

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-1
REGISTRATION STATEMENT
UNDER THE SECURITIES ACT OF 1933

DIFFUSION PHARMACEUTICALS INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

2834
(Primary Standard Industrial
Classification Code Number)

30-0645032
(I.R.S. Employer
Identification Number)

1317 Carlton Avenue, Suite 200
Charlottesville, VA 22902
(434) 220-0718

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

David G. Kalergis
Chief Executive Officer
1317 Carlton Avenue, Suite 200
Charlottesville, VA 22902
(434) 220-0718

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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New York, New York 10036
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1345 Avenue of the Americas
New York, New York 10105
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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended (the "Securities Act"), check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
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 to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Proposed maximum aggregate offering price(1)	Amount of registration fee
Common Stock, par value \$0.001 per share (2)(3)	\$ 9,200,000	\$ 1,194.16
Pre-funded warrants to purchase shares of common stock and common stock issuable upon exercise thereof (3)(5)	-	-
Warrants to purchase shares of common stock and common stock issuable upon exercise thereof (3)(5)	\$ 9,200,000	\$ 1,194.16
Underwriters' Warrant to purchase shares of Common Stock and common stock issuable upon exercise thereof (4)(5)	\$ 575,000	\$ 74.40
Total	\$ 18,975,000(6)	\$ 2,462.96

- (1) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(o) under the Securities Act. Includes the offering price of any additional securities that the underwriter has the option to purchase.
- (2) Includes securities that the underwriters have the option to purchase.
- (3) The proposed maximum aggregate offering price of the common stock proposed to be sold in the offering will be reduced on a dollar-for-dollar basis based on the aggregate offering price of the pre-funded warrants offered and sold in the offering (plus the aggregate exercise price of the common stock issuable upon exercise of the pre-funded warrants), and as such the proposed aggregate maximum offering price of the common stock and pre-funded warrants (including the common stock issuable upon exercise of the pre-funded warrants), if any, is \$9,200,000.
- (4) Represents warrants issuable to H.C. Wainwright & Co., LLC (the "Underwriter's Warrants") to purchase a number of shares of common stock equal to 5% of the number of shares of common stock and pre-funded warrants (including the shares of common stock and pre-funded warrants issued pursuant to the underwriter's exercise of its over-allotment option) being offered at an exercise price equal to 125% of the public offering price of the common stock. See "Underwriting."
- (5) Resales of the common warrants, the pre-funded warrants and the Underwriter's Warrants on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, are registered hereby. Resales of shares of common stock issuable upon exercise of the Underwriter's Warrants, the pre-funded warrants and the common stock warrants are also being registered on a delayed or continuous basis hereby.
- (6) Pursuant to Rule 416 under the Securities Act, the securities being registered hereunder include such indeterminate number of additional securities as may be issued after the date hereof as a result of stock splits, stock dividends or similar transactions.

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated October 6, 2019

PRELIMINARY PROSPECTUS

Diffusion₂n

Pharmaceuticals Inc.

Shares of Common Stock

Pre-Funded Warrants to Purchase Shares of Common Stock

Common Warrants to Purchase up to	Shares of Common Stock
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We are offering _____ shares of our common stock and common warrants to purchase up to _____ shares of common stock and the shares of common stock that are issuable from time to time upon exercise of the common warrants. We are also offering to certain purchasers whose purchase of shares of common stock in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% (or, at the election of the purchaser, 9.99%) of our outstanding common stock immediately following the consummation of this offering, the opportunity to purchase, if any such purchaser so chooses, pre-funded warrants, in lieu of shares of common stock that would otherwise result in such purchaser's beneficial ownership exceeding 4.99% (or, at the election of the purchaser, 9.99%) of our outstanding common stock. The purchase price of each pre-funded warrant will be equal to the price at which a share of common stock is sold to the public in this offering, minus \$0.001, and the exercise price of each pre-funded warrant will be \$0.001 per share. The pre-funded warrants will be immediately exercisable and may be exercised at any time until all of the pre-funded warrants are exercised in full. For each pre-funded warrant we sell, the number of shares of common stock we are offering will be decreased on a one-for-one basis. Therefore the number of common warrants sold in this offering will not change as a result of a change in the mix of the shares of our common stock and pre-funded warrants sold. The shares of common stock and pre-funded warrants, and the accompanying common warrants, can only be purchased together in this offering but will be issued separately and will be immediately separable upon issuance. Each common warrant will have an exercise price of \$ _____ per share of common stock, will be exercisable upon issuance and will expire five years from the date of issuance.

