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Diffusion Pharmaceuticals, Inc. (DFFN-NASDAQ)

DFFN: TSC to be Developed for Treatment of Hypoxic Tumors…

Based on our probability adjusted DCF model that takes into account potential future revenues from TSC in select hypoxia-related indications, DFFN is valued at $2.00/share. This model is highly dependent upon the continued clinical success of TSC and will be adjusted accordingly based upon future clinical results.

Current Price (11/29/21)	$0.39
Valuation	**$2.00**

OUTLOOK

On November 10, 2021, Diffusion Pharmaceuticals, Inc. (DFFN) announced financial results for the third quarter of 2021 and provided a business update. Based upon results obtained thus far for its lead development compound, trans sodium crocetinate (TSC), the company will be advancing it for the treatment of hypoxic solid tumors. Diffusion will be obtaining input from the U.S. FDA in early 2022 and we anticipate an update following the receipt of that input regarding the specifics of the first clinical trial. In the interim, we anticipate two additional oxygenation trials taking place – 1) the Altitude Trial will begin within the next couple of weeks and will investigate the consumption of oxygen in the presence of TSC in a simulated high altitude environment. 2) The ILD-DLCO will be a double-blind, randomized, placebo controlled study to evaluate the effects of TSC on diffusion of carbon monoxide through the lungs (DLCO) of patients with interstitial lung disease. This trial will begin in late 2021.

SUMMARY DATA

52-Week High	**$1.70**
52-Week Low	**$0.35**
One-Year Return (%)	**-49.74**
Beta	**1.39**
Average Daily Volume (sh)	**1,010,498**
Shares Outstanding (mil)	**102**
Market Capitalization ($mil)	**$40**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**10**
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	**N/A**
P/E using 2019 Estimate	**N/A**

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

ZACKS ESTIMATES

Revenue

(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2020	0 A	0 A	0 A	0 A	0 A
2021	0 A	0 A	0 A	0 E	0 E
2022					0 E
2023					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2020	-$0.07 A	-$0.10 A	-$0.07 A	-$0.06 A	-$0.30 A
2021	-$0.06 A	-$0.04 A	-$0.12 A	-$0.04 E	-$0.26 E
2022					-$0.16 E
2023					-$0.14 E

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Business Update

Developing TSC for Treatment of Hypoxic Solid Tumors

On November 10, 2021, Diffusion Pharmaceuticals, Inc. (DFFN) announced that the company is intending to develop its lead drug candidate, trans sodium crocetinate (TSC), for the treatment of hypoxic solid tumors. This is based on an increased understanding of the drug's mechanism of action from the TCOM and COVID-19 studies, the positive preclinical and clinical data compiled thus far, and the fact that TSC is currently administered intravenously. Hypoxia is common to nearly all solid tumors and it contributes both to the difficulty in treating them as well as their metastatic potential. The company has previously reported positive results from the use of TSC in treating glioblastoma (GBM), a tumor type that is known to have significant oxygen diffusion restriction (Rong *et al*., 2006), which further supports its continued development in other hypoxic tumors.

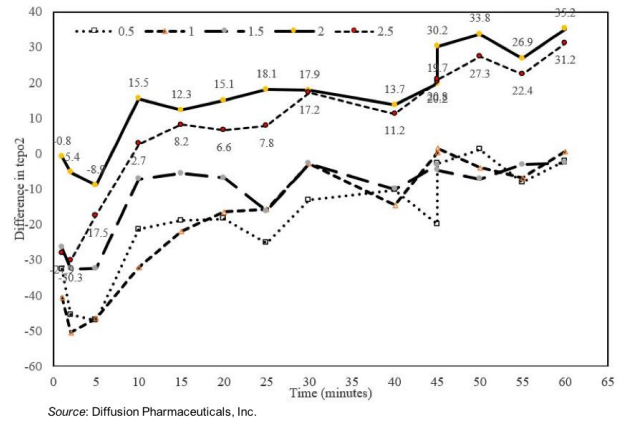
The company will be seeking input from the U.S. FDA on a trial design, currently expect to be a Phase 2 study, which they hope to receive in early 2022. However, the start date for a trial will be dependent upon the timing of the feedback from the FDA as well as the availability of drug product. We anticipate the company providing an update on timelines as well as details on the Phase 2 trial design following receipt of the FDA's feedback.

Two Additional Oxygenation Trials to Get Underway in 4Q21

Diffusion is in the process of evaluating TSC in a series of oxygenation trials to better understand its mechanism of action and clinical potential. The company has successfully completed the first of three planned studies, the TCOM study, and we anticipate the other two trials, Altitude Trial and ILD-DLCO Trial, initiating in the fourth quarter of 2021.

