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Diffusion Pharmaceuticals, Inc. (DFFN-NASDAQ)

DFFN: Data from Initial 8 Patients in Phase 3 GBM Trial Expected in mid-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 $10.00/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 (04/17/19)	$3.20
Valuation	**$10.00**

OUTLOOK

Diffusion Pharmaceuticals, Inc. (DFFN) is currently conducting the INTACT Phase 3 clinical trial of trans sodium crocetinate (TSC) in 236 patients with newly diagnosed inoperable glioblastoma multiforme (GBM). Data from the initial eight patients from the run-in portion of the trial is expected in mid-2019.

The company recently announced that the U.S. Patent Office has issued U.S. Patent 10,130,689 that covers the use of TSC with tissue plasminogen activator (tPA) for the treatment of stroke. tPA is currently the only FDA-approved therapeutic for the treatment of stroke. The company is currently planning for a Phase 2 clinical trial of TSC in acute stroke that 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.

SUMMARY DATA

52-Week High	**$9.26**
52-Week Low	**$1.94**
One-Year Return (%)	**-63.82**
Beta	**0.29**
Average Daily Volume (sh)	**52,766**
Shares Outstanding (mil)	**3**
Market Capitalization ($mil)	**$11**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**6**
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)
2018	0 A	0 A	0 A	0 A	0 A
2019	0 E	0 E	0 E	0 E	0 E
2020					0 E
2021					0 E

Earnings per Share
(Diluted)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	-$4.11 A	-$0.81 A	-$1.99 A	-$1.66 A	-$8.21 A
2019	-$0.90 E	-$0.90 E	-$0.42 E	-$0.43 E	-$2.30 E
2020					-$1.39 E
2021					-$1.28 E

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WHAT'S NEW

Business Update

Data from First Eight Patients in Phase 3 GBM Trial in mid-2019

Diffusion Pharmaceuticals, Inc. (DFFN) is currently conducting 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 therapy (RT) and chemotherapy (TMZ) or standard of care alone. We anticipate data from the run-in cohort in mid-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 RT. 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 Patent Issued for TSC in the Treatment of Stroke

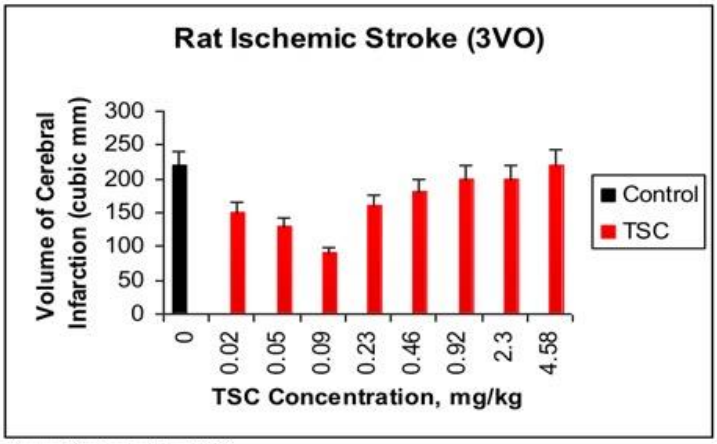
On December 17, 2018, Diffusion Pharmaceuticals, Inc. (DFFN) announced the issuance of U.S. Patent 10,130,689 that covers the use of the company's lead drug candidate, trans sodium crocetinate (TSC), with tissue plasminogen activator (tPA) for the treatment of stroke. tPA is currently the only FDA approved therapy for the treatment of stroke and is used for its anti-thrombotic activity to dissolve blood clots in patients suffering from ischemic stroke. Worldwide sales of alteplase (recombinant tPA) totaled $1.5 billion in 2017 and is expected to grow to $1.9 billion by 2022 (EvaluatePharma).

Phase 2 Trial of TSC in Stroke to Initiate in 2019

Diffusion is currently planning to conduct the Pre-Hospital Ambulance Stroke Trial – TSC (PHAST-T), which will be a randomized, double blind, placebo controlled Phase 2 trial with an anticipated enrollment of 160 ambulance-transported patients (80 active/80 placebo) 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 addition, patients are eligible to receive tPA separately in-hospital if it is determined they are suffering from an ischemic stroke. In October 2018, Diffusion received approval from the U.S. FDA to enroll patients in the study. We anticipate the trial initiating in 2019 and topline results could be available in two years following the start of the trial.

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 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 March 20, 2019, Diffusion announced financial results for 2018 and provided a business update. For the year, the company had R&D expenses of $5.8 million compared to $5.1 million in 2017. The increase was primarily due to an increased expenses associated with the Phase 3 GBM trial partially offset by a decrease in manufacturing costs. G&A expenses in 2018 were $6.2 million, which were flat compared to 2017. In 2018, there was a non-cash goodwill impairment charge of $6.9 million as a result of the sustained decrease in the company's market capitalization during the second half of 2018. There was no such charge in 2017.

The company exited 2018 with approximately $8.0 million in cash and cash equivalents. We estimate this will be sufficient to fund operations through the first half of 2019. As of March 13, 2019, the company had approximately

3.4 million common shares outstanding and when factoring in warrants and options a fully diluted share count of approximately 5.7 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 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 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 compound's unique mechanism of action and solid preclinical and clinical data seen to date.

The company recently enacted a 1-for-15 reverse split, which lowered the total shares outstanding to 3.4 million and when factoring in options and warrants the fully diluted share count is 5.7 million. Combing the net present value for each of the company's development programs along with the company's current cash position and estimated additional shares to be issued leads to a valuation of $10.00 per share.

PROJECTED FINANCIALS

Diffusion Pharmaceuticals, Inc.	2018 A	Q1 E	Q2 E	Q3 E	Q4 E	2019 E	2020 E	2021 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	$5.8	$1.5	$1.6	$1.7	$1.8	$6.6	$9.0	$11.0
General & Administrative	$6.2	$1.6	$1.6	$1.6	$1.6	$6.4	$7.5	$8.0
Goodwill Impairment	$6.9	$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	$0.0	$0.0	$0.0
Operating Income	($19.0)	($3.10)	($3.2)	($3.3)	($3.4)	($13.0)	($16.50)	($19.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.2	($0.1)	($0.1)	($0.1)	($0.1)	($0.2)	($0.2)	($0.2)
Pre-Tax Income	($18.8)	($3.1)	($3.2)	($3.3)	($3.5)	($13.2)	($16.7)	($19.2)
Income Taxes	($0.4)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Accretion of Series A preferred dividends	$8.3	$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	**($26.6)**	**($3.1)**	**($3.2)**	**($3.3)**	**($3.5)**	**($13.2)**	**($16.7)**	**($19.2)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($8.21)**	**($0.90)**	**($0.90)**	**($0.42)**	**($0.43)**	**($2.30)**	**($1.39)**	**($1.28)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	3.2	3.4	3.5	8.0	8.0	5.7	12.0	15.0

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

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