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Tonix Pharmaceuticals Holding Corp. (TNXP-NASDAQ)

TNXP: Interim Analysis for Phase 3 RELIEF Trial in Sep. 2020; Preclinical data for TNX-1800 in 4Q20…

Based on our probability adjusted DCF model that takes into account potential future revenues from TNX-102 SL in fibromyalgia and TNX-1800, TNXP is valued at $3.00/share. This model is highly dependent upon continued clinical success of the company's assets and will be adjusted accordingly based upon future clinical results.

Current Price (09/03/20)	$0.83
Valuation	**$3.00**

OUTLOOK

In July 2020, Tonix Pharmaceuticals Holding Corp. (TNXP) announced that the Phase 3 RELIEF Trial of TNX-102 SL (cyclobenzaprine HCl sublingual tablet) was fully enrolled. An interim analysis of the first 50% of randomized participants is anticipated in Sep. 2020. The potential outcomes of the interim analysis are: 1) stop the study for success; 2) continue to enroll the trial as planned; 3) continue to enroll with an increase in the total number of participants; or 4) stop the study for futility. We anticipate topline results for the trial in the fourth quarter of 2020 unless there is a recommendation for an increase in the total number of participants. In the fourth quarter of 2020 we anticipate small animal and non-human primate preclinical data for TNX-1800, the company's lead COVID-19 vaccine candidate

SUMMARY DATA

52-Week High	**$5.20**
52-Week Low	**$0.40**
One-Year Return (%)	**-80.14**
Beta	**1.63**
Average Daily Volume (sh)	**9,922,670**
Shares Outstanding (mil)	**130**
Market Capitalization ($mil)	**$109**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**1**
Insider Ownership (%)	**0**
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	**-1.0**
P/E using 2019 Estimate	**-2.3**

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

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	0 A	0 A	0 A	0 A	0 A
2020	0 A	0 A	0 E	0 E	0 E
2021					0 E
2022					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	-$12.90 A	-$9.50 A	-$5.69 A	-$2.86 A	-$19.33 A
2020	-$0.37 A	-$0.23 A	-$0.11 E	-$0.11 E	-$0.59 E
2021					-$0.33 E
2022					-$0.35 E

WHAT'S NEW

Business Update

Interim Analysis for Phase 3 RELIEF Trial in Sep. 2020

In July 2020, Tonix Pharmaceuticals Holding Corp. (TNXP) announced that the Phase 3 RELIEF trial of TNX-102 SL was fully enrolled ahead of schedule. We anticipate the results of an interim analysis on the first 50% of enrolled patients in September 2020. There are four potential outcomes from the interim analysis:

1) Stop the study early for success
2) Continue to enroll the study as planned
3) Continue to enroll the study but increase the total number of participants
4) Stop the study for futility

The RELIEF trial is a randomized, double blind, placebo controlled trial that has enrolled approximately 470 participants in the U.S. (NCT04172831). All participants assigned to TNX-102 SL will initiate on 2.8 mg daily for the first two weeks. Following that, the dosage will be increased to 5.6 mg daily for 12 weeks. The primary outcome measure is the daily diary pain severity score change from baseline to Week 14 analyzed by mixed model repeated measures with multiple imputation. Topline results, assuming the interim analysis does not recommend increasing the number of participants, are expected in the fourth quarter of 2020. For a discussion of prior data for TNX-102 SL at 2.8 mg per day in fibromyalgia, see our previous report.

The company recently announced that enrollment has initiated in the Phase 3 RALLY clinical trial of TNX-102 SL in patients with fibromyalgia. The RALLY trial is very similar in design to the RELIEF trial and is being conducted as the FDA requires two successful Phase 3 trials to support approval of TNX-102 SL in the treatment of fibromyalgia. Based on current enrollment estimates, the RALLY trial may report topline results in the second half of 2021.

Recent Research Shows Importance of T Cell Immunity to SARS-CoV-2

During the initial phase of the coronavirus pandemic, antibody response to the virus was studied as a means to estimate population-level exposure to SARS-CoV-2 and the early vaccine candidates are all centered on generating a high enough neutralizing antibody titer to offer immunological protection. However, a number of recent studies have focused on T cell responses to SARS-CoV-2, and could have important implications for their involvement in generating protective immunity.