- Transcutaneous Oxygen Monitoring (TCOM) Study: TCOM measures local oxygen tension in tissue below the skin and provides an objective measure of oxygen release and diffusion into tissues from vasculature (tcpO2). This study was designed to evaluate the exposure-reponse relationship between TSC and oxygenation through direct measurement of oxygen movement in tissues. It was a randomized, double blind, placebo controlled, pharmacokinetic and pharmacodynamic study in which thirty healthy volunteers received 100% O_2 at a rate of 6L/min before and after dosing with one of five doses of TSC (range from 0.5 mg/kg to 2.5 mg/kg) or placebo.

  Topline results showed that, compared to placebo, there was a positive, dose-dependent trend in TCOM readings after TSC administration that persisted through the measurement period. The following chart (which can be accessed here) shows the effect of TSC on tcpO2 after subtracting the median placebo response from the dose and time matched median TSC response. The results were not statistically significant, due in part to the small number of subjects in each cohort and the inherent variability of tcpO2 measurements, however the trends indicated an improvement in peripheral oxygenation compared to placebo with no evidence of hyperoxygenation. Importantly, TSC was safe and well-tolerated at all doses tested with no serious adverse events or dose-limiting toxicities.



Source: Diffusion Pharmaceuticals, Inc.

- Altitude Trial: This will be a double blind, randomized, placebo controlled trial to evaluate the effects of TSC on maximal oxygen consumption (VO2) and partial pressure of blood oxygen (PaO2) in normal healthy volunteers subjected to incremental levels of physical exertion while exposed to simulated altitude conditions that induce hypoxia. The study will be statistically powered to evaluate the difference in effect of TSC versus placebo on maximal oxygen consumption and partial pressure of blood oxygen. Topline results should be available 1-2 months following study completion.

- ILD-DLCO Trial: DLCO is a pulmonary function test that measures gas diffusion (carbon monoxide, CO, as a surrogate for oxygen) from the lungs to the bloodstream and is a standard tool for examining pulmonary disease etiology. This trial will be a double-blind, randomized, placebo-controlled study which will evaluate the effects of TSC on DLCO in patients with previously diagnosed interstitial lung disease (ILD) who have a baseline DLCO test result that is abnormal. The study will be statistically powered to evaluate the difference in effect of TSC versus placebo on improvement in DLCO as well as in a standard six-minute walk test. This study is expected to initiate late in the fourth quarter of 2021 and completing in the first quarter of 2022, with results available 1-2 months following study completion.

Financial Update

On November 10, 2021, Diffusion announced financial results for the third quarter of 2021. As expected, the company did not report any revenues in the third quarter of 2021. R&D expenses for the three months ending September 30, 2021 were $2.1 million, compared to $3.1 million for the three months ending September 30, 2020. The decrease was primarily due to winding down the clinical trials of TSC in glioblastoma brain cancer, stroke, and COVID-19. G&A expenses were $1.9 million in the third quarter of 2021, compared to $2.1 million in the third quarter of 2020. The decrease was primarily due to decreased salaries, legal, and professional fees. The company also recognized a non-recurring $8.6 million non-cash impairment charge related to the write down of DFN-529.

Diffusion exited the third quarter of 2021 with approximately $40.3 million in cash and cash equivalents. This was due in part to a public offering in February 2021 in which Diffusion raised net proceeds of approximately $31.2 million. As of November 8, 2021, Diffusion had approximately 101.9 million shares outstanding and, when factoring in stock options and warrants, a fully diluted share count of approximatley 112.5 million.

Conclusion

We're intrigued by the company's announcement regarding advancing TSC in hypoxic solid tumors and we look forward to additional details as the company gets closer to launching a Phase 2 trial. In the meantime, Diffusion will focus its attention on conducting the remaining two oxygenation trials, both of which will be funded with cash on hand. With no changes to our model our valuation remains at $2.00.

