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Tonix Pharmaceuticals Holding Corp. (TNXP-NASDAQ)

TNXP: TNX-102 SL P3 PTSD Trial Enrolling; Pipeline Expansion Adds Phase 2 Program and Two Pre-Clinical Programs…

Based on our probability adjusted DCF model that takes into account potential future revenues from TNX-102 SL PTSD, TNXP is valued at $3.00/share. This model is highly dependent upon continued clinical success of TNX-102 SL in PTSD and will be adjusted accordingly based upon future clinical results.

Current Price (09/19/19)	$0.48
Valuation	**$3.00**

OUTLOOK

Tonix Pharmaceuticals Holding Corp. (TNXP) has recently announced a number of new additions to its clinical and preclinical pipeline. The company is currently conducting the Phase 3 RECOVERY study of TNX-102 SL in patients with posttraumatic stress disorder (PTSD). The study is evaluating 5.6 mg TNX-102 SL in approximately 250 patients with civilian or military-related PTSD. We anticipate topline data in the first half of 2020. The company's PTSD pipeline also includes TNX-601 (tianeptine oxalate) and recently in-licensed TNX-1600 (triple reuptake inhibitor), both of which are intended for daytime use in treating PTSD. Tonix will also be pursuing additional indications for TNX-102 SL, including fibromyalgia (which is set to enter Phase 3 testing), Alzheimer's agitation, and alcohol use disorder. Lastly, Tonix will be developing two biologics: TNX-1300 (cocaine esterase) for cocaine intoxication and TNX-1500 (anti-CD154 antibody) for prevention of organ transplant rejection and treatment of autoimmune conditions.

SUMMARY DATA

52-Week High	**$7.20**
52-Week Low	**$0.41**
One-Year Return (%)	**-93.04**
Beta	**1.44**
Average Daily Volume (sh)	**317,627**
Shares Outstanding (mil)	**16**
Market Capitalization ($mil)	**$8**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**2**
Insider Ownership (%)	**1**
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 2018 Estimate	**-0.4**
P/E using 2019 Estimate	**-0.6**

Risk Level	**High**
Type of Stock	**Small-Value**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	0 A	0 A	0 A	0 A	0 A
2019	0 A	0 A	0 E	0 E	0 E
2020					0 E
2021					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	-$8.83 A	-$7.25 A	-$5.72 A	-$6.10 A	-$26.81 A
2019	-$1.29 A	-$0.95 A	-$0.39 E	-$0.34 E	-$2.20 E
2020					-$0.95 E
2021					-$0.70 E

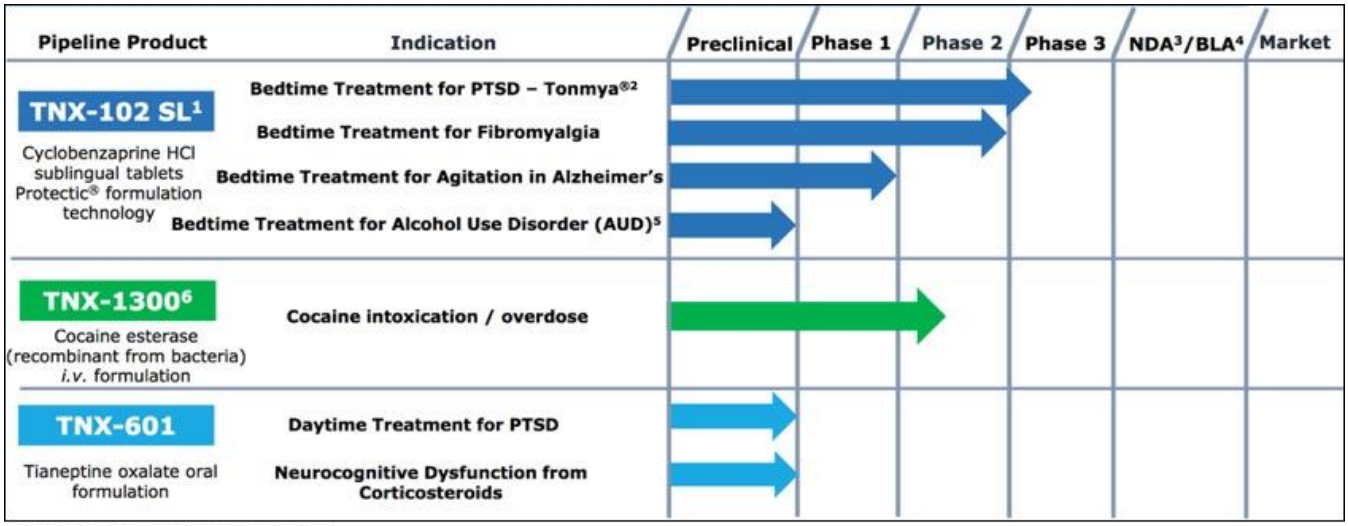
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WHAT'S NEW

