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 21, 2022

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 March 21, 2022, Diffusion Pharmaceuticals Inc. (the "Company") issued a press release announcing financial results for its fourth quarter and fiscal year ended December 31, 2021. 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 March 21, 2022, announcing financial results for the fourth quarter and fiscal year ended December 31, 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.

March 21, 2022

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

Exhibit 99.1

Diffusion Pharmaceuticals Reports 2021 Financial Results and Provides Business Update

- Altitude Trial Dosing Expected To Be Completed in 2Q2022; mid-2022 for ILD-DLCO Trial
- Phase 2 Hypoxic Solid Tumor Study Protocol Submission Planned to Support 2H22 Study Start
- $37.3M in Cash & Cash Equivalents as of Year-End; Expected to Fund Operations Through 2023

CHARLOTTESVILLE, Va., March 21, 2022 -- **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 2021 and provided a business update.

Corporate Strategy and Events

Business and financial highlights during 2021 and 2022 year-to-date include:

Declared Lead Development Program: The Company announced its intent to develop its novel, oxygen enhancing therapeutic, Trans Sodium Crocetinate ("TSC"), as an adjunct to standard of care therapy for hypoxic solid tumors in November 2021 ("Hypoxic Solid Tumor Program").

Strengthened Balance Sheet: In February 2021, the Company raised approximately $34.5 million in gross proceeds through an up-sized, follow-on public offering of its common stock with proceeds to be used to fund research and development efforts for the TSC oxygenation trials ("Oxygenation Trials") and corporate expenses. As of December 31, 2021, the Company reported a total of $37.3 million in cash and cash equivalents. As of March 18, 2022, the Company expects cash resources to fund operations through 2023.

Board Updates: Jane Hollingsworth appointed as new Board Chair in June 2021. Diana Lanchoney, M.D., and Eric Francois also elected to the Company's board of directors in June 2021.

"We are pleased with the progress we achieved in 2021. We executed our corporate, clinical, and regulatory strategies, accelerating development of our lead product candidate, TSC. The capital we raised in the first half of 2021 allowed us to design and execute critical clinical trials to assess TSC's therapeutic potential in treating hypoxia-related conditions using three unique short-term experimental clinical models of oxygenation," said Robert Cobuzzi, Jr., Ph.D., President and Chief Executive Officer of Diffusion.

Dr. Cobuzzi continued, "We believe the hard work demonstrated by our team in 2021 has laid a solid foundation for Diffusion's success in 2022. The initiation of our Altitude and ILD-DLCO trials in the last quarter of 2021 represented a significant inflection point on the route to achieving the goal of demonstrating TSC's potential to enhance the body's ability to deliver oxygen to areas where it is needed most and potentially provide a novel treatment option for a variety of conditions complicated by hypoxia. Moreover, in late 2021 we announced our intent to design and execute a clinical program to support the use of TSC as an adjunct treatment of hypoxic solid tumors as the next step in our efforts to realize TSC's potential. We believe targeting hypoxic solid tumors is appropriate for TSC given the significant unmet medical need, the compelling preclinical and clinical data accumulated to date, and the current, intravenous formulation of TSC. The team has been working closely with our advisors to design a Phase 2 study that we believe, if successful, will help patients and enhance shareholder value."

Diffusio$_2$n Pharmaceuticals Inc.

Clinical Trial Execution & Strategy

TCOM Trial: In March 2021, the Company completed enrollment and dosing of all participants in its Phase 1 trial of TSC utilizing a transcutaneous oxygen monitoring ("TCOM") device to evaluate the pharmacodynamic effects of TSC on peripheral tissue oxygenation in healthy, normal volunteers. As reported in June 2021, the topline results of the study showed TSC was safe and tolerable at all doses tested with no serious adverse events or dose-limiting toxicities. Furthermore, the Company announced that a positive trend in peripheral tissue oxygenation was observed among participants treated with TSC when compared to placebo-treated participants. This trend persisted through the one-hour, post-dosing measurement period. The Company believes the data from the TCOM Trial validate the thesis that TSC enhances oxygenation without causing hyperoxygenation. The data from the TCOM Trial have guided the design of the two additional Oxygenation Trials, as well as the design of the Hypoxic Solid Tumor Program.

