

Diffusion Pharmaceuticals, Inc.

(DFFN-NASDAQ)

DFFN: Additional Tissue Oxygenation Trial Results Expected Mid-2022...

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 (03/23/22) **\$0.26**
Valuation **\$2.00**

OUTLOOK

On March 21, 2022, Diffusion Pharmaceuticals, Inc. (DFFN) announced financial results for the fourth quarter and full year 2021 and provided a business update. The company intends to develop its lead compound, trans sodium crocetin (TSC), for the treatment of hypoxic solid tumors. Diffusion will be filing a study protocol with the U.S. FDA and we anticipate a trial initiating in the second half of 2022, subject to FDA feedback and the availability of study drug. In the interim, the company has initiated two additional oxygenation trials – 1) the Altitude Trial is investigating the consumption of oxygen in the presence of TSC in a simulated high altitude environment; and 2) The ILD-DLCO is 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. Results for the Altitude Trial should be available in mid-2022, while results for the ILD-DLCO trial should be available in the second half of 2022.

SUMMARY DATA

52-Week High **\$1.07**
52-Week Low **\$0.22**
One-Year Return (%) **-75.16**
Beta **1.41**
Average Daily Volume (sh) **858,701**

Shares Outstanding (mil) **102**
Market Capitalization (\$mil) **\$27**
Short Interest Ratio (days) **N/A**
Institutional Ownership (%) **9**
Insider Ownership (%) **2**

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-Value**
Industry **Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of \$)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2021	0 A	0 A	0 A	0 A	0 A
2022	0 E	0 E	0 E	0 E	0 E
2023					0 E
2024					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2021	-\$0.06 A	-\$0.04 A	-\$0.12 A	-\$0.03 A	-\$0.25 A
2022	-\$0.04 E	-\$0.04 E	-\$0.04 E	-\$0.04 E	-\$0.17 E
2023					-\$0.15 E
2024					-\$0.13 E

WHAT'S NEW

Business Update

Developing TSC for Treatment of Hypoxic Solid Tumors

In November 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 expected to be a Phase 2 study, which they hope to receive following submission of a clinical trial protocol. While 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 currently anticipate a trial initiating in the second half of 2022.

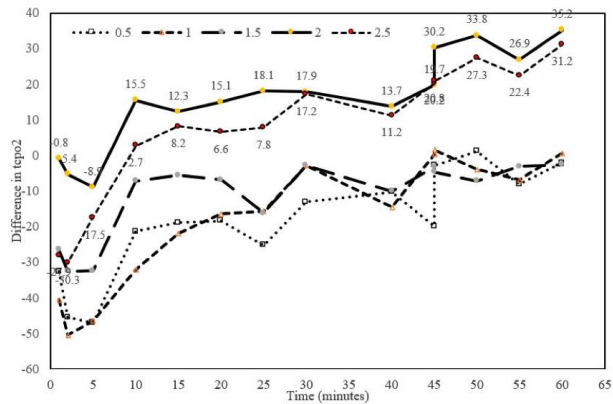
In February 2022, Diffusion [announced](#) an expansion of its Scientific Advisory Board to include five prominent radiation and medical oncologists. These advisors will be instrumental in guiding the company's new program in treating hypoxic solid tumors.

Two Additional Oxygenation Trials Underway

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. Two additional studies, the Altitude Trial and ILD-DLCO Trial, initiated 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% O₂ 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 show a clear trend in the 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 is 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. The first patient was dosed in November 2021, however the omicron wave of the COVID-19 pandemic resulted in enrollment delays and we now anticipate the study completing in the second quarter of 2022 and topline results to be available approximately 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. The trial initiated in December 2021, however the omicron wave of the COVID-19 pandemic resulted in enrollment delays and we now anticipate the study completing in mid- 2022 and topline results to be available approximately 1-2 months following study completion.

Financial Update

On March 21, 2022, Diffusion announced financial results for the fourth quarter and full year 2021. As expected, the company did not report any revenues in 2021. R&D expenses in 2021 were \$8.5 million, compared to \$9.4 million for 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 \$7.4 million in 2021, compared to \$6.4 million in 2020. The increase was primarily due to increased headcount and consulting services. The company also recognized a non-recurring \$8.6 million non-cash impairment charge related to the write down of DFN-529 in 2021.

Diffusion exited 2021 with approximately \$37.3 million in cash and cash equivalents. As of March 14, 2022, Diffusion had approximately 101.9 million shares outstanding and, when factoring in stock options and warrants, a fully diluted share count of approximately 112.3 million.