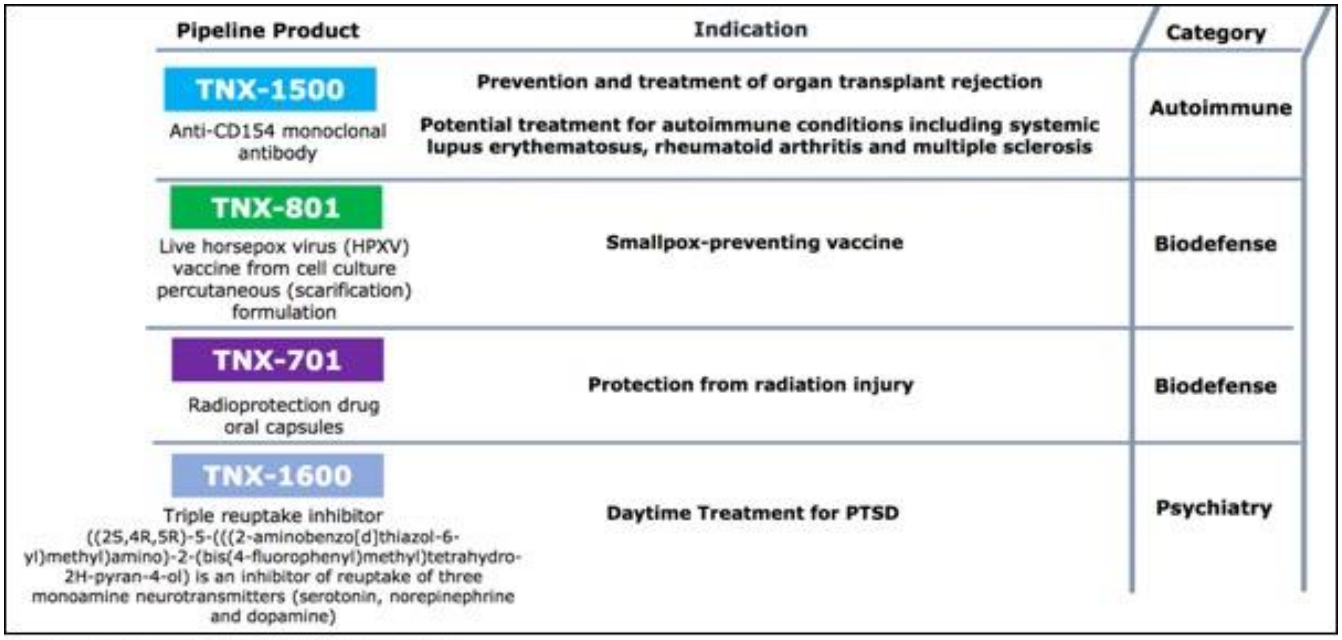
Business Update

Pipeline Expansion

In the past few months, Tonix Pharmaceuticals Holding Corp. (TNXP) has announced the addition of a number of new programs to its clinical and pre-clinical pipeline, including additional indications for its lead development compound TNX-102 SL. Below we give a brief overview of some of these programs.



Source: Tonix Pharmaceuticals Holding Corp.



