Zacks Small-Cap Research

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Tenax Therapeutics, Inc. (TENX-NASDAQ)

LEVO-CTS Misses Primary Endpoints; Vital Secondary Endpoints Achieved.

Based on our DCF model and a 15% discount rate, TENX is valued at approximately $4.00 per share. We apply a 50% probability of eventual sales of levosimendan in the United States.

Current Price (2/3/17)	$0.71
Valuation	**$4.00**

OUTLOOK

Tenax has licensed the *calcium sensitizer/K-ATP activator* levosimendan in the US and Canada to develop and commercialize for the treatment of LCOS. The drug has been approved in over 60 countries with 35 published trials supporting its safety and efficacy and has over 1 million patient exposures.

On January 31, 2017 Tenax announced the Phase 3 LEVO-CTS trial failed to achieve primary endpoints, but did show statistical significance in two of the trial's secondary endpoints. Due to the primary endpoint miss, we forecast a year delay and eventual launch of levosimendan in early 2019.

Levosimendan has a 16-year history of use in Europe with a substantial volume of literature supporting its safety and efficacy. Given the body of research reinforcing indications in LCOS, and meta-analysis supporting reductions in mortality and hospitalizations, we believe there is a possibility of FDA approval to address these unmet needs.

SUMMARY DATA

52-Week High	**$0.41**
52-Week Low	**$2.94**
One-Year Return (%)	**-73.2**
Beta	**1.01**
Average Daily Volume (sh)	**1,121,852**
Shares Outstanding (mil)	**28.1**
Market Capitalization ($mil)	**$19.9**
Short Interest Ratio (days)	**6.4**
Institutional Ownership (%)	**40**
Insider Ownership (%)	**16**
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 2016 Estimate	**N/A**
P/E using 2017 Estimate	**N/A**
Zacks Rank	**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)
2015	$0.00 A	$0.00 A	$0.00 A	$0.00 A	$0.00 A
2016	$0.00 A	$0.00 A	$0.00 A	$0.00 E	$0.00 E
2017					$0.00 E
2018					$56.3 E

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	-$0.10 A	-$0.17 A	-$0.10 A	N/A	N/A
2016	-$0.19 A	-$0.17 A	-$0.15 A	-$0.14 E	-$0.65 E
2017					-$0.39 E
2018					-$0.52 E

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WHAT'S NEW

Tenax Reports LEVO-CTS Topline Results

On January 31, 2017, Tenax Therapeutics, Inc. (NASDAQ:TENX) announced topline results from its Phase 3 LEVO-CTS trial in cardiac surgery. The trial's primary endpoints were not statistically significant, however, two secondary endpoints which include reduction in low cardiac output syndrome (LCOS) and use of postoperative secondary inotropes were statistically significant. The lack of statistical significance in the primary endpoints was surprising given the broad body of literature[1,2,3] supporting efficacy in the areas investigated. Previously conducted research has shown levosimendan's cardioprotective effects, its ability to reduce the risk of worsening congestive heart failure (CHF) or death compared with placebo in patients with decompensated CHF and improvements in short term and long term mortality when compared to placebo.

The trial's primary endpoints measured at 30 days were:

1. All-cause death or use of mechanical assist device following the start of surgery for poor cardiac function despite inotropic support and adequate fluid replacement through Day 5 (dual endpoint) **– Not statistically significant**
2. Composite of all-cause death, or perioperative nonfatal myocardial infarction, or need for renal dialysis, or use of mechanical assist device following the start of surgery for poor cardiac function despite inotropic support and adequate fluid replacement through Day 5 (quad endpoint) **– Not statistically significant**

Secondary endpoints included:

1. Duration of intensive care or coronary care unit **Not statistically significant**
2. Incidence of LCOS **- Statistically significant**
3. Postoperative use of secondary inotrope **– Statistically significant**

Other outcomes, which include occurrence of all-cause mortality from randomization through day 90 are not yet available as the end of the 90-day period has not yet been reached. We anticipate that this data will be available by the end of February 2017. It is possible that further analysis may show additional benefit of levosimendan which could be supportive of the case Tenax will make to the FDA.

