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 11, 2020

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 11, 2020, Diffusion Pharmaceuticals Inc. (the "Company") issued a press release announcing that the Company filed a Clinical Trial Application for the European Phase 1a/1b study of trans sodium crocetinate (TSC) in COVID-19 patients. A copy of the press release is attached hereto as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

Item 9.01 – Financial Statements and Exhibits

(d) Exhibits

99.1 Press release issued June 11, 2020

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 12, 2020

DIFFUSION PHARMACEUTICALS INC.

By: /s/ David G. Kalergis
Name: David G. Kalergis
Title: Chief Executive Officer

Diffusion Pharmaceuticals Files Clinical Trial Application for European Phase 1a/1b Study of TSC in COVID-19 Patients

Dosing expected to begin in Q2 2020 with first data in Q3 2020
Trial expected to enroll 224 patients over 12 months, with 24 patients immediately
U.S. IND filing planned for later this month

CHARLOTTESVILLE, Va. (June 11, 2020) – Diffusion Pharmaceuticals Inc. (NASDAQ: DFFN) ("Diffusion" or "Company") announces the submission of a Clinical Trial Application (CTA) to the Romanian National Agency for Medicines and Medical Devices (NAMMD) to initiate a Phase 1a/1b clinical trial of the Company's novel oxygenation-enhancing product candidate trans sodium crocetinate (TSC) for the treatment of hospitalized COVID-19 patients displaying severe respiratory symptoms and low oxygen levels. Low oxygen levels occur as a consequence of damage to the lungs from COVID-19 and often result in mechanical ventilation and, if that is ineffective, multiple organ failure – the leading cause of death in COVID-19 patients.

Assuming NAMMD authorization of the CTA and approval by the National ethics committee under NAMMD's accelerated seven-working-day approval process, Diffusion plans to begin the 24 patient Phase 1a portion of the clinical trial by the end of Q2 2020. The entire Phase 1a/1b trial will enroll approximately 224 patients and is expected to last approximately 12 months. First data readout on the initial 24 patients is expected in Q3 2020, followed by an interim readout on 50 patients in Q4 2020 and final data in Q2 2021.

This first European study will be facilitated by ARENSIA Exploratory Medicine GmbH and conducted at the National Institute of Infectious Diseases (NIID), Bucharest, Romania, with the Institute's Managing Director, noted infectious diseases researcher Prof. Adrian Streinu-Cercel, M.D. PhD., serving as Principal Investigator. The 1a phase will be an open-label, pharmacokinetic/ pharmacodynamic, dose-finding, safety lead-in study testing TSC in 24 hospitalized, non-ventilated COVID-19 patients with documented oxygen deficiency.

Upon completion and readout of the 1a phase of the study, the Company intends to commence at the NIID a Phase 1b adaptive-design, 200 patient, randomized, double-blinded, controlled (2:1 TSC: placebo) study with enrollment and patient observation targeted for completion in Q1 2021 and data read-out in Q2 2021. In addition to safety and oxygenation markers, the Phase 1b portion will include functional endpoints including time-to-recovery through Day 28. Trial design and optimum endpoint selection for final analyses are subject to modification based on the interim data look in Q4 2020.

The Company intends to combine these results with data from a planned similar U.S. trial to support the drug's possible approval in both Europe and the U.S. Based on detailed U.S. Food and Drug Administration (FDA) guidance from a Pre-IND Meeting Request response received last month, the Company expects to file an Investigational New Drug (IND) application later this month, with a response from the FDA expected on an accelerated basis.

"Based on both preclinical and clinical data, TSC has the potential to address the fatal oxygen deficiency that can accompany COVID-19," said Dr. Streinu-Cercel. "Given the NAMMD's regulatory acceleration program and more than 500 COVID-19 hospitalized patients here at the Institute, we expect timely authorization, enrollment and data readout for the Phase 1a portion, followed by a transition into the larger Phase 1b portion of the study."

“Rapid initiation and completion of the Phase 1a portion of this trial should provide proof-of concept data in the third quarter of this year,” said David Kalergis, chief executive officer of Diffusion. “If favorable, we expect to immediately begin the larger, randomized Phase 1b portion of the trial in Romania, with continued support from the NIID and ARENSIA Exploratory Medicine GmbH. Meanwhile, we are working with the University of Virginia Health System, iTHRIV, the University of California Health System and others for a timely start to the U.S. component of the TSC clinical development plan in COVID-19, including filing of the related IND with the FDA later this month.”

About TSC and COVID-19

Patients with COVID-19 respiratory tract infections often present with significantly impaired oxygen levels. Diffusion and its affiliated researchers believe the oxygen-enhancing mechanism of action of TSC could benefit such patients. Preclinical data indicate TSC increases oxygen availability and provides a functional benefit in animal models of acute lung injury and hemorrhagic shock. Clinical data from more than 150 patients receiving TSC for other indications demonstrate that the drug has an acceptable safety profile in both healthy and critically ill patients.

