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): May 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.)

1317 Carlton Avenue, Suite 200 **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 May 10, 2021, Diffusion Pharmaceuticals Inc. (the "Company") issued a press release announcing financial results for the three-month period ended March 31, 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 8.01 Results of Operations and Financial Condition

On May 10, 2021, the Company issued a press release reporting final results from its Phase 1b study of trans sodium crocetinate in hospitalized COVID-19 patients. A copy of that press release is attached hereto as Exhibit 99.2 and incorporated herein by reference.

Item 9.01 – Financial Statements and Exhibits

(d) Exhibits

Exhibit Number	Description
99.1	Press Release, issued May 10, 2021, announcing financial results for the three-month period ended March 31, 2021 and business update
99.2	Press Release, issued May 10, 2021, reporting final results from its Phase 1b study of trans sodium crocetinate in hospitalized COVID-19 patients

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: May 12, 2021

DIFFUSION PHARMACEUTICALS INC.

By: /s/ William Elder
Name: William Elder
Title: General Counsel

Diffusion Pharmaceuticals Inc.

Diffusion Pharmaceuticals Reports First Quarter Financial Results and Provides Business Update

CHARLOTTESVILLE, Va., May 10, 2021 -- **Diffusion Pharmaceuticals Inc. (NASDAQ: DFFN)** ("Diffusion" or the "Company"), an innovative 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 first quarter of 2021 and provided a business update.

During the first quarter, Diffusion continued to focus on progressing the development of its novel oxygen enhancing therapeutic, trans sodium crocetinate (TSC). The company's balance sheet also was fortified through a $34.5 million equity raise.

1Q21 Business and Operational Highlights

- In March 2021, the Company initiated, enrolled, and completed dosing of 30 healthy volunteers in a Phase 1 trial evaluating the pharmacodynamic effects of TSC on peripheral tissue oxygenation utilizing a transcutaneous oxygen monitoring (TCOM) device. The Company anticipates its ongoing collection and analysis of data from the study will be completed and announced by the end of the second quarter of 2021.

- In February 2021, Diffusion completed dosing and reported topline results from its Phase 1b trial evaluating TSC in hospitalized COVID-19 patients. The study evaluated the safety and tolerability of TSC when administered every six hours for up to 15 days, a dosing regimen previously untested in a clinical trial setting. Topline results, reported in mid-February 2021, showed that all doses evaluated were well tolerated and no dose-limiting toxicities or serious adverse events were observed. The Company anticipates its ongoing evaluation of secondary endpoint data will be completed and announced before the end of May 2021.

- In February 2021, the Company raised $34.5 million in gross proceeds in an offering of its common stock, issuing 33.7 million shares at a price to the public of $1.025 per share. Combined with its other cash and cash equivalents as of March 31, 2021, the Company expects existing cash and cash equivalents to be sufficient to fund its operations (including its planned clinical trials) through 2023.

1Q21 Financial Results

- Research and development expenses in the first quarter were $2.9 million compared to expenses of $1.5 million in the prior year period. The increase was primarily related to costs associated with the Company's TCOM and COVID trials, the manufacture of study materials related to these studies, and increased headcount.

- General and administrative expenses were $1.7 million during the first quarter of 2021 versus $1.4 million in the comparable quarter last year. The increase compared to the prior year period was primarily attributable to increased salaries, wages, stock-based compensation, and professional fees related to increased headcount and costs associated with the separation of former executives that will not recur in future years.

- As of March 31, 2021, Diffusion had cash and cash equivalents of approximately $46.6 million as compared to $18.5 million as of December 31, 2020.

"We met the key milestones we set for ourselves for the first quarter of 2021, including completing and announcing topline safety and tolerability results for the COVID-19 Trial, completing enrollment and treatment of the subjects in the first of the Oxygenation Trials, the TCOM study, and execution of a significant capital raise that we believe will enable us to obtain the data required to demonstrate the clinical value of TSC. For the remainder of 2021, we are focused on the design and execution of the remaining two Oxygenation Trials, which are the foundation of our redefined TSC development strategy announced in November of 2020," said Robert Cobuzzi, Jr. Ph.D., President and CEO of Diffusion.

Near-term Clinical Strategy

Data from the TCOM Trial is anticipated to be available later in the second quarter of 2021 and will be used to guide dose selection for the two additional Oxygenation Trials the Company plans to initiate and complete in the second half of 2021, both of which will be funded with cash-on-hand.

- **Induced Hypoxia Trial:** This trial will be a double-blind, randomized, placebo-controlled study which will 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 will be statistically powered to evaluate the difference in effect of TSC versus placebo on oxygen availability and consumption.

- **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.

Diffusion anticipates topline results from each study will be available within two months of their respective completion. The Company believes positive data from any one or more of the three Oxygenation Trials, if obtained, would provide evidence of a definitive effect of TSC on oxygenation. If such positive data are obtained, the Company expects to announce in the fourth quarter of 2021 up to two hypoxia-related indications in which TSC would be studied as part of its clinical development strategy aimed at supporting regulatory approval and commercialization. Diffusion intends to initiate clinical studies in the identified indications during the first quarter of 2022.

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. In addition to TSC, Diffusion's product candidate DFN-529, a novel, allosteric PI3K/Akt/mTOR Pathway inhibitor, is in early-stage development. 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, and anticipated timelines for the initiation, completion, and announcement of data from the Company's ongoing and planned Oxygenation Trials. 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 ongoing and planned studies evaluating TSC; 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.