Altitude Trial: In November 2021, Diffusion announced the dosing of the first participants in the Altitude Trial which was designed to evaluate the effects of TSC in normal healthy volunteers subjected to incremental levels of physical exertion while exposed to hypoxic and hypobaric conditions, or "simulated altitude." Due to enrollment delays experienced during early 2022 related to the omicron variant wave of the COVID-19 pandemic, the Company now anticipates completing dosing in the second quarter of 2022 and topline results are expected to be reported within one to two months of study completion.

ILD-DLCO Trial: Subsequent to receiving Investigational New Drug application clearance from the U.S. Food and Drug Administration ("FDA") in the third quarter of 2021, the Company announced the dosing of the first patient in the Phase 2 ILD-DLCO Trial in December 2021. The ILD-DLCO Trial was designed to evaluate the effects of TSC on carbon monoxide uptake through the lungs ("DLCO") and into the bloodstream of interstitial lung disease ("ILD") patients. DLCO measurement is used in the study 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 intends to evaluate the effect of TSC on lung function as measured by DLCO, as well as distance covered in a standard six-minute walk test. Due to enrollment delays experienced during early 2022 related to the omicron variant wave of the COVID-19 pandemic, the effect of the omicron variant on patients with pulmonary diseases such as ILD, and staffing issues at the facilities where the ILD-DLCO Trial is being conducted, the Company now anticipates dosing to be completed by the middle of 2022, with topline results reported within two months of study completion.

Hypoxic Solid Tumor Treatment: In November 2021, based on the available preclinical and clinical data and the significant unmet medical need, including the TCOM and COVID-19 Trial results, the Company announced its intent to focus its near-term efforts on evaluating TSC as an adjunct to standard of care in the treatment of hypoxic solid tumors as a first indication. Solid tumors, which comprise approximately 90% of all adult cancers, are often affected by hypoxia, leading to treatment resistance, metastasis, and worse prognoses. Following, among other things, analyses and discussions with the Company's oncology-focused SAB members and other external advisors over the last several months, Diffusion believes they have the necessary data to support the design and initiation of an appropriate Phase 2 trial as the first study in the Hypoxic Solid Tumor Program. The Company intends to file the study protocol with the FDA and expects to commence the trial in the second half of 2022, subject to FDA feedback and the availability of clinical drug supply.

2021 Financial Results

Diffusion had cash and cash equivalents of $37.3 million as of December 31, 2021, compared with $18.5 million as of December 31, 2020. Net cash used in operating activities during 2021 was $14.5 million, compared with $13.6 million used during 2020.

Research and development expenses were $8.5 million for 2021, compared with $9.4 million for 2020. The decrease was primarily attributable to lower project spending due to the completion and/or wind-down of the Company's clinical studies evaluating TSC in COVID-19, glioblastoma multiforme brain cancer, and stroke.

General and administrative expenses were $7.4 million for 2021, compared with $6.4 million for 2020. The increase was primarily driven by increased headcount resulting in higher compensation expense and other costs associated with the hiring of new employees, as well as an increase in expense related to consulting services.

In 2021, the Company also recognized a non-recurring $8.6 million non-cash impairment charge related to the write down of its DFN-529 IPR&D asset.

About Diffusion Pharmaceuticals Inc.

Diffusion Pharmaceuticals Inc. is a 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, including hypoxic solid tumors. 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.

Contacts
Investors:
Tiberend Strategic Advisors, Inc.
Lisa Sher/Daniel Kontoh-Boateng
lsher@tiberend.com / dboateng@tiberend.com

Media:
Kate Barrette
RooneyPartners
Kbarrette@rooneypartners.com