- A study in Sweden analyzed T cell responses in unexposed individuals, exposed family members, patients with acute or convalescent COVID-19, and patients with severe COVID-19 (Sekine *et al*., 2020). The researchers found that SARS-CoV-2-specific T cells were detectable in antibody-seronegative exposed family members and convalescent individuals with a history of asymptomatic and mild COVID-19, even in the absence of circulating anti-SARS-CoV-2 antibodies. This T cell reactivity is likely to be long lived, as memory T cells that are reactive to SARS-CoV-1 (the virus associated with the SARS outbreak in 2003) were found in patients 17 years after exposure to that virus (Le Bert *et al*., 2020). In addition, antibody responses in patients with mild COVID-19 have been shown to be short-lived (Ibarrondo *et al*., 2020). These data would suggest that the proper vaccination strategy to induce long-lived immunity to SARS-CoV-2 would be to focus on generating a robust T cell response.

- Another recent publication examined the T cell response in patients who have recovered following infection with SARS-CoV-2 (Grifoni *et al*., 2020). CD8+ and CD4+ T cells responsive to SARS-CoV-2 peptide epitopes were identified in approximately 70% and 100% of patients, respectively. The CD4+ T cell responses to spike protein were robust, with the M and N proteins being other major targets. Less common responses were seen to nsp3, nsp4, ORF3a, and ORF3. For CD8+ T cells, spike and M protein were major targets along with at least eight other viral proteins. Surprisingly, CD4+ T cells that reacted to SARS-CoV-2 were found in approximately 40-60% of unexposed individuals, which could represent cross-reactivity between T cells that react to 'common cold' coronaviruses and SARS-CoV-2. These results provide additional support to the importance of a T cell response in combating SARS-CoV-2.

Tonix's SARS-CoV-2 Vaccine Candidates Focus on T Cell Response

Tonix is developing multiple vaccines against SARS-CoV-2. Contrary to almost all other coronavirus vaccines in development, Tonix's vaccine candidates are all designed to elicit a predominantly T cell response against the spike protein or other antigens of the SARS-CoV-2 virus. This is due to the use of a live, replicating viral vector.

- TNX-1800 is the company's lead development vaccine candidate that uses the company's horsepox vector and is designed to elicit a T cell response to the SARS-CoV-2 spike protein. The virus carries a copy of the SARS-CoV-2 spike protein gene in its genome, which is then expressed following immunization. We anticipate preclinical data for small animal and non-human primates in the fourth quarter of 2020 that will report on safety and the immune response to the horsepox vector expressed spike protein. In addition, we anticipate non-human primate data from challenge studies using SARS-CoV-2 in the fourth quarter of 2020.

- TNX-1810, TNX-1820, TNX-1830 are being developed through a partnership with the University of Alberta. Each of those candidates uses the company's horsepox vector and are designed to elicit an almost exclusive T cell response to proteins from SARS-CoV-2 other than the spike protein.

- TNX-2300 is a COVID-19 vaccine candidate based on the bovine parainfluenza virus that Tonix acquired through a partnership agreement with Kansas State University. This live attenuated viral vector is designed to elicit a predominantly T cell response by co-stimulation with the CD40 ligand.

Tonix is one of only a few companies developing a SARS-CoV-2 vaccine utilizing a live, attenuated replicating viral vector that is designed to generate a predominant T cell response and the only company utilizing the horsepox vector or the bovine parainfluenza virus. Orthopoxviruses are known to induce strong innate and adaptive immune responses along with long-lasting T cell immunity (Chaudhri *et al*., 2015), which we believe will be an important feature of a successful SARS-CoV-2 vaccine.

Merck & Co., Inc. (MRK) is one of the other companies utilizing live viral vectors for developing a SARS-CoV-2 vaccine. The company previously announced the acquisition of Themis, a privately-held company that utilizes a modified measles vaccine virus (live replicating) as a vector. Merck just recently initiated a Phase 1 clinical trial for that vaccine (NCT04497298). In addition, Merck is developing a second COVID-19 vaccine using an engineered vesicular stomatitis virus (VSV), which is also a live, replicating vector. We view Merck's approach to developing a COVID-19 vaccine using live, replicating vectors as an important validation of that technology.

