UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of
the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): November 10, 2021

DIFFUSION PHARMACEUTICALS INC.

(Exact name of registrant as specified in its charter)

Delaware	**000-24477**	**30-0645032**
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

300 East Main Street, Suite 201 **Charlottesville, Virginia**	**22902**
(Address of principal executive offices)	(Zip Code)

(434) 220-0718
(Registrant's telephone number, including area code)

Not applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	DFFN	NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition

On November 10, 2021, Diffusion Pharmaceuticals Inc. (the "Company") issued a press release announcing financial results for the three-month period ended September 30, 2021 and a business update. A copy of that press release is attached hereto as Exhibit 99.1 and incorporated herein by reference.

The information included in or incorporated by reference into this Item 2.02 (including Exhibit 99.1) is being furnished pursuant to Item 2.02 of Form 8-K and shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed to be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act.

Item 9.01 – Financial Statements and Exhibits

(d) Exhibits

Exhibit Number	**Description**
99.1	Press Release, issued November 10, 2021, announcing financial results for the three-month period ended September 30, 2021 and business update
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: November 10, 2021

DIFFUSION PHARMACEUTICALS INC.
By: /s/ William Elder
Name: William Elder
Title: General Counsel

Diffusion Pharmaceuticals Reports Third Quarter Financial Results and Provides Business Update

- Announces Intent to Develop TSC to Treat Hypoxic Tumors
- Altitude Trial Expected to Commence in November 2021
- ILD-DLCO Trial Expected to Commence in Late December 2021

CHARLOTTESVILLE, Va., November 10, 2021 -- **Diffusion Pharmaceuticals Inc. (NASDAQ: DFFN)** ("Diffusion" or the "Company"), a biopharmaceutical company developing novel therapies that enhance the body's ability to deliver oxygen to areas where it is needed most, today announced financial results for the third quarter of 2021 and provided a business update.

"We believe this is an exciting time for Diffusion Pharmaceuticals. The data we have obtained over the last year from our TCOM and COVID-19 studies have enhanced our understanding of TSC dosing and its mechanism of action, which we feel provides support for the broad potential use of TSC as a treatment for conditions complicated by hypoxia. As the next step in our efforts to realize TSC's broad potential, we have chosen to target the treatment of hypoxic solid tumors as a first indication," said Robert Cobuzzi, Jr. Ph.D., President and CEO of Diffusion. Dr. Cobuzzi continued, "We believe targeting hypoxic solid tumors is right for TSC given the significant unmet medical need, the compelling preclinical and clinical data accumulated to date, and the current, intravenous formulation of TSC. As a prelude to launching the first clinical study in the program, we plan to obtain input from the U.S. Food and Drug Administration ("FDA") on its design in early 2022, and our study start date will be dependent upon FDA feedback and the availability of clinical drug supply. In the meantime, we will continue to execute on the final two Oxygenation Trials. On that, I am happy to say we plan to dose the first subject in the Altitude Trial within the next couple weeks, and in parallel we are working to initiate the ILD-DLCO Trial."

TSC Development Plans for 2021 and 2022

The Oxygenation Trials

In June 2021, Diffusion reported a positive trend in oxygenation from its Phase 1b TCOM Trial evaluating the effect of TSC versus placebo on peripheral tissue oxygenation in healthy normal volunteers using transcutaneous oxygen measurements. The data obtained from the TCOM Trial have been used to guide dose selection in the Company's two additional Oxygenation Trials–the Altitude Trial and the ILD-DLCO Trial.

- **Altitude Trial**: This trial will be a double-blind, randomized, placebo-controlled study to evaluate the effects of TSC on maximal oxygen consumption, or VO2, and partial pressure of blood oxygen, or PaO2, in normal healthy volunteers subjected to incremental levels of physical exertion while exposed to hypoxic and hypobaric conditions (i.e., simulated altitude). The study is designed to evaluate the effect of TSC versus placebo on maximal oxygen consumption and partial pressure of blood oxygen. The Company expects dosing of the first subject in the Altitude Trial in November 2021 and expects to complete the study in late December 2021 or early January 2022. The Company anticipates reporting topline results from the Altitude Trial within two months of study completion.

- **ILD - DLCO Trial:** This trial will be a double-blind, randomized, placebo-controlled study which will evaluate the effects of TSC on the diffusion of carbon monoxide through the lungs ("DLCO") in patients with previously diagnosed interstitial lung disease who have a baseline DLCO test result that is abnormal. DLCO will act as a surrogate measure of oxygen transfer efficiency, or uptake, from the alveoli of the lungs, through the plasma, and onto hemoglobin within red blood cells. 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. Diffusion anticipates initiating the ILD-DLCO Trial late in the fourth quarter of 2021 and completing the trial in the first quarter of 2022, with topline results reported within two months of study completion.

