	($4.2)	($2.0)	($3.3)	($13.0)	$13.4	$16.9	$4.1
Operating Margin	*0%*	*0.0%*	-	-	-	-	*-473.3%*	*53.6%*	*54.7%*	*22.7%*
Total Other Income	($0.1)	($0.8)	($0.9)	($2.8)	$1.2	($0.4)	($3.0)	($1.5)	($1.0)	$1.0
Pre-Tax Income	($5.9)	($6.8)	($4.5)	($7.0)	($0.8)	($3.7)	($16.0)	$11.9	$15.9	$5.1
Taxes & Other	$0	($1.2)	$0	$0	$0	$0	$0	$0	$2.4	$1.5
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*5%*	*15%*	*30%*
Net Income	($5.9)	($5.6)	($4.5)	($7.0)	($0.8)	($3.7)	($16.0)	$11.9	$13.5	$3.6
Net Margin	*0%*	*0.0%*	-	-	-	-	*-580.9%*	*47.6%*	*43.8%*	*19.7%*
Reported EPS	**($0.10)**	**($0.09)**	**($0.08)**	**($0.12)**	**($0.01)**	**($0.06)**	**($0.27)**	**$0.19**	**$0.21**	**$0.05**
YOY Growth	-	*-6.2%*	-	-	-	-	*185.7%*	*-170.6%*	*11.0%*	*-74.4%*
Weight Ave. Shares Out	58.5	59.2	59.2	59.3	59.4	59.5	59.4	62.5	64.0	66.0

Source: Zacks Small-Cap Research, Inc. *Jason Napodano, CFA*

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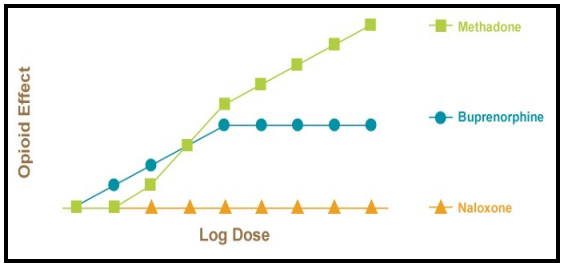
APPENDIX

…Background on buprenorphine…

Buprenorphine is a synthetic derivative of opium, chemically similar to both morphine and codeine, but has stimulatory rather than depressant effects. Buprenorphine is 25-50X more potent than morphine and is sometimes used recreationally by insufflations (crushing and inhaling the powder).

Buprenorphine is commonly used to treat addiction to heroin, and has proven superior in its efficacy and convenience to methadone. Withdrawal from buprenorphine after short-term use is generally far milder than other potent opioids, but can have a longer duration of abuse. The drug has a pharmacologic ceiling effect, which provides an increased safety margin when compared to methadone. As a result, the drug is now generally recognized as the gold standard for the treatment of opioid addiction. There are an estimated 3.7 million people addicted to opioids in the U.S., over 80% of which are prescription drugs.

	U.S.	EU
All Opioid Addiction	**3.7M**	**1.8M**
Heroin	0.6M	1.6M
Prescription Drugs	3.1M	0.2M



The product was first marketed in 1980 by British firm, Reckitt & Colman as an analgesic, available as Temgesic 0.2 mg sublingual tablets, and as Buprenex in a 0.3 mg/ml injectable formulation. In October 2002, the U.S. FDA approved Subutex as high-dose (2 mg & 8 mg) sublingual pill preparations indicated for detoxification and long-term replacement therapy in opioid dependency. As a result, the drug is now predominantly used for this purpose. Approval in France first came in 1997, and has since followed to the majority of the EU. Buprenorphine is a Schedule III controlled substance under the United Nations' Convention on Psychotropic Substances.

In October 2002, the U.S. FDA also approved Suboxone, a novel formulation of buprenorphine and naloxone, to increase the deterrence of abuse through intravenous injection. Naloxone is an opioid antagonist that blocks the high or euphoric effects for opioids such as heroine that leads to withdrawal symptoms. In October 2009, the FDA approved a generic preparation of 2 mg and 8 mg sublingual dosages of buprenorphine. Demand was so high that pharmacies began to run out of supply and Roxane Labs, the first generic filer, was unable to meet demand. In April 2010, the FDA approved a second supplier in Teva Pharmaceutical. Reckitt is now marketing a Suboxone Film, approved in August 2010, to counter generic the pending availability to the sublingual tablet.

In 2001, Grunenthal introduced Transtec (buprenorphine transdermal patch) in Europe for the treatment of chronic pain. The product is available as a 35, 52.5 and 70 ug (micrograms) per hour transdermal patches that deliver the dose over ninety-six hours. It is also used for the treatment of moderate to severe cancer pain and severe non-cancer pain not responding to non-opioids. Purdue Pharma markets Butrans in the U.S., a 5, 10, and 20 ug, 7-day transdermal patch for the management of moderate to severe chronic pain in patients requiring a continuous, around-the-clock opioid analgesic for an extended period of time. A similar transdermal product is marketed by collaboration between Mundipharma and Grunenthal in Australia under the name Norspan. We note that buprenorphine is not administered orally due to very high first-pass metabolism. The transdermal patch products can typically be worn for 3 to 7 days.

