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): July 26, 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** (Address of principal executive offices)	**22902** (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 July 26, 2022, Diffusion Pharmaceuticals Inc. issued a press release announcing plans to initiate a Phase 2 clinical trial in patients with glioblastoma multiforme incorporating innovative imaging methodology to evaluate tumor 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 July 26, 2022
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.

Dated: July 27, 2022

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

Exhibit 99.1

Diffusion Pharmaceuticals to Initiate Phase 2 Trial in Patients with Glioblastoma Multiforme Incorporating Innovative Imaging Methodology to Evaluate Tumor Oxygenation

- Diffusion aligns with FDA on design of an open-label, dose-escalation, Phase 2 safety and efficacy study of trans sodium crocetinate ("TSC") in newly diagnosed glioblastoma multiforme ("GBM") patients
- Company to evaluate effects of TSC on tumor oxygenation using an innovative positron emission tomography ("PET") hypoxia imaging methodology with data expected within one year of study initiation
- Diffusion previously obtained Orphan Drug Designation for use of TSC in conjunction with radiotherapy for the treatment of GBM

CHARLOTTESVILLE, Va., July 26, 2022--Diffusion Pharmaceuticals Inc. (NASDAQ: DFFN) ("Diffusion" or the "Company"), a biopharmaceutical company developing novel therapies to enhance the body's ability to deliver oxygen to areas where it is needed most, today announced that after collaboration with the United States Food and Drug Administration ("FDA") on the design of their Phase 2 clinical trial entitled "Open-Label, Dose-Escalation, Phase 2 Safety and Efficacy Study of TSC in Newly Diagnosed Glioblastoma ("GBM") Patients when Administered with Standard of Care ("SOC")". The trial will be designated Study 200-208. The Company expects to initiate the trial by the end of 2022 and anticipates dosing the first patient in the trial in the first quarter of 2023.

GBM is an aggressive, deadly, and treatment-resistant type of malignant brain tumor, affecting approximately 13,000 newly diagnosed patients each year in the United States. Few treatment options are available for patients with GBM, and none have extended life expectancy beyond a few months. In fact, according to the National Brain Tumor Society, the five-year survival rate for GBM is only 6.8 percent with an average survival time of eight months.

"Effective treatment of GBM remains a significant unmet need and we believe in the potential for TSC to enhance the effectiveness of standard of care therapy for GBM," said Robert Cobuzzi, Jr., Ph.D., President and Chief Executive Officer of Diffusion. These tumors are known to be hypoxic, which reduces the effectiveness of radio-, chemo-, and immunotherapeutic approaches and promotes tumor cell metastases. We have previously received Orphan Drug designation from the FDA for treatment of GBM with TSC in conjunction with radiotherapy. With the results of the TCOM and Altitude Trials, we now have better data on TSC dosing compared to the previous GBM trials, and we have used these data to design a unique trial that not only will allow us to evaluate the effects of TSC on key clinical outcomes such as survival, but the use of PET imaging also will enable us to obtain data on the direct effects of TSC on GBM tumor oxygenation well before clinical outcome data is typically available in clinical trials involving GBM patients."

The study will include a dose-escalation phase, enrolling patients in a 3+3+3 design, to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of TSC at doses of 1.5 mg/kg, 2.0 mg/kg and 2.5 mg/kg administered in combination with concomitant standard of care radiotherapy ("RT") plus temozolomide. An additional 17 subjects will be treated at the highest tolerable dose identified in the dose escalation phase. The primary objective of the study is to evaluate the safety and tolerability of TSC for the treatment of patients with newly diagnosed GBM when administered with SOC. Secondary objectives of the study are to evaluate progression-free survival at six months by magnetic resonance imaging, assessment using Response Assessment in Neuro-Oncology criteria, and to evaluate overall survival at 12 months.

Study 200-208 will vary in a variety of ways from the GBM trials conducted by Diffusion in the past, including three particularly notable differentiators:

- The 1.5 mg/kg to 2.5 mg/kg doses of TSC to be administered in the study will be 6-10-fold higher than the 0.25 mg/kg dose used in Diffusion's prior GBM trials.

- TSC will be administered five days each week approximately 30-60 minutes prior to radiotherapy, as compared to the three days per week regimen in Diffusion's prior GBM trials.

- The study trial will incorporate PET scans to directly evaluate the oxygen enhancing effects of TSC on tumor hypoxia using one of two radiotracers, 18F-FMISO or 18F-FAZA, with initial data readouts expected to be available within one year of the study's initiation.

"For patients with hypoxic tumor microenvironments such as glioblastoma, radiation can be less effective. Diffusion Pharmaceutical's proposed phase 2 trial of Trans Sodium Crocetinate (TSC) for glioblastoma patients may help to overcome the relative resistance of the hypoxic tumor to ionizing radiation. Improvements in the clinical outcomes for high-grade glioma patients are critically needed" said Dr. Jason Sheehan, MD, PhD, Neurosurgeon at University of Virginia School of Medicine.

"With Glioblastoma Awareness Day on July 20th serving as a stark reminder of the continued unmet need for this disease, our team is incredibly motivated to work with our clinical investigators to get this uniquely designed trial started to explore the potential of TSC to improve outcomes for patients suffering from this devastating diagnosis," noted Chris Galloway, MD, Chief Medical Officer of Diffusion.

About Diffusion Pharmaceuticals Inc.
Diffusion Pharmaceuticals Inc. is a biopharmaceutical company developing novel therapies to enhance the body's ability to deliver oxygen to areas where it is needed most. Diffusion's lead product candidate, TSC, is being investigated 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: the potential therapeutic value of TSC in GBM and other indications; the anticipated design of Study 200-208; anticipated timelines for the initiation, completion, and announcement of data from the Company's ongoing and planned clinical trials; and the Company's near-term strategic priorities with respect to the development of TSC and otherwise. 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 risks and uncertainties include, among other things, those related to: the novelty of the design of Study 200-208; the relevance of trends observed in the Company's Oxygenation Trials in normal healthy volunteers to the study to any indication, including GBM and other hypoxic solid tumors; the therapeutic value of TSC; the optimal doses and dosing regimens of TSC in connection with the potential treatment of GBM or any other particular disease or indication; the Company's ability to fund, design, initiate, enroll, execute, and complete Study 200-208; the clinical and regulatory relevance of the results that may be observed in the PET hypoxia imaging component of Study 200-208; the likelihood and timing of regulatory approval of TSC, if any, for the treatment of GBM 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 global supply chain disruptions on the Company's drug product manufacturing capabilities, clinical development program, and associated timelines; the Company's ability to protect and expand its intellectual property portfolio; general economic, political, business, industry, and market conditions, including the ongoing COVID-19 pandemic, inflationary pressures, and geopolitical conflicts; 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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