Our common stock is listed on the Nasdaq Capital Market under the symbol "DFFN." On October 11, 2019, the last reported sale price of our common stock on the Nasdaq Capital Market was \$1.78 per share. The public offering price per share of common stock and any pre-funded warrant and the accompanying common warrant will be determined between us and the underwriter at the time of pricing, and may be at a discount to the then current market price. There is no established public trading market for the pre-funded warrants, the common warrants and the Underwriter's Warrants and we do not expect a market to develop. Without an active trading market, the liquidity of the warrants will be limited. In addition, we do not intend to list the pre-funded warrants, common warrants or the Underwriter's Warrants on the Nasdaq Capital Market, any other national securities exchange or any other trading system.

Investing in our securities involves a high degree of risk. See the section entitled "Risk Factors" beginning on page 7 of this prospectus and in the documents incorporated by reference into this prospectus for a discussion of risks that should be considered in connection with an investment in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

	Per Share and Common Warrant	Per Pre-Funded Warrant and Common Warrant	Total
Public offering price	\$	\$	\$
Underwriting discounts and commissions (1)	\$	\$	\$
Proceeds, before expenses, to us (2)	\$	\$	\$

- (1) In addition, we have agreed to reimburse the underwriter for certain expenses and to issue the Underwriter Warrants to the underwriter. See “Underwriting” for additional information and a description of the compensation payable to the underwriters.
- (2) We estimate the total expenses of this offering payable by us, excluding the underwriting discounts and commissions, will be approximately \$

The offering is being underwritten on a firm commitment basis. We have granted the underwriter an option for a period of 30 days from the date of this prospectus to purchase up to additional shares of our common stock and/or up to additional common warrants (equal to 15% of the shares (including shares underlying the pre-funded warrants) and/or 15% of the common warrants in this offering) at a price per share equal to the combined public offering price, less the underwriting discounts and commissions.

The securities are expected to be delivered to purchasers on or about , 2019.

Sole Book-Running Manager

H.C. Wainwright & Co.

The date of this prospectus is , 2019

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ABOUT THIS PROSPECTUS

You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus. You should not assume that the information in this prospectus is accurate at any date other than the date indicated on the cover page of this prospectus or the filing date of any document incorporated by reference, regardless of its time of delivery. We are offering to sell shares of common stock, pre-funded warrants and common warrants and seeking offers to buy shares of common stock, pre-funded warrants and common warrants only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of the common stock, pre-funded warrants and common warrants.

For investors outside the United States: neither we nor the underwriter have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock, pre-funded warrants and common warrants and the distribution of this prospectus outside the United States.

PROSPECTUS SUMMARY

This summary highlights information contained in other parts of this prospectus or incorporated by reference into this prospectus from our filings with the Securities and Exchange Commission (the “SEC”). As it is only a summary, it does not contain all of the information that you should consider before purchasing our securities in this offering and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere or incorporated by reference into this prospectus. You should read the entire prospectus, the registration statement of which this prospectus is a part, and the information incorporated by reference herein in their entirety, including the “Risk Factors” and our financial statements and the related notes contained in and incorporated by reference into this prospectus, before purchasing our securities in this offering. Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus to “Diffusion,” “we,” “our,” “us” or similar references mean Diffusion Pharmaceuticals Inc.

Diffusion Pharmaceuticals Inc.

Business Overview

We are a clinical stage biotechnology company developing new treatments for life-threatening conditions by improving the body’s ability to bring oxygen to the areas where it is needed most. We are developing our lead product candidate, transcrocetinate sodium, also known as trans sodium crocetininate (“TSC”), for use in those life-threatening conditions in which cellular oxygen deprivation (“hypoxia”) is the basis for significant unmet medical needs. TSC is designed to safely and selectively target and re-oxygenate the micro-environment of hypoxic cells, and can potentially be used in many indications, including stroke, oncology and cardiovascular disease. In stroke, TSC helps promote the diffusion of oxygen into those brain cells in which oxygen-deprivation causes neuronal death resulting in patient mortality or morbidity. In cancer, TSC re-oxygenates treatment-resistant cancerous tissue, making the cancer cells up to three times more susceptible to the therapeutic effects of standard-of-care radiation therapy and chemotherapy.

A range of tissue types, including both normal and cancerous cells, has been shown to be safely re-oxygenated in our preclinical and clinical studies using TSC’s novel mechanism of action. We believe TSC’s ability to re-oxygenate normal tissue that has become oxygen-deprived provides opportunities for new therapeutic approaches to conditions ranging from stroke and emergency medicine to cardiovascular and neurodegenerative diseases. In oncology, we believe TSC’s therapeutic potential is not limited to one specific tumor type, thereby making it potentially useful to improve standard-of-care treatments in many life-threatening cancers. Given TSC’s safety profile and animal data, we could, with appropriate funding, move directly into Phase 2 studies for TSC in many such cancers. The successful completion of trials for TSC or any other potential product candidate in these or any other indication is dependent upon our ability to further raise necessary capital.