BioDelivery Sciences is currently in phase 3 trials with BEMA buprenorphine. The company's BEMA technology utilizes a small, bioerodible polymer film for application to the mucosal membranes (inner lining of cheek). BEMA films were designed to rapidly deliver a dose of drug across the mucous membranes for time sensitive conditions or to facilitate administration of drugs with poor oral (pill) absorption. BEMA buprenorphine is being designed to eliminate abuse potential by crushing sublingual tablets, a similar concept to Titan's Probuphine. However, BDSI's BEMA product requires daily dosing whereas Probuphine is a six month implant.

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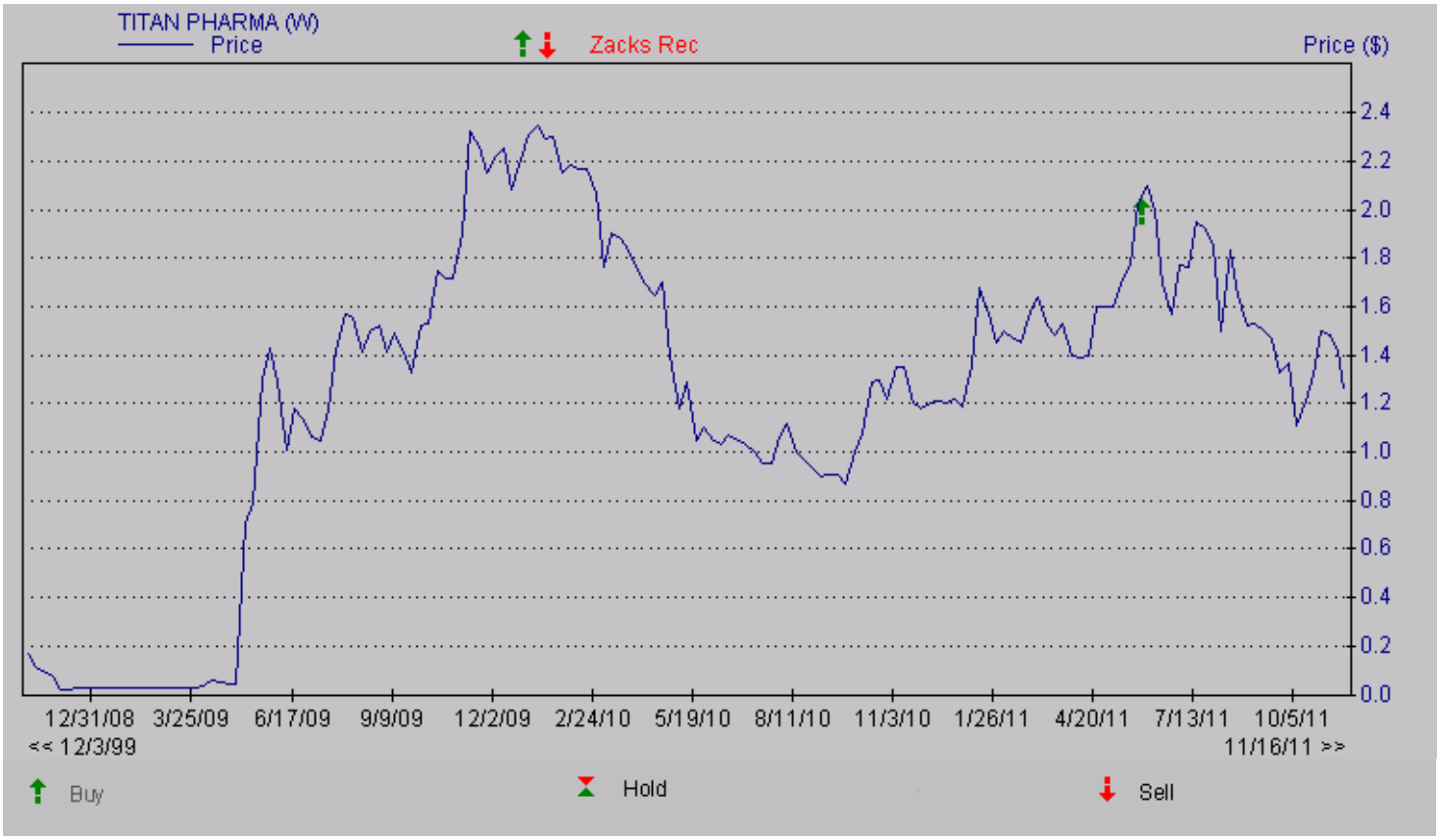
HISTORICAL RECOMMENDATIONS



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