Other trials have shown efficacy in a number of endpoints. The REVIVE[4] studies, looked at efficacy on symptoms of heart failure including death and found efficacy.[5] Other studies, which are summarized in an academic review[6] of the drug also show efficacy and safety. Despite the unexpected results from the LEVO-CTS trial, we believe that there is sufficient evidence available to support FDA approval under the right circumstances.

Originally, the Finish company Orion Pharmaceuticals (HEL: ORNBV) filed an NDA in the US for levosimendan for decompensated heart failure in 1998, but withdrew it due to additional questions by the FDA regarding safety and the breakdown of metabolites and a request for an additional trial. The drug was first approved in Sweden in 2000 and was subsequently approved and now used in 60 countries. During this period, and through additional trials, the FDA's initial questions to Orion have been answered and may provide support for an NDA.

Currently, Tenax is scheduling a meeting with the FDA to review the study results and to explore the recommended path forward. Statistical results from the trials were checked by the statistical team at the Duke Clinical Research Institute (DCRI) and double checked by statisticians at Stanford, who managed the DSMB process for LEVO-CTS, reducing the risk of a calculation error. In the next several weeks, Tenax will conduct additional analysis of the data to better understand why the endpoints failed to achieve the anticipated results. Data will be segmented by hospital, type of surgery, percent ejection fraction, blood pressure range, patient type and other variables in order to ascertain if there are any factors that interfered with the direction or statistical significance of the outcome. This may provide clarity as to why the LEVO-CTS results were at odds with favorable results shown in other studies.

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3868185/
[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5042644/
[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1994023/
[4] REVIVE (Randomised Multicenter Evaluation of Intravenous Levosimendan Efficacy) studies (REVIEV I and REVIEV II)
[5] https://www.ncbi.nlm.nih.gov/pubmed/24621834
[6] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3868185/#R115

The lack of statistical significance in the primary trial endpoints reduces the probability of FDA approval. The results also may delay a favorable response by the regulatory body as Tenax will likely be required to gather more information. Despite this setback, there are a few positives that may support eventual approval, most importantly the numerous studies that have been conducted in the last 15 years that support a wide array of benefits from the drug and the million plus patients that have been administered levosimendan. We note that safety and efficacy in at least one trial[7] was so strong, it was halted prematurely due to its clear mortality benefit. Furthermore, the statistical significance of secondary endpoints in the LEVO-CTS trial related to incidence of LCOS and reduction of use in postoperative inotropes are also supportive of favorable FDA action. It seems counterproductive to the health and safety of cardiac surgery patients for the regulatory body to deny approval for this drug given what we know; however, we do attempt to reflect this negative data point in our updated valuation.

To reflect the trial outcome, unknown progression of further requirements and increased uncertainty regarding FDA approval, we reduce the likelihood of approval from 75% to 50% and delay ultimate sales of levosimendan by one year to 2019. This adjustment reduced the target price derived from our DCF model from $9.00 to $4.00.

LEVO-CTS Trial Highlights

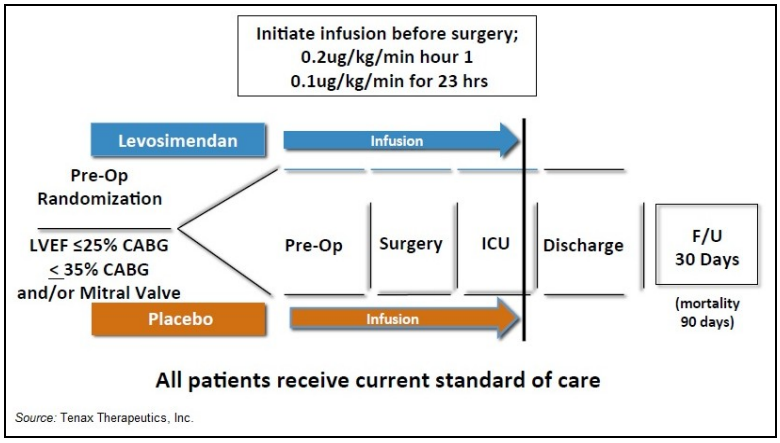
On November 18th, 2016 Tenax reported that it had completed enrollment of its target 880 patient panel size. Following the completion of enrollment, the company verified all data and locked the database, after which they analyzed the data over another multi-week period. Initial topline data was announced on January 31, 2017, which failed to show statistical significance for the primary endpoints, but did show statistical significance for two of the three secondary endpoints. Tenax is currently conducting further analysis and has scheduled a meeting with the FDA to determine what will be required to file for approval.

