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Diffusion Pharmaceuticals, Inc. (DFFN-NASDAQ)

DFFN: Phase 3 GBM Trial Underway; Planning for Phase 2 Trial in Stroke…

Based on our probability adjusted DCF model that takes into account potential future revenues from TSC in GBM, pancreatic cancer, and brain metastases, DFFN is valued at $3.50/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 (02/22/18)	$0.64
Valuation	**$3.50**

OUTLOOK

Diffusion Pharmaceuticals, Inc. (DFFN) recently announced the initiation of a Phase 3 clinical trial of trans sodium crocetinate (TSC) in patients with newly diagnosed inoperable glioblastoma multiforme (GBM). A total of 236 patients will be randomized 1:1 to receive standard of care (radiation plus chemotherapy) with TSC or placebo. The trial will take place at a total of 100 clinical sites (54 in the U.S. and 46 in the E.U.). An interim analysis may be performed in 2020 with final results likely available in 2021. The company also recently completed a $12 million financing to help fund the Phase 3 trial.

Planning is underway for a Phase 2 clinical trial of TSC in patients suffering from ischemic or hemorrhagic stroke, in which TSC would be administered to ambulance-transported patients. Assuming initiation of the trial in 2018, data could be available in 2019.

SUMMARY DATA

52-Week High	**$5.06**
52-Week Low	**$0.59**
One-Year Return (%)	**-83.46**
Beta	**-1.69**
Average Daily Volume (sh)	**693,111**
Shares Outstanding (mil)	**50**
Market Capitalization ($mil)	**$32**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**8**
Insider Ownership (%)	**16**
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)
2016	0 A	0 A	0 A	0 A	0 A
2017	0 A	0 A	0 A	0 E	0 E
2018					0 E
2019					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2016	-$0.62 A	-$0.37 A	-$0.53 A	-$0.25 A	-$1.76 A
2017	-$2.77 A	$1.89 A	-$0.37 A	-$0.31 E	-$0.61 E
2018					-$1.07 E
2019					-$1.34 E

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WHAT'S NEW

Business Update

Phase 3 GBM Trial of TSC Underway

On January 29, 2018, Diffusion Pharmaceuticals, Inc. (DFFN) announced that the first patient has been dosed in the Phase 3 clinical trial of trans sodium crocetinate (TSC), a small molecule that improves diffusion of oxygen through the bloodstream in order to increase tissue oxygenation and potentially improve outcomes associated with radiation and chemotherapy cancer treatments. The trial has been named INTACT (**IN**vestigating **T**sc **A**gainst **C**ancerous **T**umors) and is anticipated to screen 300 patients with inoperable glioblastoma multiforme (GBM) and enroll 264 such that results from 236 patients will be available for analysis. Patients will be randomized 1:1 to receive TSC along with standard of care radiation and chemotherapy (temozolimide) or standard of care alone. The primary outcome of the study is overall survival at two years between the two groups. We anticipate an interim analysis taking place in 2020 with final results available in 2021.

The Phase 3 study is a follow up to a Phase 1/2 study of 59 GBM patients with newly diagnosed GBM (Gainer *et al*., 2016). In the Phase I portion of the trial, TSC was initially administered three times per week at half-dose to three patients prior to radiation. Six additional patients received full dose TSC for six weeks in combination with radiation. No dose-limiting toxicities were identified in the nine patients during the Phase I portion of the trial. Fifty additional patients were enrolled in the Phase II trial at full dose TSC in combination with TMZ and RT. Four weeks after completion of RT, all patients resumed TMZ for five days every four weeks, but no further TSC was administered.

The results of the study were presented in relation to a historical control group, which is from a 2005 study that showed the addition of TMZ to standard of care (surgery plus radiation) increased overall survival from 12.1 months to 14.6 months (Stupp *et al*., 2005). Diffusion reported that:

- ❖ TSC plus radiation and TMZ increased the patients' chance of survival at two years by 37% compared to the historical control group. The overall survival at two years was 37% in the TSC group compared to 27% in the historical control group.

- ❖ In the subgroup of patients considered inoperable (biopsy only), the chance of survival at two years for those who received TSC was increased by 380%.

- ❖ 71 percent of people treated with TSC were alive at one year compared to 61 percent of people in the historical control group.

- ❖ Of the 37 patients with tumors able to be monitored, 27 experienced tumor regression, with 11 (30%) patients having complete tumor regression.

- ❖ No serious negative safety findings attributed to TSC were observed in the TSC study and adverse events were consistent with those seen in previous trials of GBM featuring radiation and TMZ.

