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Diffusion Pharmaceuticals, Inc. (DFFN-NASDAQ)

DFFN: Highly Encouraging Data from Run-in Portion of Phase 3 GBM Trial…

Based on our probability adjusted DCF model that takes into account potential future revenues from TSC in stroke, DFFN is valued at $1.50/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 (12/30/19)	$0.40
Valuation	**$1.50**

OUTLOOK

On Dec. 10, 2019, Diffusion Pharmaceuticals, Inc. (DFFN) presented data from the 19 patient run-in portion of the Phase 3 clinical trial of trans sodium crocetinate (TSC) at the inaugural Glioblastoma Drug Development Summit. While the number of patients who received high dose TSC was small (n=7), the company reported that six (86%) of them are still alive, which compares to 38% for the Phase 2 clinical trial and 13% for the standard of care at the same time point. The company is currently seeking a partner to continue development of TSC in GBM.

The company also recently enrolled the first patient in the Phase 2 clinical trial of TSC for the treatment of stroke. We anticipate topline results in approximately two years.

SUMMARY DATA

52-Week High	**$7.00**
52-Week Low	**$0.22**
One-Year Return (%)	**-82.22**
Beta	**-0.22**
Average Daily Volume (sh)	**4,966,029**
Shares Outstanding (mil)	**33**
Market Capitalization ($mil)	**$13**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**14**
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 A	0 A	0 A	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	-$0.81 A	-$0.63 A	-$0.60 A	-$0.17 E	-$1.46 E
2020					-$0.56 E
2021					-$0.48 E

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WHAT'S NEW

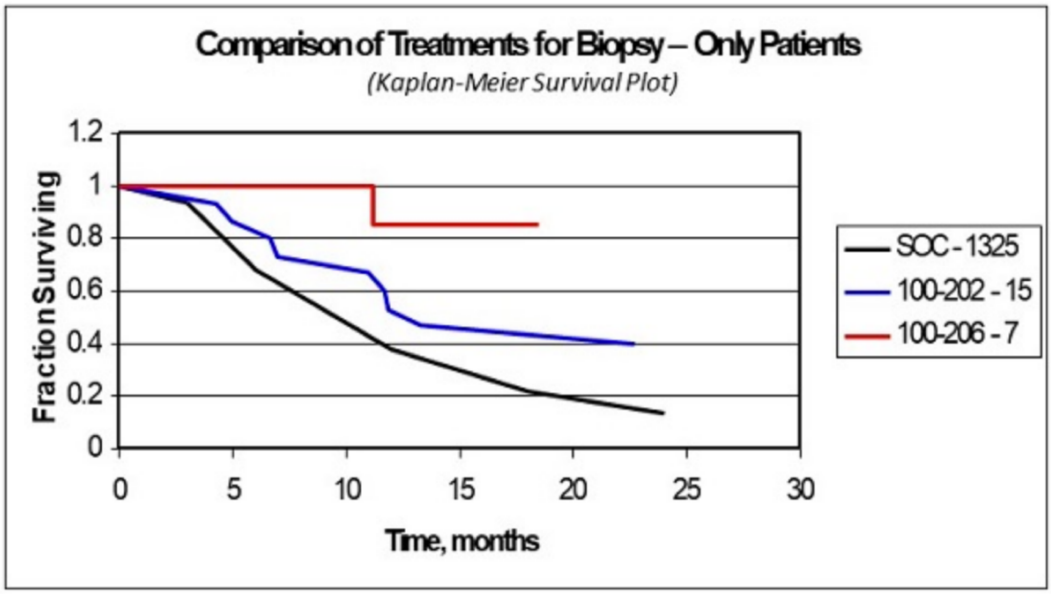
Business Update

Encouraging Data for Dose Escalation Run-in of Phase 3 GBM Trial

On December 10, 2019, Diffusion Pharmaceuticals, Inc. (DFFN) announced the presentation of highly encouraging data from the 19 patient run-in portion of the Phase 3 **IN**vestigating **T**sc **A**gainst **C**ancerous **T**umors (INTACT) clinical trial of TSC in patients with glioblastoma (GBM). The data was presented by Diffusion's Chief Scientific Officer, Dr. John Gainer, at the inaugural Glioblastoma Drug Development Summit, which took place from Dec. 10-11, 2019.

