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): February 11, 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 Information.

Diffusion Pharmaceuticals Inc. (the "Company") is updating certain information concerning its business, clinical studies, and development plans, certain other matters, and certain risks related thereto. A copy of that information is attached 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

99.1 Certain Information Concerning the Business, Clinical Studies, and Development Plans of Diffusion Pharmaceuticals Inc.

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: February 12, 2021

DIFFUSION PHARMACEUTICALS INC.

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

Exhibit 99.1

NOTE REGARDING FORWARD-LOOKING STATEMENTS

The information contained includes express and implied forward-looking statements. By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics and industry change, and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained herein, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition, liquidity and prospects may differ materially from the forward-looking statements contained herein. In addition, even if our results of operations, financial condition, liquidity, and prospects are consistent with the forward-looking statements contained herein, they may not be predictive of actual results or reflect unanticipated developments in future periods.

Forward-looking statements appear in a number of places throughout the information contained herein. We 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. Forward-looking statements also include statements regarding our intentions, beliefs, projections, outlook, analyses, or expectations, including our intentions, beliefs, projections, outlook, analyses, or expectations concerning, among other things:

- our ability to obtain additional financing;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the success and timing of our clinical and preclinical studies, including our ability to enroll subjects in our ongoing clinical studies at anticipated rates;
- our ability to obtain and maintain regulatory approval of our product candidates and, if approved, our products, including the labeling under any approval we may obtain;
- our plans and ability to develop and commercialize our product candidates and the outcomes of our research and development activities;
- the accuracy of our estimates of the size and characteristics of the potential markets for our product candidates, the rate and degree of market acceptance of any of our product candidates that may be approved in the future, and our ability to serve those markets;
- the success of products that are or may become available which also target the potential markets for our product candidates;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the performance of third parties, including contract research organizations, manufacturers, and outside consultants to whom we outsource certain operational and staff functions;
- obtaining and maintaining intellectual property protection for our product candidates and our proprietary technology;
- our ability to operate our business without infringing the intellectual property rights of others;
- regulatory developments in the U.S., European Union, and other foreign jurisdictions;
- recently enacted and future legislation regarding the healthcare system, including trends towards managed care and healthcare cost containment, the impact of any significant spending reductions or cost controls affecting publicly funded or subsidized healthcare programs, or any replacement, repeal, modification, or invalidation of some or all of the provisions of the U.S. Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act;
- any significant breakdown, infiltration or interruption of our information technology systems and infrastructure;
- our ability to satisfy the continued listing requirements of the NASDAQ Capital Market or any other exchange on which our securities may trade in the future;
- our ability to continue as a going concern;
- uncertainties related to general economic, political, business, industry, and market conditions, including the recent U.S. presidential election;
- the ongoing COVID-19 pandemic; and

- other risks and uncertainties, including those discussed elsewhere in our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and our other public filings.

As a result of these and other factors, known and unknown, actual results could differ materially from our intentions, beliefs, projections, outlook, analyses, or expectations expressed in any forward-looking statements contained herein. Accordingly, we cannot assure you that the forward-looking statements contained herein will prove to be accurate or that any such inaccuracy will not be material. You should also understand that it is not possible to predict or identify all such factors, and you should not consider any such list to be a complete set of all potential risk or uncertainties. In light of the foregoing and the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Any forward-looking statement contained herein speaks only as of the date of such statement, and, except as required by applicable law or by the rules and regulations of the SEC, we undertake no obligation to update such statements to reflect events or circumstances after the date of this Form 8-K or to reflect the occurrence of unanticipated events. Comparisons of current and any prior period results are not intended to express any ongoing or future trends or indications of future performance, unless explicitly expressed as such, and should only be viewed as historical data.

BUSINESS SUMMARY

This summary highlights selected information about the Company and does not contain all of the information that you need to consider in making a decision to invest in our securities. You should carefully read the information included herein and in our other public filings with the Securities and Exchange Commission ("SEC"), including the risks of investing in our securities discussed under the heading "Risk Factors" herein, in our Annual Report on Form 10-K for the year ended December 31, 2019, and in our subsequent Quarterly Reports on Form 10-Q.

Overview

We are an innovative, clinical stage biopharmaceutical company developing novel therapies that enhance the body's ability to deliver oxygen to the areas where it is needed most. Our lead product candidate, trans sodium crocetinate ("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.

