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Diffusion Pharmaceuticals, Inc. (DFFN-NASDAQ)

DFFN: TSC to be Tested as Treatment for ARDS Caused by COVID-19…

Based on our probability adjusted DCF model that takes into account potential future revenues from TSC in stroke, DFFN is valued at $1.75/share. This model is highly dependent upon the continued clinical success of TSC and will be adjusted accordingly based upon future clinical results.

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Current Price (05/19/20)	$1.11
Valuation	**$1.75**

OUTLOOK

In April 2020, Diffusion Pharmaceuticals, Inc. (DFFN) announced the company's pre-IND submission to the FDA for the use of trans sodium crocetinate (TSC) as a treatment for acute respiratory distress syndrome (ARDS) caused by COVID-19. Shortly thereafter, the FDA indicated that the review time for the company's IND will be significantly shortened under the Coronavirus Treatment Acceleration Program (CTAP). We anticipate Diffusion submitting the IND immediately following receipt of the FDA's response to the pre-IND submission. Talks have already initiated with institutions in the U.S. and Eastern Europe so that the trial can get underway as quickly as possible.

SUMMARY DATA

52-Week High	**$5.40**
52-Week Low	**$0.22**
One-Year Return (%)	**-75.50**
Beta	**0.81**
Average Daily Volume (sh)	**11,014,797**
Shares Outstanding (mil)	**46**
Market Capitalization ($mil)	**$51**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**8**
Insider Ownership (%)	**6**
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	**N/A**
P/E using 2019 Estimate	**N/A**

Risk Level	**High**
Type of Stock	**Small-Blend**
Industry	**Med-Biomed/Gene**

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 E	0 E	0 E	0 E
2021					0 E
2022					0 E

Earnings per Share
(Diluted)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	-$0.81 A	-$0.63 A	-$0.60 A	-$0.25 A	-$1.76 A
2020	-$0.07 A	-$0.06 E	-$0.07 E	-$0.07 E	-$0.27 E
2021					-$0.23 E
2022					-$0.23 E

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WHAT'S NEW

Business Update

Waiting for Response on Pre-IND Submission for TSC in COVID-19 ARDS

On April 27, 2020, Diffusion Pharmaceuticals, Inc. (DFFN) announced the company's Pre-IND submission to the U.S. FDA for the use of the company's lead development compound, trans sodium crocetinate (TSC), for the treatment of acute respiratory distress syndrome (ARDS) as a result of infection with the novel coronavirus, SARS-CoV-2, which causes coronavirus disease 2019 (COVID-19). We anticipate the company receiving a response from the FDA on the Pre-IND submission very soon, after which the IND will be submitted.

The FDA indicated that it will be reviewing Diffusion's IND under the Coronavirus Treatment Acceleration Program (CTAP), which was designed to significantly shorten review times for select COVID-19 submissions. Concurrently, the company is in discussions with institutions located in areas with severe COVID-19 outbreaks in both the U.S. and Eastern Europe so that enrollment can begin as quickly as possible.

ARDS and TSC

The current coronavirus epidemic is resulting in severe disease for a small percentage of patients, many of which end up on a ventilator as a result of ARDS, which is a condition where the small blood vessels of the lung leak fluid that fills up the alveoli, thus preventing proper oxygen exchange (Stevens *et al*., 2018). This can lead to a hypoxic environment in the patient signified by a low blood oxygen level and subsequent lack of oxygen in vital organs, thus a treatment that can increase oxygenation should help to alleviate these symptoms.

There are many causes of ARDS, including infections (e.g., pneumonia), severe burns, pancreatitis, inhalation of smoke or chemicals, or other serious illnesses. An excessive inflammatory response appears to be involved in the pathogenesis of ARDS (Li *et al*., 2019). Current treatment options involve supportive care while the lungs heal, which involves oxygen therapy supplied through a ventilator. There are no pharmacological treatments specifically for ARDS and approximately 40% of hospitalized patients die from it (Siegel *et al*., 2020).

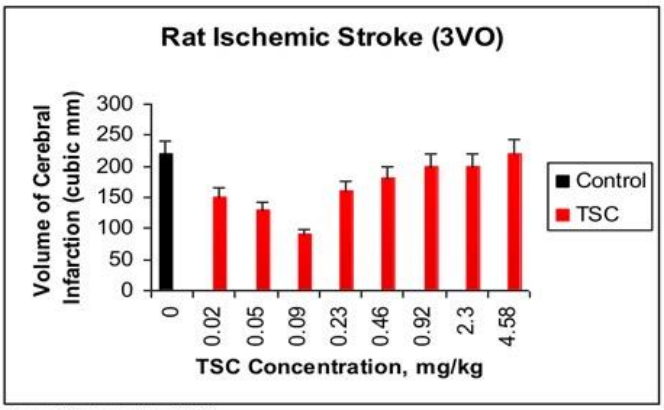
In a model of acute lung injury that mimics ARDS, TSC was shown to increase arterial PO_2 immediately after administration without affecting the lungs (Gainer *et al*., 2005). This is in addition to multiple other examples of TSC increasing oxygenation in animal models, including in hemorrhagic shock (Giassi *et al*., 2002) and in a 10% oxygen environment (Singer *et al*., 2000). Thus, we believe there is ample support for testing TSC in the treatment of ARDS.