  In addition, with the clearance of the Investigational New Drug application ("IND") to support the ILD-DLCO Trial from the Pulmonary, Allergy, and Critical Care division of the FDA received during the third quarter, Diffusion now has open INDs for TSC with four FDA divisions: Pulmonary, Allergy, and Critical Care; Cardiology and Nephrology, Neurology and Oncology.

The Company believes these Oxygenation Trials remain integral to the overall development plan for TSC, as they are intended to provide further information regarding TSC's mechanism of action and dose-response characteristics, as well as to support what the Company believes is the broad therapeutic potential of TSC to treat a variety of conditions complicated by hypoxia. More specifically, the Altitude Trial is designed to provide information on TSC's effects on oxygen consumption, and the ILD-DLCO Trial is designed to evaluate the effects of TSC on the uptake of oxygen through the lungs.

Using TSC to Treat Hypoxic Solid Tumors

While the Company intends to continue developing data to support TSC's broad potential uses, it has announced that its near-term focus will be the design and execution of a clinical program to support the use of intravenously administered TSC as a treatment for hypoxic solid tumors.

Diffusion Pharmaceuticals Inc.

“Solid tumors comprise approximately 90% of all adult cancers, and according to the American Cancer Society, roughly 1.9 million new cancer cases will be diagnosed in the U.S. alone during 2021. Hypoxia is a common complicating factor in nearly all solid tumors, directly contributing to treatment resistance and metastatic potential. Tumor hypoxia has been studied for decades and continues to be an area of unmet need that negatively influences treatment outcomes independent of modality” said Chris Galloway, M.D., Chief Medical Officer of Diffusion. Dr. Galloway went on to state, “We believe TSC’s unique mechanism of action along with its safety profile has the potential to improve treatment success of solid tumors coincident with standard of care therapy. Diffusion has existing pre-clinical and clinical evidence of TSC’s potential positive effects in solid tumors, and now further informative exposure-response data from recently completed studies like the Oxygenation Trials and our COVID-19 trial. Building upon this we are actively working to design a targeted development plan in multiple solid tumor types and plan to submit a briefing document to the FDA in early 2022. In parallel, data from the upcoming Altitude and ILD-DLCO Trials will be used to refine and enhance our understanding of TSC’s dose and effects that conceivably translate into a multitude of oncology and non-oncology indications.”

3Q21 Financial Results

- Research and development expenses in the third quarter were $2.1 million compared to expenses of $3.1 million in the prior year period, a decrease of $1.0 million. This decrease was attributable to the completion of the Company’s clinical trial evaluating TSC in COVID-19 patients in February and the wind-down of the Company’s glioblastoma multiforme and stroke trials, and partially offset by increased headcount and costs related to the startup of the Altitude and ILD-DLCO Trials.

- General and administrative expenses were $1.9 million during the third quarter of 2021 versus $2.1 million in the comparable quarter last year. The decrease compared to the prior year period was primarily attributable to executive separation payments in the prior year period partially offset by increased salaries, wages, stock-based compensation, and professional fees related to increased headcount in 2021.

- The Company recognized a non-recurring, non-cash asset impairment charge of $8.6 million during the third quarter of 2021 versus $0.0 in the comparable quarter last year. The charge was related to the full impairment of the in-process research and development asset associated with the Company’s DFN-529 product candidate, which was acquired in January 2016 in connection with the reverse merger of Diffusion Pharmaceuticals LLC and RestorGenex Corporation.

- The Company’s third quarter 2021 operating loss was $12.6 million as compared with an operating loss of $5.2 million in the third quarter of 2020, with the increase primarily attributable to the $8.6 million non-cash asset impairment charge described above. Excluding the asset impairment charge, the Company’s operating loss decreased by $1.3 million.

- As of Sept 30, 2021, Diffusion had cash and cash equivalents of approximately $40.3 million as compared to $18.5 million as of December 31, 2020. The increase was primarily attributable to the proceeds of the Company’s public offering of common stock in February 2021. Diffusion estimates that it has sufficient cash to fund operations and capital expenditures through 2023.

About Diffusion Pharmaceuticals Inc.
Diffusion Pharmaceuticals Inc. is an innovative biopharmaceutical company developing novel therapies that enhance the body's ability to deliver oxygen to areas where it is needed most. Diffusion's lead product candidate, TSC, is being developed to enhance the diffusion of oxygen to tissues with low oxygen levels, also known as hypoxia, a serious complication of many of medicine's most intractable and difficult-to-treat conditions. For more information, please visit us at www.diffusionpharma.com.

