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Diffusion Pharmaceuticals, Inc. (DFFN-NASDAQ)

DFFN: Phase 2 Clinical Trial of TSC in Acute Stroke to Commence in 2019…

Based on our probability adjusted DCF model that takes into account potential future revenues from TSC in GBM, pancreatic cancer, and stroke, DFFN is valued at $3.00/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 (12/10/18)	$0.24
Valuation	**$3.00**

OUTLOOK

Diffusion Pharmaceuticals, Inc. (DFFN) is currently planning for a Phase 2 clinical trial of the company's lead asset, trans sodium crocetinate (TSC), in acute stroke. The Pre-Hospital Ambulance Stroke Trial – TSC (PHAST-T) will test the administration of TSC by Emergency Medical Technicians in ambulance-transported patients within two hours of onset of suspected stroke. We anticipate this trial commencing in 2019.

Diffusion is also currently conducting the INTACT Phase 3 clinical trial of TSC in 236 patients with newly diagnosed inoperable glioblastoma multiforme (GBM). The first patients were dosed in January 2018 and we anticipate an interim analysis being performed at the earlier of two years follow-up for all subjects or 198 events (deaths).

SUMMARY DATA

52-Week High	**$1.73**
52-Week Low	**$0.24**
One-Year Return (%)	**-82.91**
Beta	**-1.56**
Average Daily Volume (sh)	**402,604**
Shares Outstanding (mil)	**51**
Market Capitalization ($mil)	**$12**
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-Value**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	0 A	0 A	0 A	0 A	0 A
2018	0 A	0 A	0 A	0 E	0 E
2019					0 E
2020					0 E

Earnings per Share
(Diluted)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	-$2.78 A	-$1.00 A	$0.20 A	$0.06 A	-$1.94 A
2018	-$0.27 A	-$0.05 A	-$0.13 A	-$0.06 E	-$0.42 E
2019					-$0.24 E
2020					-$0.26 E

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WHAT'S NEW

Business Update

Phase 2 Trial of TSC in Stroke Patients to Commence in 2019

In early 2018, Diffusion Pharmaceuticals, Inc. (DFFN) announced the acceptance of an abstract titled "PreHospital Acute Stroke Therapy with Trans Sodium Crocetinate (PHAST-TSC)" to be presented at the International Stroke Conference. The abstract discussed the design and rationale for a planned Phase 2 study of trans sodium crocetinate (TSC), a small molecule that improves diffusion of oxygen through the bloodstream in order to increase tissue oxygenation, in patients with acute ischemic (from a clot) or hemorrhagic (from a bleed) stroke. The Pre-Hospital Ambulance Stroke Trial – TSC (PHAST-T) 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. The trial is novel in that patients will be treated in the ambulance on the way to the hospital. In October 2018, Diffusion received approval from the U.S. FDA to enroll patients in the study. We anticipate the trial initiating in 2019, subject to available funding, and topline results could be available in two years following the start of the trial.

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 $1.5 billion in 2017 and is expected to grow to $1.9 billion by 2022 (EvaluatePharma).

Phase 3 GBM Trial Enrolling Patients

Early in 2018, Diffusion announced that the first patient has been dosed in the Phase 3 **IN**vestigating **T**sc **A**gainst **C**ancerous **T**umors (INTACT) clinical trial. The trial 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. Following a dose-escalation run-in period, in which eight patients will receive ascending doses of TSC along with temozolimid (TMZ) for two 28-day cycles, patients will be randomized 1:1 to receive TSC along with standard of care radiation and chemotherapy (TMZ) or standard of care alone. The eighth patient from the run-in portion of the study should complete in January 2019, and we anticipate data from this cohort in the second quarter of 2019. The primary outcome of the study is overall survival at two years between the two groups. An interim analysis will take place at the earlier of a) two years follow-up for all subjects or b) 198 events (deaths). At 198 events the study will be 80% powered with an estimated overall survival time of 10 months for patients on standard of care and 14.9 months for patients treated with TSC in addition to standard of care.