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Exhibit 99.2

Diffusion Pharmaceuticals Inc.

Diffusion Pharmaceuticals Reports Final Results from Its Phase 1b Study of Trans Sodium Crocetinate in Hospitalized COVID-19 Patients

CHARLOTTESVILLE, Va., May 10, 2021 -- **Diffusion Pharmaceuticals Inc. (NASDAQ: DFFN)** ("Diffusion" or the "Company"), an innovative biopharmaceutical company developing novel therapies that enhance the body's ability to deliver oxygen to areas where it is needed most, today announced final results from the Phase 1b study evaluating trans sodium crocetinate (TSC) in hospitalized COVID-19 patients. Data from the open-label study were reviewed by an independent Safety Monitoring Committee (SMC).

Topline results based upon analyses of primary endpoint data from the trial were announced in February 2021, indicating that TSC was safe and well-tolerated when administered on a more frequent dosing regimen than previously tested in a clinical trial setting.

The Company and the SMC have concluded analyses of the trial's planned secondary and exploratory endpoints, which included time to improvement in WHO ordinal scale by day 7 and through day 29, time on oxygen supplementation, and hospital length of stay. While this study was not designed or powered to evaluate efficacy, the Company and SMC observed that patients receiving the 1.5 mg/kg dose had improved outcomes in these secondary and exploratory endpoints compared to those receiving lower doses. In addition, no patients required dialysis or developed acute kidney injury and there were no reports of pulmonary embolism or deep vein thrombosis. One death was reported during the study, a patient who received the lowest dose and which was determined by the SMC to be not drug related.

The SMC went on to recommend the Company consider additional preliminary work before initiating a registrational study, including the testing of higher TSC doses and a continuous intravenous infusion. Of note, the first of the Company's three planned Oxygenation Trials, the TCOM study, tested TSC at doses up to 2.5 mg/kg.

"We learned a lot from this safety and tolerability trial, not only is TSC safe with more frequent dosing, but across a wider range of doses than previously tested. We are encouraged by the trends in the data suggesting TSC improved relevant clinical outcomes, recognizing the conclusions we can draw are limited due to the study not being designed or powered to evaluate efficacy" said Chris Galloway, M.D., Chief Medical Officer. "We believe the observations and recommendations of the SMC further support the importance of our three, small, controlled Oxygenation Trials as efficient means to demonstrate TSC's enhancement of oxygenation with more clarified dosing and, if successful, allowing us to design later phase trials to support commercially-focused development in specific indication(s)."

Trial Design

- The trial enrolled 24 patients divided into four sequential cohorts of six patients, with each patient in a dose cohort receiving the same intravenous doses of 0.25 mg/kg, 0.5 mg/kg, 1.0 mg/kg, or 1.5 mg/kg, depending on the patient's cohort.

- All patients were administered intravenous doses of TSC every six hours for a minimum of five days and up to 15 days.

"This study of TSC in COVID-19 patients was initiated to determine if TSC is safe and well tolerated when given in multiple doses per day in a patient population suffering from an acute respiratory infection. The medical and scientific communities have since come to understand COVID-19 is a much more complex disease, and the study itself was complicated to conduct. So, we are very happy the trial achieved its primary objective, demonstrating safety and tolerability, and the results of the secondary endpoint analyses confirm our belief in the value of executing our ongoing Oxygenation Trials," said Robert Cobuzzi, Jr., Ph.D., President and CEO of Diffusion.

Near-Term Clinical Strategy

Diffusion has initiated a series of three short-term Oxygenation Trials in the United States in 2021, funded with cash-on-hand. The first of these studies, the TCOM Trial, initiated, enrolled, and completed dosing in March 2021.

- **TCOM Trial:** This trial was a randomized, double-blind, placebo controlled, pharmacokinetic and pharmacodynamic study of TSC that enrolled and dosed 30 healthy volunteers. Trial participants were randomized into one of six subgroups, each of which received a single intravenous dose of placebo or one of five different doses of TSC ranging from 0.5 mg/kg to 2.5 mg/kg. All trial participants received supplemental oxygen during equivalent monitoring periods before and after TSC or placebo was administered while being continuously monitored with TCOM sensors applied to the lower extremity. The primary endpoint evaluates the relative change in TCOM readings from baseline after TSC administration. Diffusion anticipates that the ongoing collection and analyses of the TCOM trial data will be completed and announced by the end of the second quarter of 2021.

- **Induced Hypoxia Trial:** This trial will be a double-blind, randomized, placebo-controlled study which will 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 will be statistically powered to evaluate the difference in effect of TSC versus placebo on oxygen availability and consumption.

- **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.

Diffusion anticipates initiating and completing the DLCO Trial and Induced Hypoxia Trial in the second half of 2021, with topline results from each study available within two months of their respective completion. The Company believes positive data from any one or more of the three Oxygenation Trials, if obtained, would provide evidence of a definitive effect of TSC on oxygenation. If such positive data are obtained, the Company expects to announce in the fourth quarter of 2021 the hypoxia-related indications in which TSC would be studied as part of its clinical development strategy aimed at supporting regulatory approval and commercialization. Diffusion intends to initiate clinical studies in the identified indications during the first quarter of 2022.

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