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): April 27, 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 April 27, 2020, Diffusion Pharmaceuticals Inc. (the "Company") issued a press release announcing the pre-IND submission to the U.S. Food and Drug Administration (FDA) of a planned clinical program using trans sodium crocetinate (TSC) in COVID-19 patients displaying severe respiratory symptoms and low oxygen levels. 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 April 27, 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: April 29, 2020

DIFFUSION PHARMACEUTICALS INC.

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

Exhibit 99.1

Diffusion Pharmaceuticals Inc.

Diffusion Pharmaceuticals Announces Pre-IND Submission to the FDA of Design for TSC Trials to Treat Acute Respiratory Distress Syndrome in COVID-19

- *Program to focus on enhanced blood oxygenation and reduction in patient progression to Intensive Care Units*
- *Patient enrollment planned for both the U.S. and Eastern Europe*

CHARLOTTESVILLE, Va. (April 27, 2020) – Diffusion Pharmaceuticals Inc. (NASDAQ: DFFN) ("Diffusion" or "the Company"), a cutting-edge biotechnology company developing new treatments for life-threatening medical conditions by improving the body's ability to deliver oxygen to the areas where it is needed most, today announced the pre-IND submission to the U.S. Food and Drug Administration (FDA) of a planned clinical program using trans sodium crocetinate (TSC) in COVID-19 patients displaying severe respiratory symptoms and low oxygen levels. Under federal regulations, the FDA has up to 60 days to hold an advisory meeting with the Company, but for COVID-19-related submissions, the FDA has announced its intention to significantly shorten this period under its Coronavirus Treatment Acceleration Program. Clinical trial start-up preparations are continuing as the Company awaits the FDA's response.

To aid in timely trial enrollment, Diffusion is conducting expedited discussions with institutions located in areas of severe COVID-19 incidence, both in the U.S. and in Eastern Europe, to determine their possible participation.

Acute Respiratory Distress Syndrome (ARDS) develops in nearly all patients hospitalized with COVID-19, triggered by lack of sufficient oxygen to vital organs as a consequence of damage to the lungs. In severe cases, patients need to receive life support through mechanical ventilation. In general, ARDS carries a high mortality rate (up to 40% in those on a breathing machine, and likely higher in COVID-19-related ARDS). Diffusion believes that through successful implementation of its TSC/COVID-19 clinical program, TSC's oxygen-enhancing mechanism of action could provide an important new treatment option for this life-threatening unmet medical need. Further, the Company believes that TSC's novel mechanism of action would be compatible with many of the COVID-19 treatment modalities currently used or under development.

Although the number, design and projected enrollment of the clinical trials are subject to change, Diffusion's pre-IND submission for TSC envisions three studies to be conducted in rapid succession. The first is an open-label study that will examine the basic safety of the TSC dosing paradigm in up to 12 COVID-19 patients who have been admitted to Intensive Care Units (ICUs.) In addition to the primary endpoint of safety, blood gas and pulse oximetry data also will be collected to observe TSC's possible effect on increasing oxygenation in these oxygen-starved patients.

The second trial is planned as a larger, double-blinded, randomized, placebo-controlled study to confirm safety in the ICU patient population and determine the statistical significance of any effect on the patient's oxygenation status from TSC, again using blood gas analysis and pulse oximetry. The number of patients enrolled will be determined by statistical considerations. Data also will be collected for other endpoints including mortality.

Assuming results from the second study warrant program continuation, the third study, also double-blinded, randomized and placebo controlled, would enroll a statistically determined number of hospitalized COVID-19 patients who have not yet been admitted to an ICU, and therefore may not have arterial blood lines in place. While pulse oximetry readouts and other parameters will be monitored for possible improvements in patient status, the primary goal of this third study, intended to be a registration trial, will be to show that TSC lowers the probability of COVID-19 patient admittance to the ICU. Diffusion believes that achieving this goal would provide an important new tool for healthcare professionals as they fight to prevent the cascade of negative effects from oxygen deficiency in hospitalized COVID-19 patients, which too often lead to disease progression and mortality. Meeting this goal could also provide significant cost savings to the health care system, lessening the use of critical resources associated with ICU admittance and fostering TSC's more widespread use.

Diffusion's COVID-19 program is a cooperative research effort with the University of Virginia Health System (UVA) and the Integrated Translational Research Institute of Virginia (iTHRIV.) iTHRIV is a National Institutes of Health (NIH)-funded Clinical and Translational Awards (CTSA) program. Dr. Andrew Southerland, Associate Professor of Neurology and Public Health Sciences at UVA, serves as lead Principal Investigator, working with co-investigator Dr. Alex Kadl, Assistant Professor of Medicine and Pharmacology in the UVA Division of Pulmonary & Critical Care Medicine.

"Despite 50 years of research," said Dr. Kadl, " there are no pharmaceutical therapies for ARDS. We further know that maintaining adequate blood oxygenation with needed mechanical ventilation can cause further harm and damage to the lungs. Improving oxygenation with TSC may prevent severe hypoxia and the need for mechanical ventilation, giving the lungs the time needed to recover from COVID-19 infection."

"We believe TSC's novel oxygen-enhancing mechanism could have a direct effect on the systemic hypoxemia in COVID-19 patients, altering the downward spiral of disease progression and decreasing the necessity for ARDs-related admissions to the ICU," said David Kalergis, chief executive officer of Diffusion. "We are committed to working with hospitals and regulatory authorities both in the U.S. and Eastern Europe to forge the fastest possible pathway to TSC's approval, consistent with good clinical practices."

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 Office of Naval Research, which was seeking a way to treat multiple organ failure and its resulting mortality caused by the systemic hypoxemia from blood loss on the battlefield. Evolutions in research have led to Diffusion's focus today: Fueling Life by taking on some of medicine's most intractable and difficult-to-treat diseases, including multiple organ failure, stroke and glioblastoma multiforme (GBM) brain cancer. In each of these diseases, hypoxia – oxygen deprivation of essential tissue in the body – has proved to be a significant obstacle for medical providers and is the target for TSC's novel mechanism.

In July 2019 the Company reported favorable safety data in a 19-patient dose-escalation run-in study to its Phase 3 INTACT program, using TSC to target inoperable GBM. Further findings from the dose-escalation run-in study, released in December 2019, also showed possible signals of enhanced survival and patient performance. 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 is expected to be minimal until the COVID-19 pandemic abates. The Company is also currently partnering with the University of Virginia and iTHRIV in a research program to develop its novel small molecule TSC as a treatment for Acute Respiratory Distress Syndrome (ARDS) from COVID-19, specifically targeting the associated multiple organ failure.

Preclinical data supports the potential for TSC as a treatment for other conditions where hypoxia plays a major role, such as myocardial infarction, peripheral artery disease, and neurodegenerative conditions such as Alzheimer's and Parkinson's disease. In addition, 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 protocol described above, which is a pre-IND submission, will be ultimately acceptable to the FDA for an IND submission 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; moreover, if this or a revised protocol is acceptable to the FDA for an IND submission, there can be no assurance as to when the FDA might provide such guidance or when the program might be able to commence, if at all; the uncertainty that as of yet the FDA has no 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; 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 sufficiency of the company’s cash, 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.

Contacts:
David Kalergis, CEO
Diffusion Pharmaceuticals Inc.
(434) 825-1834
dkalergis@diffusionpharma.com
or
LHA Investor Relations
Kim Sutton Golodetz
(212) 838-3777
kgolodetz@lhai.com

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