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): June 30, 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 June 30, 2021, Diffusion Pharmaceuticals Inc. (the "Company") issued a press release announcing topline results from the Company's Phase 1 trial of its lead product candidate, 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 and is incorporated herein by reference.

Item 9.01 – Financial Statements and Exhibits

(d) Exhibits

Exhibit Number	**Description**
99.1	Press Release, issued June 30, 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: June 30, 2021

DIFFUSION PHARMACEUTICALS INC.

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

Exhibit 99.1

Diffusion Pharmaceuticals Reports Positive Trend in Oxygenation from TCOM Trial

Trial Dosed Healthy Volunteers with Trans Sodium Crocetinate

CHARLOTTESVILLE, Va., June 30, 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 topline results from the Company's Phase 1 trial of its lead product candidate, trans sodium crocetinate ("TSC").

In this trial, transcutaneous oxygen monitoring ("TCOM") was used to measure the direct pharmacodynamic effects of TSC on peripheral tissue oxygenation in healthy normal volunteers. Topline results were based upon analyses of primary endpoint data, which indicate, as compared to placebo, a positive dose-response trend in TCOM readings after TSC administration that persisted through the measurement period. Due in part to the small number of healthy subjects in each cohort, and the inherent variability of tcpO2 measurement, the magnitude of effect was not statistically significant; however, the trends in the primary endpoint data indicated an improvement in peripheral oxygenation compared to placebo, with no evidence of hyperoxygenation. Furthermore, TSC was safe and well-tolerated at all doses tested with no serious adverse events or dose-limiting toxicities.

"The positive trend observed in the TCOM trial is very encouraging," said Chris Galloway, M.D., Diffusion's Chief Medical Officer. "We believe the data further clarify TSC's exposure-response relationship and successfully build on our clinical development strategy. These data will inform study design for upcoming trials and our ongoing investigation of the timing of administration to maximize clinical efficacy. We also believe the TCOM data complement recent data obtained from our COVID-19 trial and further support our ongoing execution of our three well-controlled Oxygenation Trials, where each study is uniquely designed to differentially investigate TSC's novel mechanism of action. We expect the individual and collective data from these studies will inform our late phase programs and clinical indications to pursue for commercialization of TSC."

The TCOM Trial was the first of three Oxygenation Trials the Company plans to conduct in 2021. The designs of these studies are as follows:

Oxygenation Trial Designs

- **TCOM Trial:** This recently completed clinical 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 evaluated the relative change in TCOM readings from baseline after TSC administration compared to placebo.

- **Altitude Trial (induced hypoxia):** 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 trial will evaluate the difference in effect of TSC 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 an abnormal baseline DLCO test result. 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 evaluate the difference in effect of TSC on improvement in DLCO, as well as distance covered in a standard six-minute walk test.

Diffusion anticipates initiating and completing the DLCO and Altitude Trials in the second half of 2021, with topline results from each study available within two months of their respective completion. These results will further guide the selection of indications and doses to be pursued for future development of TSC. In the fourth quarter of 2021, the Company expects to announce the initial hypoxia-related indications in which TSC would be studied as part of its clinical development strategy aimed at supporting regulatory approval and, if approved, commercialization. Diffusion intends to initiate clinical studies in the identified indications during the first half of 2022.

“It is exciting to see the effects on oxygenation in the TCOM study. These results along with the other two Oxygenation Trials form the cornerstone of our revised TSC development strategy implemented over the last nine months”, said Robert Cobuzzi, Jr., Ph.D., President and CEO of Diffusion. “We are executing well as a team, meeting our stated commitments and we continue to evolve as an organization.”

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 near-term strategic priorities, anticipated timelines for the initiation, completion, and announcement of data from the Company's ongoing and planned oxygenation trials, 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 completion of the full analyses of the data from the TCOM Trial, including secondary endpoint data; the Company's ability to design, initiate, enroll, execute, and complete its ongoing and planned studies evaluating TSC; the optimal doses and dosing regimens of TSC in connection with the potential treatment of any particular disease or indication; 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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