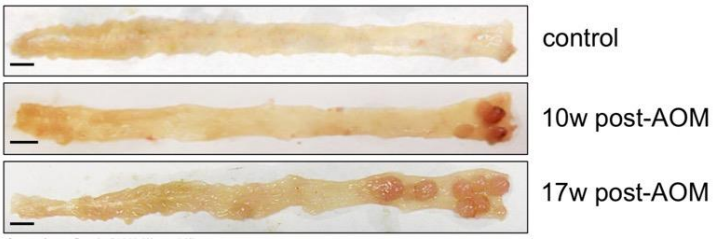
According to the WHO, there are 29 COVID-19 vaccines in clinical development and 138 COVID-19 vaccines in preclinical development. Six vaccines are currently in Phase 3 trials, including those from University of Oxford/AstraZeneca, Moderna, and BioNTech/Pfizer. Initial results from these Phase 3 trials could be available in the fourth quarter of 2020, however since each of those is predominantly focused on an antibody response we are unsure of the durability for any protective effects seen.

Update on TNX-1700

In 2019, Tonix licensed TNX-1700 (recombinant Trefoil Family Factor 2, rTFF2) from Columbia University for the treatment of gastric and pancreatic cancers. Columbia, together with the company, recently presented a poster at the 2020 American Association of Cancer Research (AACR) Virtual Annual Meeting II on a study that investigated the role of PD-L1 in colorectal cancer (CRC) tumorigenesis along with the role of myeloid derived suppressor cells (MDSCs) in combination with PD-1 blockade[1]. Thus far, except for a very small minority of patients, PD-1 therapy has been ineffective against CRC, thus representing a significant opportunity for compounds that could increase the response rate of CRC patients to PD-1 therapy.

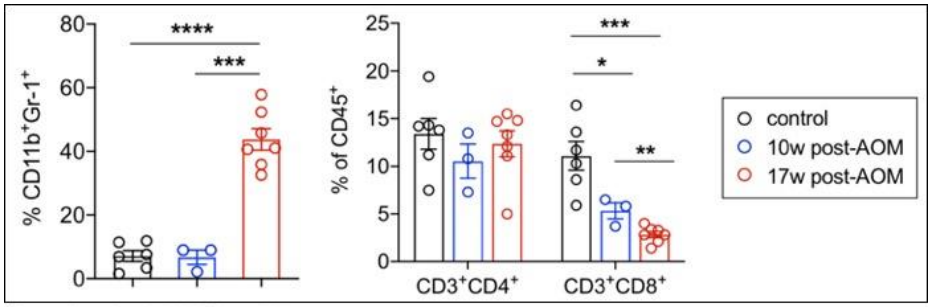
To analyze the effect of rTFF2 in CRC the azoxymethane/dextran sodium sulfate (AOM/DSS) mouse model was utilized. This model efficiently recapitulates the histopathological characteristics of colitis-associated CRC, including distally-located tumors and invasive adenocarcinomas (Parang *et al*., 2016). The following figure shows colons from AOM/DSS treated mice with tumors readily visible by 10 weeks.

[1] Woosook Kim, et al., "Stabilized recombinant trefoil factor 2 (TFF2-CTP) enhances anti-tumor activity of PD-1 blockade in mouse models of colorectal cancer [abstract]," In: Proceedings of the Annual Meeting of the American Association for Cancer Research 2020, *Cancer Res*, 80(16 Suppl):Abstract nr 6640[doi: 10.1158/1538-7445.AM2020-6640]



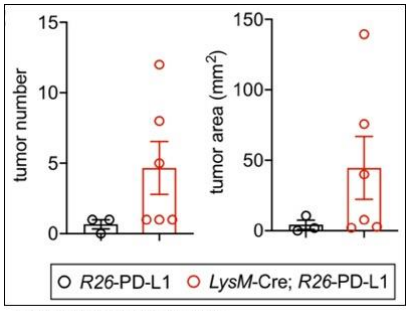
Source: Cancer Res, April 2020, Woosook Kim

The following figure on the left shows that the AOM/DSS model leads to an expansion of myeloid cells (red circles), particularly CD11b+Gr-1+ MDSCs, compared to untreated mice (black circles). In addition, there is a significant decrease in the amount of intratumoral CD8+ T cells, suggesting a decreased immune response, as shown in the following figure on the right.