Update on Phase 2 Stroke Trial

Diffusion is currently conducting the the Phase 2 on-ambulance trial of the company's lead asset, trans sodium crocetinate (TSC), for the treatment of stroke. The Pre-Hospital Administration of Stroke Therapy-TSC (PHAST-TSC) trial is expected to enroll 160 patients who will be treated in the ambulance (80 active/80 placebo) within two hours of a suspected stroke on the way to the hospital regardless of whether they are suffering from an ischemic or hemorrhagic stroke. In addition, patients are eligible to receive tissue plasminogen activator (tPA) separately in-hospital if it is determined they are suffering from an ischemic stroke. A total of 23 hospitals, working in conjunction with 150 emergency medical transport groups, are expected to participate in the trial across central Virginia and in Los Angeles County. Enrollment has initiated in both locations, however due to the ongoing coronavirus epidemic the company expects delays in enrollment. Specifically, the LA County Fire Department has ceased training of first responders that had been scheduled to participate in the trial due to the necessity to respond to the pandemic.

The primary endpoint of the study will be the extent of disability at 90 days using the utility-weighted modified Rankin Scale (UW-mRS) (Chaisinanunkul *et al*., 2015). Secondary endpoints will examine functional independence, activities of daily living, and health-related quality of life.

Preclinical models show that TSC could be an effective treatment for both ischemic and hemorrhagic stroke (Manabe *et al*., 2010; Wang *et al*., 2014). The following figure, shown at the 2019 International Stroke Conference, shows a dose dependent reduction in infarct volume in a rat model of ischemia-reperfusion where TSC was administered 10 minutes following onset of ischemia.



Source: Southerland *et al.*, 2019

In another rat model of ischemia-reperfusion, which involved two hours of ischemia followed by 22 hours of reperfusion, treatment with TSC one and a half hours after onset of ischemia led to a significant reduction in infarct volume of 32%. In a third model of ischemia-reperfusion, which involved two hours of reperfusion followed by an additional four hours of one vessel occlusion, treatment with TSC significantly reduced infarct volume by 34%. Lastly, in an intracerebral hemorrhage model in which TSC was administered three hours after collagenase injection, there was a significant reduction in hemispheric swelling and hemorrhage volume in animals treated with TSC. It is important that TSC be effective, or at least not detrimental, regardless of the type of stroke. Otherwise, its use would be contraindicated prior to the diagnosis of the type of stroke and by that time it may be too late to be effective.

There are approximately 800,000 strokes every year in the U.S., and they are responsible for the deaths of approximately 140,000 individuals (CDC). Strokes cost the U.S. healthcare system an estimated $34 billion every year (Benjamin *et al*., 2017).

Financial Update

On May 12, 2020, Diffusion announced financial results for the first quarter of 2020. As expected, the company did not report any revenues. R&D expenses were $1.5 million for the first quarter of 2020, compared to $1.7 million for the first quarter of 2019. The decrease was primarily due to a decrease in costs associated with the Phase 3 GBM trial. G&A expenses were $1.3 million for the first quarter of 2020, compared to $1.2 million for the first quarter of 2019. The slight increase was primarily due to increased professional expenses.

As of Mar. 31, 2020, Diffusion had approximately $10.8 million in cash and cash equivalents. In April and May 2020, the company received gross proceeds of approximately $4.8 million from the exercise of 6,385,496 warrants and the exchange and exercise of another 5 million warrants. On May 18, 2020, the company announced a private direct offering of approximately 11.4 million shares sold at $1.05 per share for gross proceeds of approximately $12 million. We estimate that the company has sufficient capital to fund operations into 2022.

We estimate that following the most recent direct offering that Diffusion has approximately 57.4 million shares of common stock and when factoring in stock options and warrants a fully diluted share count of approximately 79.9 million shares.

Conclusion

We believe there is plenty of data to support the use of TSC as a treatment for ARDS and we look forward to the company initiating a clinical trial soon. The fact that the FDA will be expediting the review of the company's IND is encouraging and shows that the agency believes it could have a positive impact on the treatment of ARDS patients. We preliminarily believe treating COVID-19 patients with TSC is a $250 million opportunity and based on a 30% probability of success we value the opportunity at $57 million. In addition to adding in the opportunity in COVID-19 to our model we have pushed back the timeline for TSC in stroke, and these changes have moved our valuation to $1.75.

PROJECTED FINANCIALS

Diffusion Pharmaceuticals, Inc.	2019 A	Q1 A	Q2 E	Q3 E	Q4 E	2020 E	2021 E	2022 E
TSC (GBM)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
TSC (Stroke)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Grants & Collaborative Revenue	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$6.6	$1.5	$1.5	$1.7	$2.0	$6.8	$8.0	$10.0
General & Administrative	$4.8	$1.4	$1.2	$1.3	$1.3	$5.2	$5.2	$5.5
Goodwill Impairment	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Depreciation	$0.1	$0.0	$0.0	$0.0	$0.0	$0.1	$0.1	$0.1
Operating Income	($11.6)	($3.0)	($2.8)	($3.1)	($3.3)	($12.1)	($13.3)	($15.6)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.1	($0.0)	$0.0	$0.0	$0.0	($0.0)	($0.2)	($0.2)
Pre-Tax Income	($11.5)	($2.9)	($2.8)	($3.1)	($3.3)	($12.1)	($13.5)	($15.8)
Income Taxes	$0.3	($0.4)	$0.0	$0.0	$0.0	($0.4)	$0.0	$0.0
Accretion of Series A preferred dividends	$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	**($11.8)**	**($2.6)**	**($2.8)**	**($3.1)**	**($3.3)**	**($11.7)**	**($13.5)**	**($15.8)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($1.76)**	**($0.07)**	**($0.06)**	**($0.07)**	**($0.07)**	**($0.27)**	**($0.23)**	**($0.23)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	6.7	34.5	46.0	46.0	50.0	44.1	60.0	70.0

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

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