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): March 25, 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 8.01 Other Events

On March 25, 2021, Diffusion Pharmaceuticals Inc. (the "Company") issued a press release announcing the completion of enrollment and dosing in the Company's Phase 1 trial of its novel, oxygen enhancing therapeutic, trans sodium crocetinate ("TSC"), utilizing a transcutaneous oxygen monitoring device to evaluate the effects of TSC on peripheral tissue oxygenation. A copy of the press release is attached hereto as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 – Financial Statements and Exhibits

(d) Exhibits

Exhibit Number	**Description**
99.1	Press Release, issued March 25, 2021

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: March 25, 2021

DIFFUSION PHARMACEUTICALS INC.

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

Diffusion Pharmaceuticals Completes Enrollment and Dosing in TCOM Study

CHARLOTTESVILLE, Va., March 25, 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 it has completed enrollment and dosing of all participants in the Company's Phase 1 trial of its novel, oxygen enhancing therapeutic, trans sodium crocetinate ("TSC"), utilizing a transcutaneous oxygen monitoring (TCOM) device to evaluate the pharmacodynamic effects of TSC on peripheral tissue oxygenation.

The TCOM trial is the first in a series of three short-term Oxygenation Trials that Diffusion plans to conduct in the United States in 2021. Together, these Oxygenation Trials will serve as a prospective exploration of the relationship between the level of TSC exposure (dose) and response (change in oxygenation) and the Company expects positive data from any of the three Oxygenation Trials, if obtained, will guide the next phases of TSC's clinical development and commercialization plans. The Company intends to fund these three studies with cash-on-hand.

The TCOM 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 and each received a single intravenous dose of placebo or one of five different doses of TSC ranging from 0.5-2.5 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 in the second quarter of 2021.

"We expect the results of the TCOM trial to provide important information about TSC's ability to enhance oxygen delivery to tissues, while further clarifying dose and duration of effects" said Christopher Galloway, M.D., Chief Medical Officer of Diffusion. "I am ever grateful to the volunteers and thrilled that the trial was able to fully enroll so quickly. We now eagerly await the objective analysis of the trial, recognizing we have two other Oxygenation Trials yet to be conducted this year."

Near-term Clinical Strategy
In addition to the TCOM trial, the Company plans to initiate the following two, additional Oxygenation Trials in the third quarter of 2021:

- **Hypoxia Trial:** This is expected to 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.

- **DLCO Trial:** This is expected to be a double-blind, randomized, placebo-controlled study which will evaluate the effects of TSC on the diffusion of carbon monoxide through the lungs, also known as 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 Company expects positive data from any of the three Oxygenation Trials will drive the next steps in the TSC clinical development strategy, which is focused on demonstrating the therapeutic value of TSC in a applicable patient population affected by hypoxia. Assuming success in any one or more of the Oxygenation Trials, Diffusion expects to identify and announce the specific, hypoxia-related indication(s) on which it will focus further clinical development in the fourth quarter of 2021. The Company then plans to initiate a Phase 2 clinical outcome study evaluating TSC in the announced indication(s) 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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