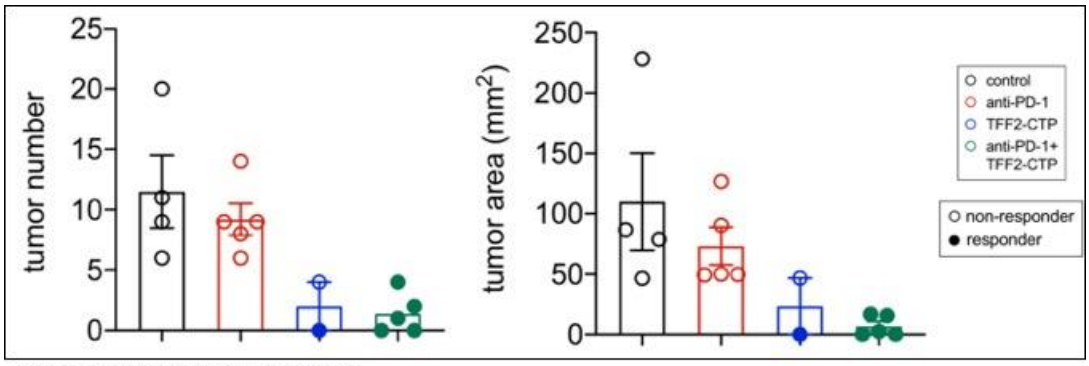
Source: Cancer Res, April 2020, Woosook Kim

To investigate the role of PD-L1 in CRC development, mice overexpressing PD-L1 specifically in myeloid cells were generated using a Cre-lox system. The following graph shows that tumor numbers were higher and tumors were larger in mice that expressed PD-L1 in myeloid cells (denoted by LysM-Cre; R26-PD-L1).



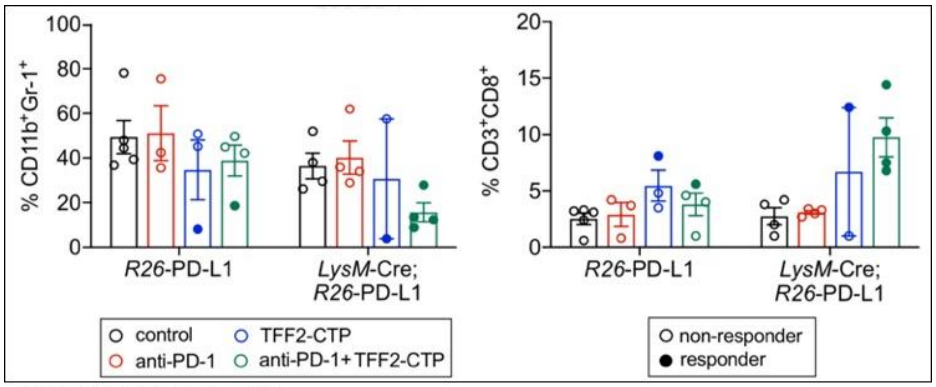
Source: Cancer Res, April 2020, Woosook Kim

TFF2 was previously shown to inhibit CRC growth through suppression of the expansion of MDSCs. For the current study, PD-L1 was specifically expressed in myeloid cells in the AOM/DSS model. Treatment with anti-PD-1 with or without TFF2 showed that the combination treatment resulted in a significant decrease in the number of tumors formed as well as a decrease in the size of the tumors. Interestingly, these results were only seen in mice that expressed PD-L1 in myeloid cells.



Source: Cancer Res, April 2020, Woosook Kim

This decrease in tumor number and size in responders was accompanied by an increase in CD8+ tumor-infiltrating cells and a decrease in myeloid cells, as shown in the following figures (green bars/circles). Once again, this effect was only seen in animals that expressed PD-L1 in MDSCs (LysM-Cre;R26-PD-L1).



Source: Cancer Res, April 2020, Woosook Kim

In summary, anti-PD-1 monotherapy does not affect tumor number or size in a mouse model of CRC, however when combined with TFF2 the efficacy of anti-PD-1 therapy is increased. This anti-tumor activity appears to be the result of an increase in tumor infiltrating CD8+ T cells and a decrease in MDSCs. These results point to the potential for TFF2 to be used in combination with anti-PD-1 therapy in treating CRC patients.

Update on TNX-1900

In June 2020, Tonix announced the acquisition of TNX-1900, a proprietary, patented enhanced formulation of intranasally administered oxytocin that has demonstrated activity in various non-clinical studies in migraine prophylaxis and neuropsychiatric models. The company recently presented the preclinical results of TNX-1900 at the American Academy of Neurology first ever Sports Concussion Conference that investigated the efficacy of intranasal oxytocin in relieving pain and associated depressive behavior following traumatic brain injury (TBI). The presentation can be accessed here.