Since the study lacked a control arm it is difficult to draw definitive conclusions regarding the activity of TSC, however we have been unable to identify another publication that discusses tumor regression in GBM patients, thus it is difficult to put this data fully into context. Gainer *et al*. cite anecdotal evidence of a maximum regression of 25% typically seen with standard RT through discussions with those who administer RT to GBM patients, thus 30% of patients experiencing complete tumor regression appears to be unprecedented.

Diffusion decided to focus on patients with inoperable GBM in the INTACT trial for the following reasons:

- ✓ The Phase 1/2 clinical trial showed a 380% increase in survival at two years in inoperable patients compared to a historical control group.
- ✓ The number of patients required will only be 236, compared to approximately 400 that would be required if all newly diagnosed GBM patients were included.
- ✓ Inoperable GBM patients fare much worse using SOC treatment and need better treatment options.
- ✓ Reducing the number of patients will provide significant cost savings.

Planning Underway for Phase 2 Trial in Stroke Patients

On January 24, 2018, Diffusion announced the acceptance of an abstract titled "PreHospital Acute Stroke Therapy with Trans Sodium Crocetinate (PHAST-TSC)" which was presented at the International Stroke Conference Jan. 24-26, 2018. The abstract discusses the design and rationale for a planned Phase 2 study of TSC in patients with acute ischemic (from a clot) or hemorrhagic (from a bleed) stroke. It will be a randomized, double blind, placebo controlled trial with an anticipated enrollment of 160 ambulance-transported patients treated within two hours of the onset of a suspected stroke. If funding allows for the trial to begin in 2018, results could be available in 2019.

Preclinical models show that TSC could be an effective treatment for both ischemic and hemorrhagic stroke (Wang *et al*., 2014). In a 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 second 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). The only FDA approved treatment for acute ischemic stroke is tissue plasminogen activator (t-PA), although its use can aggravate outcomes in hemorrhagic stroke and increase hemorrhagic transformation in some ischemic strokes (Larrue *et al*., 2001). Worldwide sales of alteplase (recombinant t-PA) totaled $1.4 billion in 2016 and is expected to grow to $1.9 billion by 2022 (EvaluatePharma).

Financial Update

On January 18, 2018, Diffusion announced the pricing of a $12 million underwritten public offering of a total of 15 million shares of common stock together with 15 million warrants. The public offering price was $0.80 per share with the warrants having an exercise price of $0.80 and a five-year expiration date. In addition, the company granted the underwriter (H.C. Wainwright & Co.) a 30-day option to purchase up to 2.25 million additional shares of common stock. In addition, since the company raised >$10 million, all outstanding Series A convertible shares will be automatically converted to common shares.

Valuation

Diffusion's valuation is derived from a risk-adjusted discounted cash flow model that takes into account potential future revenues from the sale of TSC in GBM, pancreatic cancer, and brain metastases. For all indications we assume that the company will partner and receive 15% royalties on net sales.

For GBM, we model for a new drug application (NDA) to be filed in 2021, and approval in 2022. For pancreatic cancer, we model for the Phase 2 trial to initiate in 2018, an NDA filing in 2022, and approval in 2023. For brain metastases, we model for a Phase 2/3 trial to initiate in 2020, an NDA filing in 2023 and approval in 2024.

Combing the net present value for each of the company's development programs along with the company's current cash position and estimated additional capital necessary leads to a valuation of $3.50 per share. The stock is currently trading at a significant discount to this valuation and we believe that investors could use the current downturn to add to or establish a position.

PROJECTED FINANCIALS

Diffusion Pharmaceuticals, Inc.	2016 A	Q1 A	Q2 A	Q3 A	Q4 E	2017 E	2018 E	2019 E
TSC (GBM)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
TSC (Pancreatic Cancer)	$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	$7.3	$1.0	$1.2	$1.8	$2.0	$5.9	$10.0	$17.0
General & Administrative	$11.1	$1.6	$1.8	$1.6	$2.5	$7.4	$9.0	$9.5
Other Expenses	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($18.4)	($2.6)	($3.0)	($3.3)	($4.5)	($13.4)	($19.0)	($26.5)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	($0.0)	($26.1)	$23.4	$8.4	($0.0)	$5.8	($0.2)	($0.2)
Pre-Tax Income	($18.4)	($28.6)	$20.4	$5.1	($4.5)	($7.6)	($19.2)	($26.7)
Income Taxes Paid	($0)	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($18.0)**	**($28.6)**	**$20.4**	**$5.1**	**($4.5)**	**($7.6)**	**($19.2)**	**($26.7)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($1.76)**	**($2.77)**	**$1.89**	**$0.37**	**($0.31)**	**($0.61)**	**($1.07)**	**($1.34)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	10.2	10.3	10.8	13.9	14.5	12.4	18.0	20.0

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

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