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.

New Chief Financial Officer

On September 21, 2018, Diffusion announced the appointment of William "Bill" Hornung as Chief Financial Officer. Mr. Hornung was previously the company's Chief Business Officer. He has over 20 years of experience in the industry and prior to his time with Diffusion he most recently served as Vice President of Finance at PTC Therapeutics, Inc. Prior to PTC, he was responsible for planning and operations of The Liposome Company and also served as Chief Financial Officer of ContraVir Pharmaceuticals.

Financial Update

On November 13, 2018, Diffusion announced financial results for the third quarter of 2018. Net loss for the third quarter of 2018 was $6.7 million compared to net income of $5.1 million in the third quarter of 2017. The large increase in net loss was due a $8.4 million gain for the change in fair value of common stock warrant liabilities in the third quarter of 2017 that was due to the decrease in the market value of the company's common stock and not indicative of ongoing operations.

R&D expenses for the third quarter of 2018 were $1.2 million, compared to $1.8 million during the third quarter of 2017. The decrease was primarily due to decreased costs associated with the Phase 3 GBM trial. G&A expenses in the third quarter of 2018 and 2017 were both $1.6 million. The company also recognized a non-cash goodwill impairment charge of $4.2 million during the third quarter of 2018 as a result of a decrease in the company's market capitalization. There was no goodwill impairment charge in the third quarter of 2017.

As of September 30, 2018, the company had approximately $11.0 million in cash and cash equivalents. We believe the company has sufficient capital to fund operations through September 2019. As of November 1, 2018, the company had approximately 50.6 million common shares outstanding and when factoring in warrants and options a fully diluted share count of approximately 85.1 million.

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 stroke. 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 2023, and approval in 2024. For pancreatic cancer, we model for the Phase 2 trial to initiate in 2020, an NDA filing in 2024, and approval in 2025. For stroke,

we model for a Phase 2 trial to initiate in 2019, an NDA filing in 2023 and approval in 2024. We believe total peak sales for TSC of over a billion dollars are possible based on the compounds unique mechanism of action and solid preclinical and clinical data seen to date.

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 $3.00 per share.

PROJECTED FINANCIALS

Diffusion Pharmaceuticals, Inc.	2017 A	Q1 A	Q2 A	Q3 A	Q4 E	2018 E	2019 E	2020 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	$5.1	$1.8	$1.4	$1.2	$1.5	$5.9	$7.0	$9.0
General & Administrative	$6.2	$1.5	$1.7	$1.6	$1.6	$6.3	$7.0	$7.5
Goodwill Impairment	$0.0	$0.0	$0.0	$4.2				
Depreciation	$0.1	$0.0	$0.0	$0.0	$0.0	$0.1	$0.0	$0.0
Operating Income	($11.3)	($3.4)	($3.1)	($7.0)	($3.1)	($12.3)	($14.0)	($16.5)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$8.9	($0.1)	($0.0)	$0.0	$0.0	($0.1)	($0.2)	($0.2)
Pre-Tax Income	($2.4)	($3.3)	($3.0)	($6.9)	($3.1)	($12.4)	($14.2)	($16.7)
Income Taxes	($1.1)	$0.0	($0.3)	($0.2)	$0.0	($0.5)	$0	$0
Accretion of Series A preferred dividends	($1.3)	$8.3	$0.0	$0.0	$0.0	$8.3	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($2.6)**	**($11.6)**	**($2.7)**	**($6.7)**	**($3.1)**	**($20.2)**	**($14.2)**	**($16.7)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($1.94)**	**($0.27)**	**($0.05)**	**($0.13)**	**($0.06)**	**($0.42)**	**($0.24)**	**($0.26)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	12.4	42.1	50.5	50.6	50.7	48.5	60.0	65.0

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

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