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TNX-102 SL (cyclobenzaprine HCl sublingual tablets)

1) PTSD (RECOVERY Trial): Tonix is currently conducting the Phase 3 RECOVERY trial in patients with posttraumatic stress disorder (PTSD). The RECOVERY trial is a randomized, double blind, placebo controlled study of TNX-102 SL over 12 weeks with the primary endpoint being the Week 4 change in CAPS-5 score from

baseline between TNX-102 SL and placebo-treated patients. The Week 12 change in CAPS-5 score is a key secondary endpoint.

In addition to the primary endpoint being at Week 4 instead of Week 12, the RECOVERY trial incorporates other important changes compared to the Phase 3 HONOR trial that we think helps to increase the likelihood for success, including:

a) Inclusion will be limited to individuals with PTSD who experienced their trauma within the past nine years, while the HONOR trial included individuals who experienced a trauma from 2001 or later. A retrospective analysis showed a treatment effect in patients treated within nine years of trauma, while treated patients who were > nine years from their trauma failed to separate from placebo.
b) The study will include both civilian and military PTSD patients, while the HONOR trial had limited inclusion to only those with military-related PTSD.
c) The total number of study subjects is anticipated to be approximately 250, compared to approximately 550 subjects that were to be enrolled in the HONOR trial.

Management has indicated that thus far enrollment is going well and we believe that will continue to be the case. We anticipate topline results in the first half of 2020.

2) Fibromyalgia: In April 2019, Tonix announced receipt of the FDA meeting minutes following a clinical guidance meeting which indicated the agency supports the advancement of TNX-102 SL as a centrally acting non-opioid analgesic for the management of fibromyalgia. Two positive Phase 3 trials will support the registration of 5.6 mg TNX-102 SL in fibromyalgia along with long-term safety exposure data from the PTSD program.

Tonix previously tested 2.8 mg TNX-102 SL in fibromyalgia in the Phase 3 AFFIRM trial, a 12-week, randomized, double blind, placebo controlled trial of 519 patients who were administered either 2.8 mg TNX-102 SL or placebo at bedtime in a 1:1 randomization. The trial did not achieve statistical significance in the primary efficacy endpoint of the proportion of patients who reported a 30% or greater decrease in pain from baseline (P=0.095). The pre-specified statistical method utilized for the primary efficacy analysis counted all patients who withdrew from the study as non-responders, even if the reason for leaving the study had nothing to do with efficacy or tolerability. Another standard statistical method that takes into account the reasons for discontinuation showed statistical significance in the 30% responder analysis (P=0.012). Additionally, the same pain data analyzed by mean pain, an FDA accepted pain endpoint, demonstrated significant separation from placebo by mixed model repeated measures (MMRM) analysis (P<0.001).

While the AFFIRM trial did not meet the primary efficacy endpoint, 2.8 mg TNX-102 SL did show statistically significant effects on two other key secondary endpoints, Patient Global Impression of Change (PGIC) and Fibromyalgia Impact Questionnaire-Revised (FIQ-R) function and symptom domain scores, which assess global improvement, a range of fibromyalgia symptoms, and functional improvement.

New approaches to treat fibromyalgia are needed, as approximately one-third of patients are on chronic opiates. Given that 2.8 mg TNX-102 SL showed clinical benefit in a number of different outcomes, we believe that increasing the dose to 5.6 mg is likely to provide evidence to support its approval in the management of fibromyalgia. The company will need to secure additional funding to advance the fibromyalgia program as well as finalize and submit a new Phase 3 protocol and statistical analysis plan for FDA acceptance.

3) Agitation in Alzheimer's: Agitated behaviors (e.g., irritability, restlessness, aggression) are a significant issue in patients with Alzheimer's disease (AD). Reports indicate that agitation occurs in approximately 50% of AD patients (Alzheimer's Association) and is a leading cause of institutionalization (Cohen *et al*., 1997). While a number of hypotheses have been put forth to explain the cause of agitation in AD, there is currently no agreed upon theory. There are also no FDA approved therapies for treating agitation in AD.