TSC was designed to enhance the level of organization among water molecules by increasing the amount of hydrogen bonding. This creates a less dense matrix of water molecules, which facilitates the diffusion of oxygen molecules from areas of high to low oxygen concentrations, such as from oxygenated red blood cells into tissues where the oxygen is used to power the cells. In animal models, this diffusion-enhancing mechanism of action has been observed to affect hypoxic tissue preferentially while avoiding excessive oxygen-related tissue toxicity, also known as hyperoxia.

TSC previously has been demonstrated safe and tolerable in certain dosages in over 180 subjects included in our clinical programs across a variety of medical conditions often complicated by hypoxia, including our clinical studies conducted in patients afflicted with glioblastoma multiforme brain cancer ("GBM"), peripheral artery disease with intermittent claudication, and stroke, as well as our Phase 1b clinical trial evaluating TSC in hospitalized COVID-19 patients, designated as Protocol 100-303, initiated in September 2020 (the "100-303 COVID Trial"). In each of these conditions and many others, hypoxia is a significant contributor to morbidity and mortality, and a considerable treatment obstacle for medical providers.

In addition to TSC, the Company's product candidate DFN-529, a novel, allosteric PI3K/Akt/mTOR pathway inhibitor, is in early-stage development. The Company previously completed two Phase 1 clinical trials evaluating DFN-529 in age-related macular degeneration, and DFN-529 was also previously in preclinical development in oncology, specifically GBM.

100-303 COVID Trial

On September 10, 2020, we announced the dosing of the first two patients in our 100-303 COVID Trial evaluating TSC in hospitalized COVID-19 patients at the NIID in Bucharest, Romania. The primary endpoint of the 100-303 COVID Trial was to evaluate the safety and tolerability of TSC administered every six (6) hours for up to 15 days, a more frequent dosing regimen than has been used in our previous clinical studies. Secondary endpoints included pharmacokinetic measurement of TSC levels after dosing, relative improvements in blood oxygen levels, and certain other clinical parameters related to COVID-19.

On February 9, 2021, we completed dosing of the twenty-fourth and final patient in the 100-303 COVID Trial. No dose-limiting toxicities were observed among any patients who received doses of 0.25 mg/kg, 0.5 mg/kg, or 1.0 mg/kg every 6 hours. Data for the final 1.5 mg/kg dose group of patients are currently being prepared for review by the trial's external safety monitoring committee. Diffusion anticipates the committee will hold its initial meeting to evaluate the data from the final dose group on Friday, February 12, 2021. We will announce the topline, safety and tolerability data for the final dose group promptly following completion of the committee's evaluation. Analyses of the secondary endpoint data are anticipated to be completed and announced before the end of the first quarter of 2021.

Anticipated Next Steps in TSC Development Program

Looking beyond the 100-303 COVID Trial, the next step we have planned in the development of TSC is the design and execution of clinical studies using short-term, experimental models to evaluate the clinical effects of TSC on oxygenation. To date, TSC has been administered to more than 180 subjects in clinical studies. Data from these clinical studies have contributed significantly to our understanding of the safety, tolerability, and pharmacokinetics of TSC. In addition, potential indications of efficacy have been observed in two studies, including a small study in patients with peripheral artery disease with claudication and also in a post hoc analysis of patients with unresected GBM tumors. However, neither of these studies was statistically powered to formally evaluate efficacy, so we believe that further, robust clinical development of TSC requires a prospective exploration of the relationship between dose and oxygenation. To this end, we plan to conduct these short-term clinical studies over the coming months.

The first study (the “TCOM Study”), which we expect to initiate in March 2021, will measure the effects of TSC on peripheral tissue oxygenation using a device called a transcutaneous oximeter (“TCOM”). This device directly measures the release of oxygen from the blood vessels through the skin and is commonly used to predict the likelihood of wound healing, the potential for success with hyperbaric therapy, and to map the appropriate location for limb amputation. The TCOM Study is designed as a double-blind, randomized, placebo-controlled study in healthy volunteers breathing 100% oxygen. The TCOM Study will test escalating doses of TSC in an attempt to establish a dose-response relationship on enhanced oxygen delivery and will be statistically powered to evaluate the effect on tissue oxygenation levels versus placebo. We anticipate this study to be completed in the second quarter of 2021, with topline results available within one to two months following study completion.