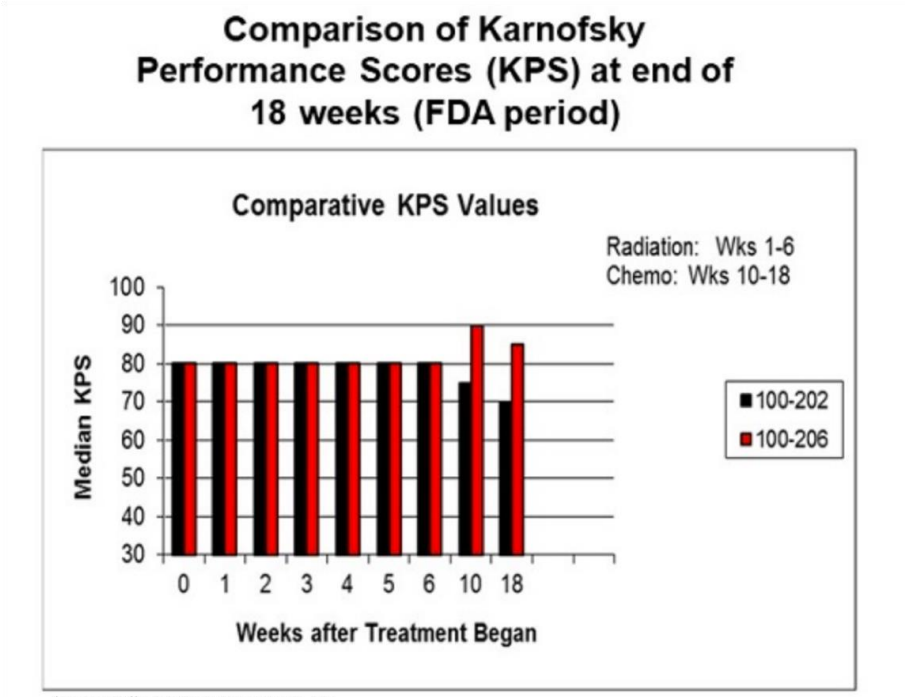
Patients in the INTACT trial have GBM but are not eligible for surgery, thus the standard of care treatment is radiation therapy for six weeks, followed by 28 days of rest, and then six cycles of temozolomide (TMZ). The INTACT protocol calls for patients to receive TSC both during radiation treatment and during the chemotherapy phase.

The company recently completed the 19-patient, open label, single arm, dose escalation run-in portion of the INTACT trial, which was required since a higher dose of TSC was to be administered, compared to the dose that was given during the Phase 1/2 trial in 59 newly diagnosed GBM patients (Gainer *et al*., 2016). The company reported that there were no safety signals associated with administration of TSC. In addition, six of the seven patients that received the highest dose of TSC during their treatment are still alive, as shown in the following Kaplan-Meier survival plot. The current data showing an 86% "fraction surviving" compares favorably to just 38% for the Phase 2 clinical trial and only 13% for standard of care at the same time point.



Source: Diffusion Pharmaceuticals, Inc.

Patient's Karnofsky Performance Scores (KPS), which measure the ability to perform daily activities, also *increased* from baseline following completion of high dose TSC treatment, as shown in the following graph. This contrasts with what was seen in the Phase 2 clinical trial (denoted 100-202) in which KPS began decreasing by week 10 and continued to decrease out to week 18.



Source: Diffusion Pharmaceuticals, Inc.

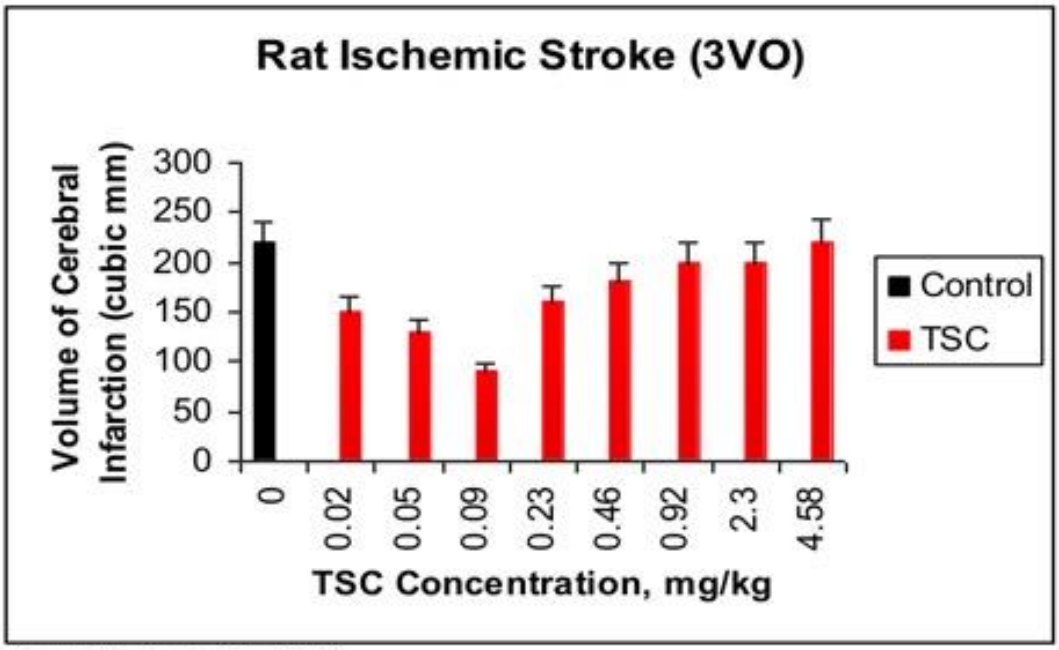
Patients with inoperable GBM have a very grim prognosis, thus the data presented by Diffusion is highly encouraging for this group of patients. In addition, there were no safety signals and TSC continues to be very well tolerated. The company is currently seeking a partner to continue development of TSC in GBM.