Cyclobenzaprine has multiple activities that include antagonism of the 5-HT_{2A} receptor, the alpha-1 adrenergic receptor, and histamine H_1 receptor, thus potentially being able to impact mood, anxiety, and psychosis, the three main areas in which symptoms of agitation are generally seen.

The FDA has cleared the IND such that a Phase 2 clinical trial can initiate in patients with agitation in AD. In addition, the agency has granted Fast Track designation for TNX-102 SL in agitation in AD. While the company has yet to disclose how the study will be funded, we believe a partnership is the most likely scenario.

4) Alcohol Use Disorder: The National Institute on Alcohol Abuse and Alcoholism estimates that there are approximately 16 million people in the U.S. with alcohol dependence or abuse. There are currently three FDA approved medicines to treat alcohol dependence including Antabuse®, Vivitrol®, and Campral®. Vivitrol® is an extended release version of naltrexone that is administered by injection once monthly. Sales of Vivitrol totaled $303 million in 2018 ($86 million for AUD), and it is expected to generate approximately $120 million in revenue in AUD in 2022 (EvaluatePharma).

   Sleep disturbance is a common problem for those recovering from alcohol dependence and is an independent risk factor for relapse to alcohol (Arnedt *et al*., 2007). TNX-102 SL can improve sleep quality, thus making it a good candidate for AUD treatment. Tonix will be meeting with the FDA in the fourth quarter of 2019 for a pre-IND meeting, and upon receiving clearance for the IND, TNX-102 SL for AUD will be Phase 2 ready.

PTSD Programs

Tonix has a total of three programs in PTSD, including TNX-102 SL, which is currently in a Phase 3 clinical trial in PTSD. The rationale for multiple programs includes: 1) leveraging the company's core expertise in PTSD drug development; 2) the heterogeneity of PTSD symptoms means that different patients may respond to different medicines; 3) the severity of PTSD indicates that different combinations of drugs may be optimal for certain patients.

1) TNX-601: Tonix is developing TNX-601 for the daytime treatment of PTSD (as opposed to TNX-102 SL, which is administered at bed time). It is a novel formulation of tianeptine, which is thought to exert its antidepressant effects through indirect action on glutamate receptors (both AMPA and NMDA) that causes release of brain-derived neurotrophic factor (BDNF) (McEwen *et al*., 2010). This is in contrast to antidepressant drugs such as Spravato® (esketamine), which was recently approved by the FDA for the treatment of depression, which acts directly on the NMDA receptor.

   Tianeptine is currently available as a depression treatment in the E.U., Asia, and Latin America, but is not approved in the U.S. or U.K. Tonix has discovered a novel salt and polymorph of tianeptine that could lead to improved stability, consistency, and manufacturing. Due to its reported pro-cognitive and anxiolytic effects, TNX-601 may treat PTSD by a different mechanism of action compared to TNX-102 SL.

2) TNX-1600: This is a multifunctional neuromodulator that inhibits norepinephrine, serotonin, and dopamine transporters with Ki values of 6, 21, and 30 nM, respectively. In addition, it has little to no affinity for other CNS receptors. In a rodent model for traumatic stress exposure, TNX-1600 was shown to attenuate acquisition and retention of fearful memories in rats exposed to traumatic stress, was efficacious in the forced swim test (indicative of anti-depressant activity), and did not stimulate locomotor activity (indicative of a low abuse potential).

Cocaine Intoxication

TNX-1300: In May 2019, Tonix announced the in-licensing of TNX-1300, a double-mutant cocaine esterase (CocE) for the treatment of cocaine intoxication. This is a Phase 2 asset and has received breakthrough therapy designation by the U.S. FDA. TNX-1300 is a recombinant enzyme derived from a *Rhodococcus* species that utilizes cocaine as a sole source of carbon and nitrogen. A previous Phase 2 clinical trial conducted by Reckitt Benckiser Pharmaceuticals, the previous licensee to the product, with 29 cocaine abusers showed that TNX-1300 reduced cocaine plasma concentration by 90% within two minutes and cocaine-induced physiological effects were significantly reduced compared to placebo (Nasser *et al*., 2014). With approximately 500,000 emergency room visits every year for treatment of cocaine use, and approximately 50% of those visits leading to hospitalization, there is a potentially substantial market opportunity for the treatment of cocaine intoxication.