The second planned study (the “DLCO Study”) will measure the diffusion of carbon monoxide through the lungs (“DLCO”) 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. As with the TCOM procedure, DLCO testing is commonly performed as part of standard pulmonary function testing and aids in the diagnosis or dyspnea (a.k.a. shortness of breath), as well as tracking improvement or progression over time on prescribed treatments. We plan to use the DLCO Study to evaluate the diffusion enhancing effects of TSC in patients with previously diagnosed interstitial lung disease who have a baseline DLCO test result that is abnormal. The DLCO Study will be designed as a double-blind, randomized, placebo-controlled study of escalating doses of TSC in an attempt to establish a dose-response relationship and will be statistically powered to evaluate the effect versus placebo. We anticipate this study to be initiated in the second quarter and be completed in the third quarter of 2021, with topline results available within one to two months of study completion.

Assuming we are successful in these next steps, we believe that the data from these studies will provide definitive proof of effect on enhanced oxygenation from uptake in the lungs to delivery at the tissue level, and also provide important dose-response data that will guide our efforts to optimize our clinical development strategy focusing on the hypoxia continuum (agnostic of the causation or therapeutic space), including the specification of relevant patient populations and indications and our corresponding regulatory strategy.

CERTAIN INFORMATION REGARDING OUR COMMON STOCK

The number of shares of our common stock outstanding on February 10, 2021 was 68,018,555, excluding:

- 2,240,204 shares of common stock issuable upon the exercise of outstanding stock options and vesting of restricted stock units under the Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan, as amended (the "2015 Equity Plan"), and with respect to such options, at a weighted-average exercise price of $8.28 per share;

- 5,100,066 shares of common stock issuable upon the exercise of outstanding warrants (including shares of common stock issuable upon exercise of the Warrants), at a weighted-average exercise price of $10.34 per share; and

- 2,105,744 shares of common stock reserved for future issuance under the 2015 Equity Plan.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below and under the section captioned "Risk Factors" contained in our most recent Annual Report on Form 10-K, as revised and supplemented by our subsequent Quarterly Reports on Form 10-Q, together with the other information contained or herein and in our other public filings with the SEC before making a decision to invest in our securities. We cannot assure you that any of the events discussed in the risk factors below will not occur. These risks could have a material and adverse impact on our business, results of operations, financial condition and cash flows, and our future prospects would likely be materially and adversely affected. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment.

Our stock price is volatile, and your investment may suffer a decline in value.

The closing market price for our common stock has varied between a high of $1.60 on July 21, 2020, and a low of $0.25 on March 17, 2020, in the twelve-month period ended February 10, 2021. As a result of fluctuations in the price of our common stock, you may be unable to sell your shares at or above the price you paid for them. The market price of our common stock is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market, industry and other factors, including the risk factors described under the section captioned "Risk Factors" contained in our Annual Report on Form 10-K for the year ended December 31, 2019 and our subsequent Quarterly Reports on Form 10-Q. The market price of our common stock may also be dependent upon the valuations and recommendations of the analysts who cover our business. If the results of our business do not meet these analysts' forecasts, the expectations of investors or the financial guidance we provide to investors in any period, the market price of our common stock could decline.

In addition, the stock markets in general, and the markets for biotechnology stocks in particular, have experienced significant volatility that has often been unrelated to the financial condition or results of operations of particular companies. These broad market fluctuations may adversely affect the trading price of our common stock and, consequently, adversely affect the price at which you could sell any shares of our common stock that you purchase. In the past, following periods of volatility in the market or significant price declines, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Future sales of our common stock in the public market or other financings could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market, the perception that these sales might occur, or other financings could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. A substantial portion of the outstanding shares of our common stock are freely tradable without restriction or further registration under the Securities Act unless these shares are owned or purchased by "affiliates" as that term is defined in Rule 144 ("Rule 144") promulgated under the Securities Act of 1933, as amended. In addition, shares of common stock issuable upon exercise of outstanding warrants and options, as well as shares reserved for future issuance under our incentive stock plan, will be eligible for sale in the public market to the extent permitted by applicable vesting requirements, if any, and, in some cases, subject to compliance with the requirements of Rule 144. As a result, these shares will be eligible to be freely sold in the public market upon issuance, subject to restrictions under the securities laws.

Events outside of our control, including public health crises such as the COVID-19 pandemic, could negatively affect our business and our operating results.

The COVID-19 pandemic has resulted in significant financial market volatility, and its impact on the global economy and our operations remains uncertain. While we have business continuity plans in place to help mitigate the impact of COVID-19, a continuation or worsening of the pandemic could have a material adverse impact on our business, results of operations and financial condition and on the market price of our common stock.

On March 12, 2020, the World Health Organization declared COVID-19 to be a pandemic. In an effort to contain and mitigate the spread of COVID-19, many countries worldwide have imposed quarantines, business closures and unprecedented restrictions on travel. The outbreak and government measures taken in response, have had a significant impact, both direct and indirect, on economic activity, as worker shortages have occurred, supply chains have been disrupted, facilities and production have been suspended and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services has fallen.