About Diffusion Pharmaceuticals Inc.

Diffusion Pharmaceuticals Inc. is an innovative biotechnology company developing new treatments that improve the body’s ability to deliver oxygen to the areas where it is needed most, offering new hope for the treatment of life-threatening medical conditions. Diffusion’s lead drug trans sodium crocetinate (TSC) was originally developed in conjunction with the U.S. Office of Naval Research, which was seeking a way to treat multiple organ failure and its resulting mortality caused by low oxygen levels from blood loss on the battlefield. Evolutions in research have led to Diffusion’s focus today on addressing some of medicine’s most intractable and difficult-to-treat diseases, including multiple organ failure from respiratory distress, stroke and glioblastoma multiforme (GBM) brain cancer. In each of these diseases, lack of available oxygen presents a significant obstacle for medical providers and is the target for TSC’s novel mechanism. The Company is currently partnering with both U.S. and European-based institutions in an expedited research program to develop TSC as a treatment for the low oxygen levels and associated multiple organ failure in COVID-19 patients.

In 2019, the Company reported favorable safety data in a 19-patient dose-escalation run-in to its Phase 3 INTACT program using TSC to target inoperable GBM. That trial is currently paused while the Company prioritizes its resources to address COVID-19. Diffusion’s in-ambulance PHAST-TSC trial for acute stroke began enrolling patients last year. Given the heightened responsibilities of the Company’s emergency medical services providers, enrollment in this trial, while not officially paused, is expected to be minimal until the COVID-19 pandemic abates.

Preclinical data supports the potential for TSC as a treatment for other conditions where low oxygen availability plays an important role, such as myocardial infarction, peripheral artery disease, and neurodegenerative conditions such as Alzheimer’s and Parkinson’s disease. In addition to the development of TSC, RES-529, the Company’s PI3K/AKT/mTOR pathway inhibitor that dissociates the mTORC1 and mTORC2 complexes, is in preclinical testing for GBM.

Diffusion is headquartered in Charlottesville, Virginia – a hub of advancement in the life science and biopharmaceutical industries – and is led by CEO David Kalergis, a 30-year industry veteran and company co-founder.

Forward-Looking Statements

To the extent any statements made in this news release deal with information that is not historical, these are forward-looking statements under the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements about the company's plans, objectives, expectations and intentions with respect to future operations and products, the potential of the company's technology and product candidates, and other statements that are not historical in nature, particularly those that utilize terminology such as "would," "will," "plans," "possibility," "potential," "future," "expects," "anticipates," "believes," "intends," "continue," "expects," other words of similar meaning, derivations of such words and the use of future dates. Forward-looking statements by their nature address matters that are, to different degrees, uncertain. Uncertainties and risks may cause the Diffusion's actual results to be materially different than those expressed in or implied by such forward-looking statements. Particular uncertainties and risks include: the uncertainty as to whether the FDA will approve the IND submission for commencement of a trial in the U.S.; or that the FDA will not require significant changes that might take significant time to implement, if at all, or that any such required changes will be financially feasible; there can be no assurance as to when the program in the U.S. might be able to commence, if at all; the uncertainty that as of yet the FDA has not approved a trial evaluating TSC for the treatment of ARDS, or if approved, such a trial possibly entailing significant additional time, effort and expense, particularly in light of the difficulty of doing business during the COVID-19 pandemic; the uncertainty as to whether the protocol for the Romanian trial will be ultimately acceptable to the Romanian healthcare regulatory authorities and local ethics committees or that such regulators will not require significant changes that might take significant time to implement, if at all, or that any such required changes will be financially feasible; moreover, if this or a revised protocol is acceptable to the Romanian regulators, there can be no assurance as to when they might provide such guidance or when the program might be able to commence, if at all; the uncertainty that as of yet the Romanian regulators have not approved a trial evaluating TSC for the treatment of ARDS, or if approved, such a trial possibly entailing significant additional time, effort and expense, particularly in light of the difficulty of doing business during the COVID-19 pandemic; whether Diffusion can enroll and complete the trials and provide data on the timelines indicated; whether Diffusion can efficiently transition from the Phase 1a to Phase 1b portion of the Romanian trials; whether the data from the Romanian trials can be combined with data generated any U.S. trials; whether Diffusion has sufficient funding to complete the trials described; Diffusion's ability to maintain its Nasdaq listing, market conditions, the difficulty of developing pharmaceutical products, obtaining regulatory and other approvals and achieving market acceptance; general business and economic conditions; the company's need for and ability to obtain additional financing or partnering arrangements; and the various risk factors (many of which are beyond Diffusion's control) as described under the heading "Risk Factors" in Diffusion's filings with the United States Securities and Exchange Commission. All forward-looking statements in this news release speak only as of the date of this news release and are based on management's current beliefs and expectations. Diffusion undertakes no obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

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