Phase 2 Stroke Trial Underway

On October 17, 2019, Diffusion announced that the first patient has been enrolled in the Phase 2 on-ambulance trial of the company's lead asset, trans sodium crocetinate (TSC), for the treatment of stroke. The Pre-Hospital Administration of Stroke Therapy-TSC (PHAST-TSC) trial is expected to enroll 160 patients who will be treated in the ambulance (80 active/80 placebo) within two hours of a suspected stroke on the way to the hospital regardless of whether they are suffering from an ischemic or hemorrhagic stroke. In addition, patients are eligible to receive tissue plasminogen activator (tPA) separately in-hospital if it is determined they are suffering from an ischemic stroke. A total of 23 hospitals, working in conjunction with 150 emergency medical transport groups, are expected to participate in the trial across central Virginia and in Los Angeles County. Enrollment has initiated in Virginia and we expect enrollment to commence at the University of Los Angeles before the end of 2019.

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, shown at the 2019 International Stroke Conference, 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 November 11, 2019, Diffusion announced financial results for the third quarter of 2019. As expected, the company did not report any revenues. R&D expenses for the third quarter of 2019 were $1.7 million compared to $1.2 million for the third quarter of 2018. The increase was primarily due to increased costs associated with the Phase 2 stroke trial. G&A expenses were $1.3 million during the third quarter of 2019 compared to $1.6 million during the third quarter of 2018. The decrease was primarily due to decreased salaries, wages, and stock-based compensation.

Diffusion exited the third quarter of 2019 with approximately $6.1 million in cash and cash equivalents. On November 15, 2019, the company announced the closing of a public offering that we anticipate will raise net proceeds of approximately $3.3 million through the sale of approximately 5.1 million common shares (with the same number of Series I and II warrants) and approximately 6.3 million pre-funded warrants to purchase a share of common stock (with the same number of Series I and Series II warrants). On Dec. 12, 2019, the company announced a $3.5 million registered direct offering of approximately 6.3 million shares at a purchase price of $0.5585 per share along with approximately 6.3 million warrants with an exercise price of $0.4335.

The company had 24.2 million shares outstanding as of Dec. 10, 2019, thus after the most recent financing we estimate the total shares outstanding are 30.5 million and when factoring in stock options and warrants the fully diluted share count is approximately 54.7 million.

Conclusion

The run-in data for the Phase 3 GBM trial are really encouraging, and we are hopeful that it will be enough to entice a potential partner so that the Phase 3 trial can continue, as there seems to certainly be enough preliminary signs of efficacy to warrant TSC's advancement in that indication.

Now that the PHAST-TSC trial is underway we look forward to updates regarding patient enrollment and we estimate that topline data will be available in approximately two years. Based on the large number of strokes that occur in the U.S. every year, and the billions of dollars that treating stroke victims costs the healthcare system each year, we believe that TSC could become a blockbuster drug in the treatment of stroke and we estimate for potential peak revenues of over $1 billion worldwide. However, we have reduced the value of the GBM indication in our valuation model as the company will not move forward in GBM without a partner, although with the encouraging data from the 19-patient run-in portion of the Phase 3 trial we believe the chances for a partnership have increased. Our valuation currently stands at $1.50 per share.

PROJECTED FINANCIALS

Diffusion Pharmaceuticals, Inc.	2018 A	Q1 A	Q2 A	Q3 A	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	$1.7	$1.5	$1.7	$1.8	$6.8	$9.0	$11.0
General & Administrative	$6.2	$1.2	$1.1	$1.3	$1.6	$5.2	$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	$0.1	$0.0	$0.0
Operating Income	($19.0)	($2.9)	($2.6)	($3.052)	($3.4)	($12.0)	($16.5)	($19.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.2	($0.0)	($0.0)	$0.0	($0.1)	($0.2)	($0.2)	($0.2)
Pre-Tax Income	($18.8)	($2.9)	($2.6)	($3.0)	($3.5)	($12.2)	($16.7)	($19.2)
Income Taxes	($0.4)	($0.2)	($0.1)	($0.2)	$0.0	($0.5)	$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)**	**($2.7)**	**($2.5)**	**($2.8)**	**($3.5)**	**($11.7)**	**($16.7)**	**($19.2)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($8.21)**	**($0.81)**	**($0.63)**	**($0.60)**	**($0.17)**	**($1.46)**	**($0.56)**	**($0.48)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	3.2	3.4	3.9	4.7	20.0	8.0	30.0	40.0

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

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