Conclusion

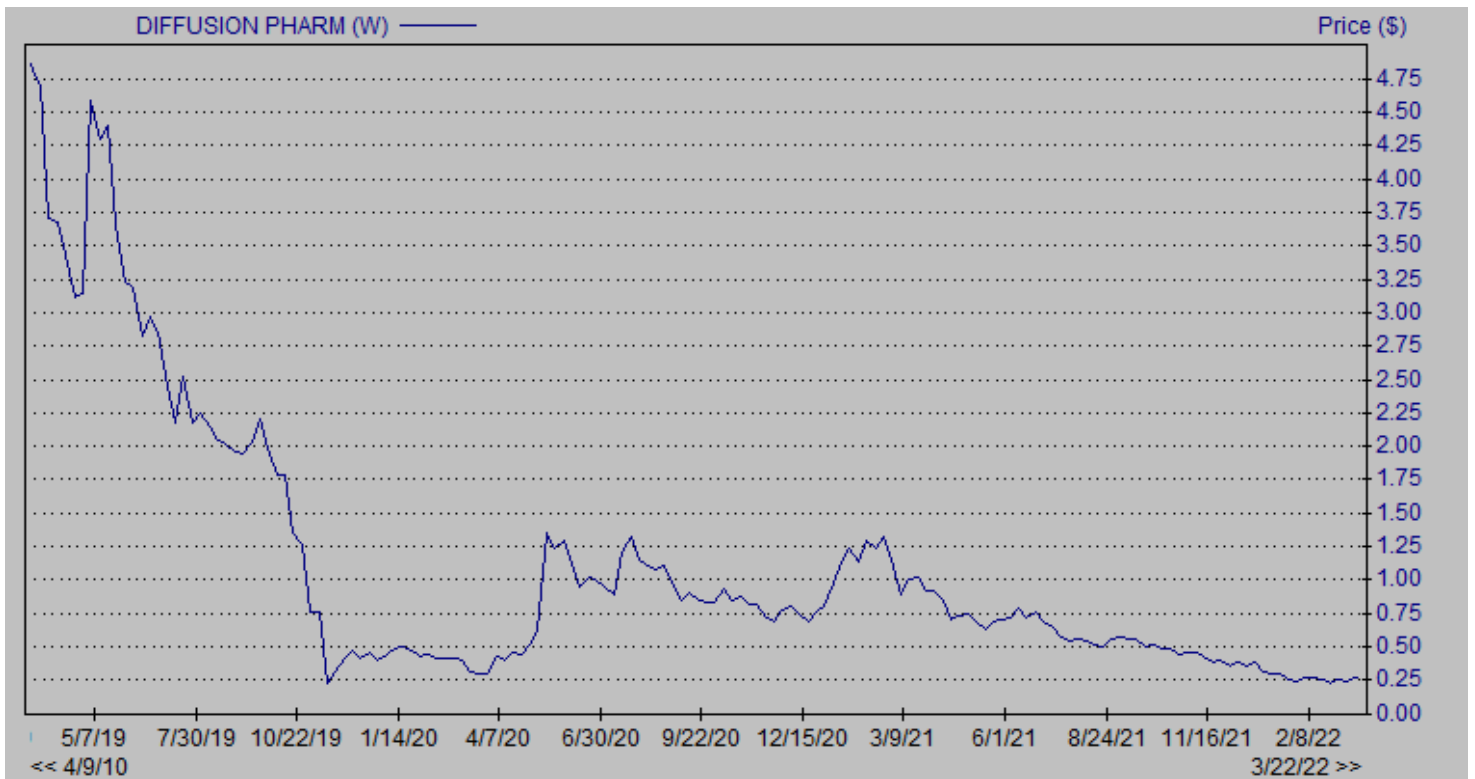
We look forward to updates from the company regarding the ongoing oxygenation trials and we anticipate topline results from the Altitude Trial in mid-2022 and the ILD-DLCO trial in the second half of 2022. In addition, we anticipate an update from the company regarding the hypoxic solid tumor program after it receives feedback from the FDA on the clinical trial protocol, with a trial expected to initiate in the second half of 2022. With no changes to our model our valuation remains at \$2.00.

PROJECTED FINANCIALS

Diffusion Pharmaceuticals, Inc.	2021 A	Q1 E	Q2 E	Q3 E	Q4 E	2022 E	2023 E	2024 E
TSC (Hypoxic Tumors)	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>YOY Growth</i>	-	-	-	-	-	-	-	-
TSC (Other Indications)	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>YOY Growth</i>	-	-	-	-	-	-	-	-
Grants & Collaborative Revenue	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>YOY Growth</i>	-	-	-	-	-	-	-	-
Total Revenues	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>YOY Growth</i>	-	-	-	-	-	-	-	-
Cost of Sales	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>Product Gross Margin</i>	-	-	-	-	-	-	-	-
Research & Development	\$8.5	\$2.0	\$2.3	\$2.4	\$2.6	\$9.3	\$10.0	\$11.0
General & Administrative	\$7.4	\$1.8	\$1.8	\$1.9	\$1.9	\$7.5	\$7.5	\$8.0
Impairment Charge	\$8.6	\$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	(\$24.7)	(\$3.8)	(\$4.2)	(\$4.4)	(\$4.5)	(\$16.9)	(\$17.6)	(\$19.1)
<i>Operating Margin</i>	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	\$0.1	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0
Pre-Tax Income	(\$24.5)	(\$3.8)	(\$4.2)	(\$4.4)	(\$4.5)	(\$16.9)	(\$17.6)	(\$19.1)
Income Taxes	(\$0.4)	\$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	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0
Net Income	(\$24.1)	(\$3.8)	(\$4.2)	(\$4.4)	(\$4.5)	(\$16.9)	(\$17.6)	(\$19.1)
<i>Net Margin</i>	-	-	-	-	-	-	-	-
Reported EPS	(\$0.25)	(\$0.04)	(\$0.04)	(\$0.04)	(\$0.04)	(\$0.17)	(\$0.15)	(\$0.13)
<i>YOY Growth</i>	-	-	-	-	-	-	-	-
Basic Shares Outstanding	97.6	101.9	102.0	102.0	102.1	102.0	120.0	150.0

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

HISTORICAL STOCK PRICE



Source: Zacks Small Cap Research

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