TBI disrupts the usual functioning of the brain and is typically brought on by a bump, blow, blast, or jolt to the head (CDC). Some of the consequences of TBI are post traumatic headache (PTH), changes in memory, attention, and concentration, changes in mood (irritability, anxiety, depression, etc.), and sleep disturbances. TBI may also develop alongside posttraumatic stress disorder (PTSD). Approximately 1.7 million TBIs occur every year in the U.S.

The preclinical data presented by Tonix showed that intranasal oxytocin, but not IV oxytocin, attenuates pain responses in a rat model of TBI without addictive potential. The effects could be blocked by an oxytocin antagonist, showing that the results were driven specifically via oxytocin receptors. Lastly, intranasal oxytocin attenuated post-TBI mood effects such as anxious and depressive behaviors in the elevated plus maze and forced swim models, respectively.

Financial Update

On August 10, 2020, Tonix announced financial results for the second quarter of 2020. As expected, the company did not report any revenues for the second quarter of 2020. Net loss available to common stockholders for the second quarter of 2020 was $14.2 million, or $0.23 per share, compared to $5.8 million, or $9.42 per share, for the second quarter of 2019. R&D expenses for the second quarter of 2020 were $10.6 million, compared to $3.6 million for the second quarter of 2019. The increase was primarily due to the acquisition of technologies of Trigemina, Inc., timing of development milestones related to the Phase 3 trial of TNX-102 SL, and increased activities relating to COVID-19 vaccine work. G&A expenses for the second quarter of 2020 were $3.6 million, compared to $2.4 million for the second quarter of 2019. The increase was primarily due to increased legal fees, patent prosecution, and maintenance costs.

The company exited the second quarter of 2020 with approximately $55.0 million in cash and cash equivalents. In July 2020, Tonix completed a registered direct public offering in which 20.94 million shares were sold for $0.50 per share resulting in net proceeds of approximately $9.6 million.

As of August 7, 2020, Tonix had approximately 130.3 million shares outstanding and when factoring in reasonably priced warrants and stock options a fully diluted share count of approximately 141.9 million.

Conclusion

Tonix has a number of important inflection points occurring before the end of 2020, including the interim readout for the Phase 3 RELIEF trial in September 2020, topline data for the RELIEF trial in the fourth quarter of 2020 (pending the outcome of the interim analysis), and preclinical efficacy data for TNX-1800. We have made a few changes to our model, including increasing the potential peak sales for TNX-102 SL in FM to $400 million, assigning a valuation for the preclinical pipeline of $50 million, and decreasing the discount rate to 12%. Our new valuation is $3.00 per share.

PROJECTED FINANCIALS

Tonix Pharmaceuticals	2019 A	Q1 A	Q2 A	Q3 E	Q4 E	2020 E	2021 E	2022 E
TNX-102 SL (FM)	$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	$18.2	$4.7	$10.6	$11.0	$11.0	$37.2	$38.0	$40.0
SG&A	$10.6	$2.6	$3.6	$3.0	$3.0	$12.2	$12.0	$13.0
Operating Income	($28.8)	($7.3)	($14.2)	($14.0)	($14.0)	($49.5)	($50.0)	($53.0)
Operating Margin	-	-	-	-	-	-	-	-
Interest & Other Income	$0.2	$0.0	$0.0	$0.1	$0.1	$0.2	$0.4	$0.4
Pre-Tax Income	($28.6)	($7.3)	($14.2)	($13.9)	($13.9)	($49.3)	($49.6)	($52.6)
Preferred Stock Deemed Dividend	$2.5	$1.26	$0.0	$0.0	$0.0	$1.3	$0.0	$0.0
Warrant Deemed Dividend	$0.0	$0.45	$0.0	$0.0	$0.0	$0.5	$0.0	$0.0
Taxes & Other	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($31.1)	($9.0)	($14.2)	($13.9)	($13.9)	($51.0)	($49.6)	($52.6)
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($19.33)**	**($0.37)**	**($0.23)**	**($0.11)**	**($0.11)**	**($0.59)**	**($0.33)**	**($0.35)**
YOY Growth	*-92.8%*	-	-	-	-	*-97.0%*	*-43.8%*	*6.0%*
Weighted Shares Outstanding	1.6	24.0	62.4	130.0	130.0	86.6	150.0	150.0

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

HISTORICAL STOCK PRICE

Source: Zacks Small Cap Research

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