Prevention of Organ Transplant Rejection

TNX-1500: This is a third-generation anti-CD154 monoclonal antibody that was developed in-house by Tonix. The company recently announced the signing of a research collaboration with Massachusetts General Hospital, led by transplantation experts such as Dr. Richard N. Pierson III, to develop TNX-1500 as a treatment for the prevention of organ transplant rejection and potentially to be utilized in conjunction with 'humanized' pig organs through xenotransplantation. CD154, also known as CD40 ligand (CD40L), is a member of the tumor necrosis factor (TNF) super family and is expressed on the surface of activated T cells to mediate helper T cell function. While no anti-CD154 monoclonal antibodies have been approved, in 2016 Boehringer Ingelheim entered into a collaboration with

AbbVie for the development of two monoclonal antibodies (including an antagonistic anti-CD40 antibody) that included an upfront payment of $595 million.

Financial Update

On August 12, 2019, Tonix announced financial results for the second quarter of 2019. As expected, the company did not report any revenues for the second quarter of 2019. R&D expenses in the second quarter of 2019 were $3.6 million compared to $4.1 million for the second quarter of 2018. The decrease was primarily due to the timing of development milestones related to the HONOR trial, which was completed in 2018. G&A expenses in the second quarter of 2019 were $2.4 million compared to $2.1 million for the second quarter of 2018. The increase was primarily due to an increase in legal fees and insurance expenses. Net loss for the second quarter of 2019 was $5.8 million, or $0.95 per share, compared to a net loss of $6.1 million, or $7.23 per share, in the second quarter of 2018.

Tonix exited the second quarter of 2019 with approximately $12.2 million in cash and cash equivalents. In July 2019, the company completed a public offering of 9 million shares of its common stock at a price of $0.60 per share that resulted in net proceeds of approximately $4.8 million. We estimate the company has sufficient capital to fund operations through the first quarter of 2020.

As of August 8, 2019, Tonix had approximately 15.4 million shares and when factoring in reasonably priced options and warrants a fully diluted share count of 21.2 million.

Conclusion

Tonix has vastly expanded its pipeline over the past few months and is setting up to advance each of the development candidates following release of the Phase 3 data from the RECOVERY trial, which we anticipate in the first half of 2020. In the meantime, the company will not be spending significant resources on any of the pipeline candidates but is instead focused on the successful execution of the RECOVERY trial. Due to the recent financing our valuation has decreased to $3 per share.