The additional analysis will examine how the drug performed in a number of subgroups including hospital, procedure type (CABG vs. valve replacement), by physician and other variables. Furthermore, data is not yet available for all-cause mortality from randomization through Day 90. Results from the full trial will be presented on March 19, 2017 at the American College of Cardiology 66th Annual Scientific Session in Washington, D.C.

Phase 3 LEVO-CTS Trial Design

In 2014, Tenax initiated the *"Levosimendan in Patients With Left Ventricular Systolic Dysfunction Undergoing Cardiac Surgery On Cardiopulmonary Bypass"* (LEVO-CTS) Phase 3 trial to evaluate the efficacy of levosimendan in the reduction of the incidence of morbidity and mortality in cardiac surgery patients at risk of LCOS when levosimendan is administered before and during cardiopulmonary bypass. The LEVO-CTS trial is a double-blind, randomized, placebo-controlled study that looks at the 30-day composite event rate of all-cause death, perioperative myocardial infarction, the need for dialysis, or the use of mechanical assist (intra-aortic balloon pump, left ventricular assist device, extracorporeal membrane oxygenation) in patients with left ventricular systolic dysfunction (reduced ejection fraction) preoperatively undergoing cardiac surgery via cardiopulmonary bypass. Duke Clinical Research Institute (DCRI) is conducting the trial, and helped design the Phase 3 protocol.

Exhibit I – Phase 3 Protocol



[7] Zairis MN, Apostolatos C, Anastassiadis F, et al. Comparison of the effect of levosi-mendan,or dobutamine or placebo in chronic low output decompensated heart failure. CAlcium Sensitizer or Inotrope or NOne in low output heart failure (CASINO) study. Program and abstracts of the European Society of Cardiology, Heart Failure Update; 2004; June 12–15; Wroclaw, Poland. 2004.

Co-primary endpoints in the trial include: (1) The all-cause death at 30 days or use of mechanical assist device following the start of surgery for poor cardiac function despite inotropic support and adequate fluid replacement) through Day 5, and (2) Composite of all-cause death (at 30 days), or perioperative nonfatal MI [CK-MB >10xULN or >100 ng/mL, CK-MB >5xULN or 50 ng/mL with new Q wave (>0.04 seconds wide in two contiguous leads) or new left bundle branch block)] (through Day 5), or need for renal dialysis (through Day 30), or use of mechanical assist device following the start of surgery for poor cardiac function despite inotropic support and adequate fluid replacement) (through Day 5). Secondary endpoints, which also intend to show the pharmacoeconomic benefit of the drug, include duration of ICU/CCU stay following surgery, and the incidence of LCOS. The safety endpoint is all-cause mortality through day 90, and since this an event-driven trial, there was a event rate check at 200 patients with interim analysis at 450 patients to check for futility or profound efficacy and to ensure safety.

It appears that low left ventricular ejection fraction (LVEF) cardiac surgery patients represent a high-risk population that experiences a higher incidence of LCOS and more severe outcomes. Based on levosimendan's established clinical profile that has demonstrated potential benefits in LCOS, we see the potential in the drug to reduce mortality and morbidity in cardiac surgery patients at risk for LCOS, as well as lowering hospital related and readmission costs.