Forward-Looking Statements
This press release includes express and implied forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including regarding the Company's anticipated cash runway, its near-term strategic priorities, anticipated timelines for the initiation, completion, and announcement of data from the Company's planned Oxygenation Trials and hypoxic solid tumor program, the relevance and significance of any such data, and the potential therapeutic value of TSC. The Company may, in some cases, use terms such as "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately," or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Although the Company believes that it has a reasonable basis for each forward-looking statement contained herein, forward-looking statements by their nature involve risks and uncertainties, known and unknown, many of which are beyond the Company's control and, as a result, the Company's actual results could differ materially from those expressed or implied in any forward-looking statement. Particular risk and uncertainties include, among other things, those related to: the Company's ability to design, initiate, enroll, execute, and complete its planned studies evaluating TSC; the optimal doses and dosing regimens of TSC in connection with the potential treatment of any particular disease or indication, including solid tumors complicated by hypoxia; the likelihood and timing of regulatory approval of TSC, if any, for the treatment of solid tumors complicated by hypoxia or any other indication, or the nature of any feedback the Company may receive from the U.S. Food and Drug Administration or other regulatory bodies; the impact of supply chain and other supplier issues on the Company's clinical development program and associated timelines; the Company's ability to protect and expand its intellectual property portfolio; the Company's ability to maintain compliance with the continued listing standards of Nasdaq; general economic, political, business, industry, and market conditions, including the ongoing COVID-19 pandemic; and the other factors discussed under the heading "Risk Factors" in the Company's filings most recent Annual Report on Form 10-K and other filings with the U.S. Securities and Exchange Commission. Any forward-looking statements in this press release speak only as of the date hereof (or such earlier date as may be identified) and, except as required by applicable law, rule, or regulation, the Company undertakes no obligation to update any such statements after the date hereof.

Diffusio$_2$n Pharmaceuticals Inc.

Contacts

Investors:
Tiberend Strategic Advisors, Inc.
Maureen McEnroe, CFA/ Lisa Sher
mmcenroe@tiberend.com/ lsher@tiberend.com

Media:
Kate Barrette
RooneyPartners
Kbarrette@rooneyco.com

DIFFUSION PHARMACEUTICALS, INC.
UNAUDITED CONDENSED STATEMENTS OF OPERATIONS
(in thousands, except share and per share amounts)

	Three Months ended September 30,		Nine Months Ended September 30,	
	2021	**2020**	**2021**	**2020**
Operating expenses:				
Research and development	$ 2,105,815	$ 3,137,553	$ 6,994,866	$ 6,845,203
Intangible asset impairment charge	8,639,000	—	8,639,000	—
General and administrative	1,930,082	2,112,375	5,510,365	4,964,440
Depreciation	19,100	24,192	67,302	78,233
Loss from operations	12,693,997	5,274,120	21,211,533	11,887,876
Other income:				
Interest income	(50,710)	(29,233)	(146,354)	(89,246)
Loss from operations before income tax benefit	(12,643,287)	(5,244,887)	(21,065,179)	(11,798,630)
Income tax benefit	(443,893)	(805,676)	(443,893)	(1,675,381)
Net loss	$ (12,199,394)	$ (4,439,211)	$ (20,621,286)	$ (10,123,249)
Deemed dividend arising from warrant exchange	—	—	—	(1,950,378)
Net loss attributable to common stockholders	$ (12,199,394)	$ (4,439,211)	$ (20,621,286)	$ (12,073,627)
Per share information:				
Net loss per share of common stock, basic and diluted	$ (0.12)	$ (0.07)	$ (0.21)	$ (0.24)
Weighted average shares outstanding, basic and diluted	101,903,979	64,011,342	98,810,420	50,216,239

DIFFUSION PHARMACEUTICALS, INC.
CONDENSED BALANCE SHEETS
(in thousands, except share and par value amounts)

	September 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 40,335,045	$ 18,515,595
Prepaid expenses, deposits and other current assets	380,097	260,825
Total current assets	40,715,142	18,776,420
Property and equipment, net	81,896	149,198
Intangible asset	—	8,639,000
Right of use asset	67,886	149,162
Other assets	15,579	15,771
Total assets	$ 40,880,503	$ 27,729,551
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 678,036	$ 545,844
Accrued expenses and other current liabilities	2,002,981	1,776,470
Current operating lease liability	67,886	113,469
Total current liabilities	2,748,903	2,435,783
Deferred income taxes	—	443,893
Noncurrent operating lease liability	—	35,693
Total liabilities	2,748,903	2,915,369
Stockholders' Equity:		
Common stock, $0.001 par value:		
1,000,000,000 shares authorized; 101,903,979 and 64,015,441 issued and outstanding at September 30, 2021 and December 31, 2020, respectively	101,904	64,016
Additional paid-in capital	164,560,366	130,659,550
Accumulated deficit	(126,530,670)	(105,909,384)
Total stockholders' equity	38,131,600	24,814,182
Total liabilities and stockholders' equity	$ 40,880,503	$ 27,729,551