As the pandemic continues, and if conditions worsen, we may experience adverse effects on our operational activities and our financial condition. It is unclear which adverse effects may be material, and it remains uncertain the degree to which these adverse effects would impact our future operational activities and financial condition. With the recent relaxation of restrictions on business operations and in-person gatherings there has been a resurgence in COVID-19 infections in numerous jurisdictions, resulting in the reinstatement of stricter restrictions and shutdowns. It is expected that there will be an ebb and flow to the pandemic with different jurisdictions having higher levels of infections than others over the course of the pandemic. In addition to existing travel restrictions, jurisdictions may continue or reinstate border closures, impose, or reimpose prolonged quarantines and further restrict travel and business activity.

As a result of the ongoing COVID-19 pandemic, we have experienced and may continue to experience disruptions that could severely impact our business and clinical trials. Any negative impact that the COVID-19 pandemic has had or will continue to have on recruiting or retaining patients in our clinical trials, the ability of our suppliers to provide materials for our product candidates, or the regulatory review process could cause additional delays with respect to product development activities, which could materially and adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, affect our ability to raise additional capital, and have a material adverse effect on our financial results. In addition, our clinical trial patients who contract COVID-19 may have adverse health outcomes that could impact the results of our clinical trials.

The COVID-19 pandemic has resulted in significant financial market volatility and uncertainty and continues to rapidly evolve. The extent to which the outbreak impacts our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the outbreak, new information that may emerge concerning the severity of COVID-19 and the actions to contain COVID-19 or treat its impact, among others. A continuation or worsening of the levels of market disruption and volatility seen in the recent past could have an adverse effect on our ability to access capital, on our business, results of operations and financial condition, and on the market price of our common stock.

Our product candidates, if approved, will face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration.

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition, and a strong emphasis on developing proprietary therapeutics. Numerous companies are engaged in the development, patenting, manufacturing, and marketing of health care products competitive with those that we are developing. For example, in January 2021, the Company became aware of a third party affiliated with a former outside consultant of the Company which claims to be in early-stage development of a product candidate that purportedly may operate through a similar mechanism of action to TSC. While it is unclear if this particular product candidate would, if developed and approved, actually be competitive with TSC or any of our other product candidates, we face competition from a number of sources, such as pharmaceutical companies, generic drug companies, biotechnology companies and academic and research institutions, many of which have greater financial resources, marketing capabilities, sales forces, manufacturing capabilities, research and development capabilities, clinical trial expertise, intellectual property portfolios, experience in obtaining patents and regulatory approvals for product candidates and other resources than us.

Many pharmaceutical companies currently offer products, and continue to develop additional alternative product candidates and technologies, for indications similar to those targeted by our product candidates. We anticipate that, if we obtain regulatory approval of any of our product candidates, we will face significant competition from other approved therapies including therapies manufactured, sold, and distributed by companies with a broad range of other product offerings, large direct sales forces and long-term customer relationships with our expected target physicians, which could inhibit our market penetration efforts. If approved, our product candidates may also compete with unregulated, unapproved, and off-label treatments. Certain of our product candidates, if approved, will present novel therapeutic approaches for the approved indications and will have to compete with existing therapies, some of which are widely known and accepted by physicians and patients. To compete successfully in this market, we will have to demonstrate that the relative cost, safety, and efficacy of our products, when and if approved, provide an attractive alternative to existing and other new therapies. Such competition could lead to reduced market share for our product candidates and contribute to downward pressure on the pricing of our product candidates, which could harm our business, financial condition, operating results, and prospects.

The Bylaws of the Company include a forum selection clause, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees, or agents.

Our Bylaws, as amended (the "Bylaws"), require that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim for breach of a fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our Certificate of Incorporation or our Bylaws or (iv) any action asserting a claim governed by the internal affairs doctrine, in each case subject to said Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein.

This exclusive forum provision will not apply to claims under the Exchange Act, but will apply to other state and federal law claims including actions arising under the Securities Act (although our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder). Section 22 of the Securities Act, however, creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Accordingly, there is uncertainty as to whether a court would enforce such a forum selection provision as written in connection with claims arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the foregoing provisions. This forum selection provision in our Bylaws may limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees, or agents, which may discourage lawsuits against us and such persons. It is also possible that, notwithstanding the forum selection clause included in our Bylaws, a court could rule that such a provision is inapplicable or unenforceable.