PROJECTED FINANCIALS

Diffusion Pharmaceuticals, Inc.	2020 A	Q1 A	Q2 A	Q3 A	Q4 E	2021 E	2022 E	2023 E
TSC (COVID)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
TSC (Other Indications)	$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	$9.4	$2.9	$2.0	$2.1	$2.6	$9.6	$12.0	$12.5
General & Administrative	$6.4	$1.7	$1.8	$1.9	$1.8	$7.3	$7.5	$8.0
Impairment Charge	$0.0	$0.0	$0.0	$8.6	$0.0	$8.6	$0.0	$0.0
Depreciation	$0.1	$0.0	$0.0	$0.0	$0.0	$0.1	$0.1	$0.1
Operating Income	($16.0)	($4.7)	($3.8)	($12.7)	($4.4)	($25.7)	($19.6)	($20.6)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.1	($0.0)	($0.1)	$0.1	$0.0	($0.0)	$0.0	$0.0
Pre-Tax Income	($15.9)	($4.6)	($3.8)	($12.6)	($4.4)	($25.7)	($19.6)	($20.6)
Income Taxes	($1.7)	$0.0	$0.0	$0.0	$0.0	$0.0	$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
Deemed Dividend from warrant exchange	$2.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Net Income	**($16.1)**	**($4.6)**	**($3.8)**	**($12.6)**	**($4.4)**	**($25.7)**	**($19.6)**	**($20.6)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.30)**	**($0.06)**	**($0.04)**	**($0.12)**	**($0.04)**	**($0.26)**	**($0.16)**	**($0.14)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	53.8	83.4	101.9	101.9	102.1	97.3	120.0	150.0

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

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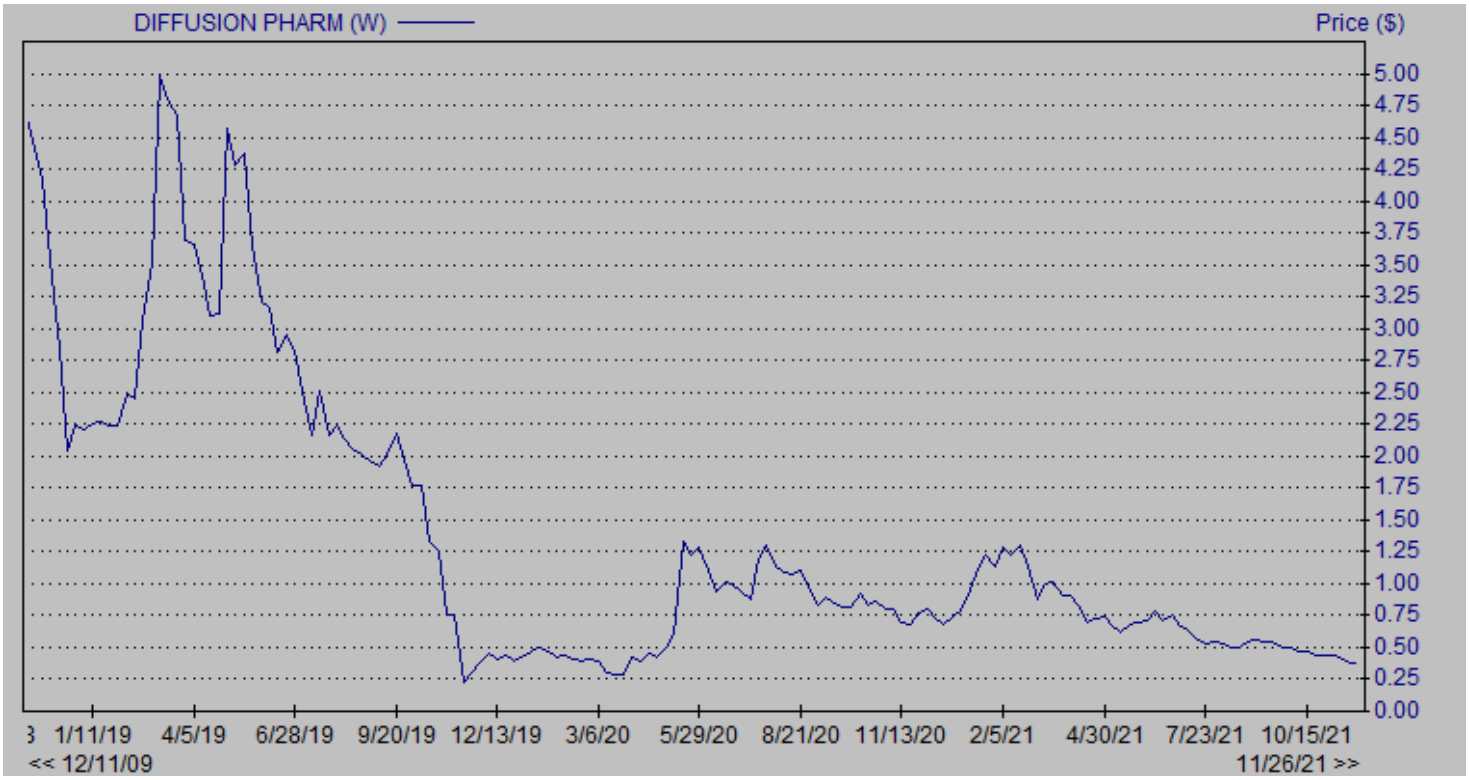
HISTORICAL STOCK PRICE



Source: Zacks Small Cap Research

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