The Path Forward for Tenax

Below we summarize upcoming milestones and events for Tenax:

- Meeting with FDA to review LEVO-CTS results prior to end of 1Q:17
- Collection of 90-day mortality data and further analysis of results
- Presentation of LEVO-CTS results March 19, 2017 at the American College of Cardiology 66th Annual Scientific Session in Washington, D.C.
- Address FDA requirements

Conclusion

Due to the unanticipated failure in the LEVO-CTS primary endpoints, there is a great deal of uncertainty as to what next steps for Tenax will be. Our original assessment of levosimendan found the drug to be a relatively low risk pursuit given the long-term and broad usage history and support the drug has globally for use in cardiac surgery. Given the favorable data available from other studies and due to the potential levosimendan has to address a critical care condition with high unmet medical need, there remains a case for FDA approval despite the LEVO-CTS trial results. There are currently no pharmacologic agents that are approved for the management, prevention and/or treatment of post-cardiac surgery LCOS, and furthermore given the statistically significant results on this secondary endpoint, we do believe there remains a possibility the FDA grants approval.

With approximately $20 million of cash estimated on the balance sheet as of January 2017, we believe that Tenax has sufficient cash to fund activities through mid-year 2018, which may allow Tenax to address many of the additional information requests from the FDA, up to but not including an additional Phase 3 trial. Given that there is currently no R&D being conducted and Tenax is in a wait and see mode, operational expenses will be at a minimum, which we reflect in our updated model. Based on our estimates, the company will need additional capital if a further trial is needed. Further funding will also be required if approval is granted to support milestone payments and Tenax's future commercialization activities including hiring a salesforce and launching levosimendan for LCOS.

We update our forecast for approval of levosimendan in the U.S. to occur in 4Q:18, with the year delay relative to our prior estimates necessary to gather additional information for the FDA. At this point our estimates are purely conjecture as we lack any guidance from the regulatory agency regarding their needs. We will adjust our estimates as more information becomes available regarding the upcoming meeting with the FDA, an event we foresee occurring in the next month or two.

PROJECTED FINANCIALS

Tenax Therapeutics, Inc. - Income Statement[8]

Tenax Therapeutics, Inc.	Q1 A	Q2 A	Q3 A	Q4 E	Jan 1- Dec 31 CY - 16 E	2017 E	2018 E
Total Revenues	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**
YOY Growth							
Cost of goods sold	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Product Gross Margin						*# DIV/0!*	*# DIV/0!*
Research and development	$3.9	$3.4	$3.2	$2.4	$13.0	$5.2	$1.0
General & administration	$1.8	$1.2	$1.3	$1.6	$5.9	$6.0	$15.0
Restructuring & Other Opex	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Finance costs	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Income from operations	($5.7)	($4.7)	($4.5)	($4.0)	($18.9)	($11.2)	($16.0)
Operating Margin						*# DIV/0!*	*# DIV/0!*
Interest Income (expense)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Other expense	($0.3)	($0.0)	($0.2)	$0.0	($0.6)	$0.0	$0.0
Pre-Tax Income	($5.4)	($4.6)	($4.3)	($4.0)	($18.3)	($11.2)	($16.0)
Income Taxes Paid	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($5.4)**	**($4.6)**	**($4.3)**	**($4.0)**	**($18.3)**	**($11.2)**	**($16.0)**
Net Margin						*# DIV/0!*	*# DIV/0!*
Reported EPS	**($0.19)**	**($0.17)**	**($0.15)**	**($0.14)**	**($0.65)**	**($0.39)**	**($0.52)**
YOY Growth					*80%*	*8%*	*34%*
Basic Shares Outstanding	28.12	28.12	28.12	28.90	28.31	29.00	31.00

Source: Company Filing // Zacks Investment Research, Inc. Estimates

[8] In 2016, Tenax changed its reporting calendar from an April 30 fiscal year end to a December 31 fiscal year end. As such, the company does not have comparable financial results for 2015.

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