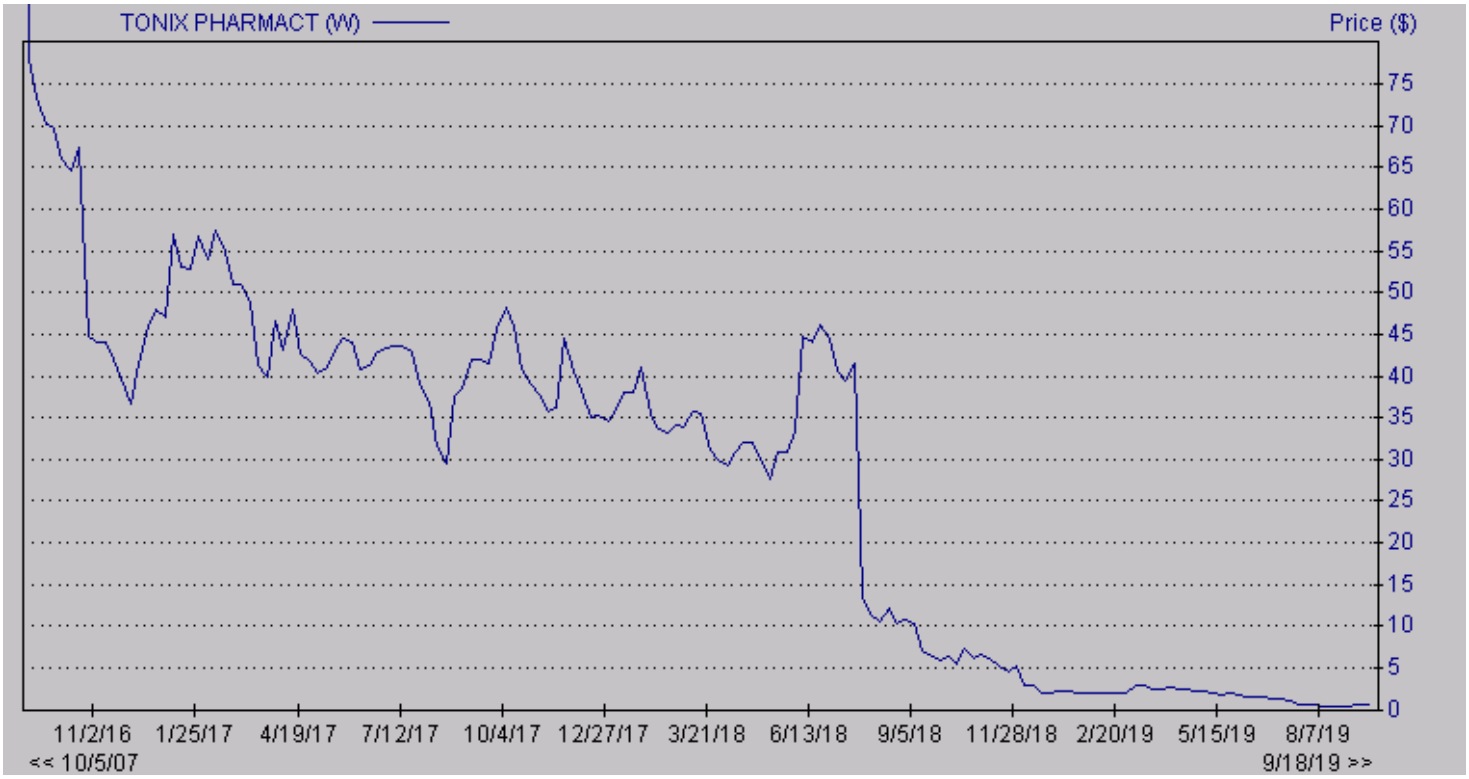
PROJECTED FINANCIALS

Tonix Pharmaceuticals	2018 A	Q1 A	Q2 A	Q3 E	Q4 E	2019 E	2020 E	2021 E
TNX-102 SL (PTSD)	$0	$0	$0	$0	$0	$0	$0	$0
Research & Collaborations	$0	$0	$0	$0	$0	$0	$0	$0
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
CoGS	$0.0	$0	$0	$0	$0	$0.0	$0.0	$0.0
Product Gross Margin	-	-	-	-	-	-	-	-
R&D	$17.6	$3.9	$3.6	$4.0	$4.1	$15.6	$16.0	$16.3
SG&A	$8.8	$2.4	$2.4	$1.9	$2.1	$8.8	$7.8	$8.2
Operating Income	($26.3)	($6.3)	($5.9)	($5.9)	($6.2)	($24.3)	($23.8)	($24.5)
Operating Margin	-	-	-	-	-	-	-	-
Interest & Other Income	$0.2	$0.1	$0.1	$0.1	$0.0	$0.1	$0.1	$0.1
Pre-Tax Income	($26.1)	($6.2)	($5.8)	($5.8)	($6.2)	($24.2)	($23.7)	($24.4)
Preferred Stock Deemed Dividend	$3.3	$0	$0	$0	$0	$0	$0	$0
Taxes & Other	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($29.4)	($6.2)	($5.8)	($5.8)	($6.2)	($24.2)	($23.7)	($24.4)
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($26.81)**	**($1.29)**	**($0.95)**	**($0.39)**	**($0.34)**	**($2.20)**	**($0.95)**	**($0.70)**
YOY Growth	*-15.4%*	-	-	-	-	*-91.8%*	*-56.9%*	*-26.5%*
Weighted Shares Outstanding	1.1	4.8	6.2	15.0	18.0	11.0	25.0	35.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

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