We believe that TSC has potential applications in stroke and emergency medicine. A Phase 2 trial in cooperation with UCLA and the University of Virginia to test TSC in the treatment of acute stroke has received approval for enrollment by the FDA, with the first enrolled patient expected in the fourth quarter of 2019. This trial, which will feature in-ambulance dosing of TSC, is named the PreHospital Acute Stroke Therapy - TSC (PHAST - TSC) and is expected to enroll 160 patients, with 80 in the treatment arm and 80 in the control arm. We believe in-ambulance dosing of TSC could significantly cut the time in which the stroke-related oxygen deprivation to brain cells goes untreated, potentially leading to a better outcome for stroke victims treated in this manner. Subject to receipt of adequate funding to support the PHAST – TSC trial, we expect to data readout during the first half of 2021.

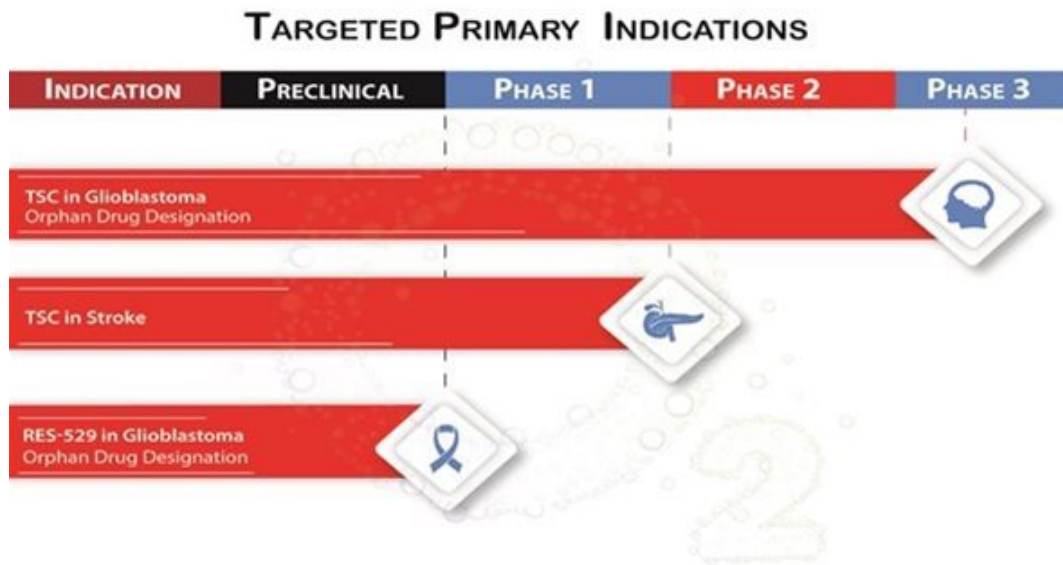
Our primary oncology program targets TSC against treatment-resistant brain cancer. A Phase 2 clinical program, completed in the second quarter of 2015, evaluated 59 patients with newly diagnosed glioblastoma multiforme (“GBM”), a particularly deadly form of primary brain cancer. GBM affects approximately 12,000 patients annually in the United States and approximately 35,000 patients annually worldwide. This open label, historically controlled study demonstrated a favorable safety and efficacy profile for TSC when combined with GBM’s standard of care, including a 37% improvement in overall survival over the control group at two years. A particularly strong efficacy signal was seen in the inoperable patients, where survival of TSC-treated patients at two years was increased by almost four-fold over the controls. In December 2017, the Company initiated the INvestigation of TSC Against Cancerous Tumors (INTACT) Phase 3 trial in the newly diagnosed inoperable GBM patient population. The trial is designed to enroll 236 patients in total, with 118 in the treatment arm and 118 in the control arm.

The trial began with an open label 8 patient safety run-in for which enrollment has completed and is now closed. With the FDA’s permission, a total of 19 patients were enrolled to ensure 8 complete data sets. The INTACT Trial Data Safety Monitoring Board (DSMB) met in the third quarter of 2019 and recommended that the study be continued. The board concluded that no adverse safety signal had been observed, and unanimously recommended continuing the study as planned using the highest tested dose of TSC – 1.5 mg/kg – during the adjuvant treatment chemotherapy period with temozolomide. Commencement of enrollment in the randomization portion of the INTACT Phase 3 Trial is contingent upon our entering into a strategic partnership providing the necessary resources to undertake the full trial.

In addition to the TSC programs, we are exploring alternatives regarding how best to capitalize upon our product candidate RES-529, which may include possible out-licensing and other options. RES-529 is a novel PI3K/Akt/mTOR pathway inhibitor which has completed two Phase 1 clinical trials for age-related macular degeneration and was in preclinical development in oncology. RES-529 has shown activity in both in vitro and in vivo glioblastoma animal models and has been demonstrated to be orally bioavailable and capable of crossing the blood-brain barrier.

Summary of Current Product Candidate Pipeline

The following table, as of June 30, 2019, summarizes the targeted primary indications for Diffusion’s lead molecule, TSC, and RES-529:

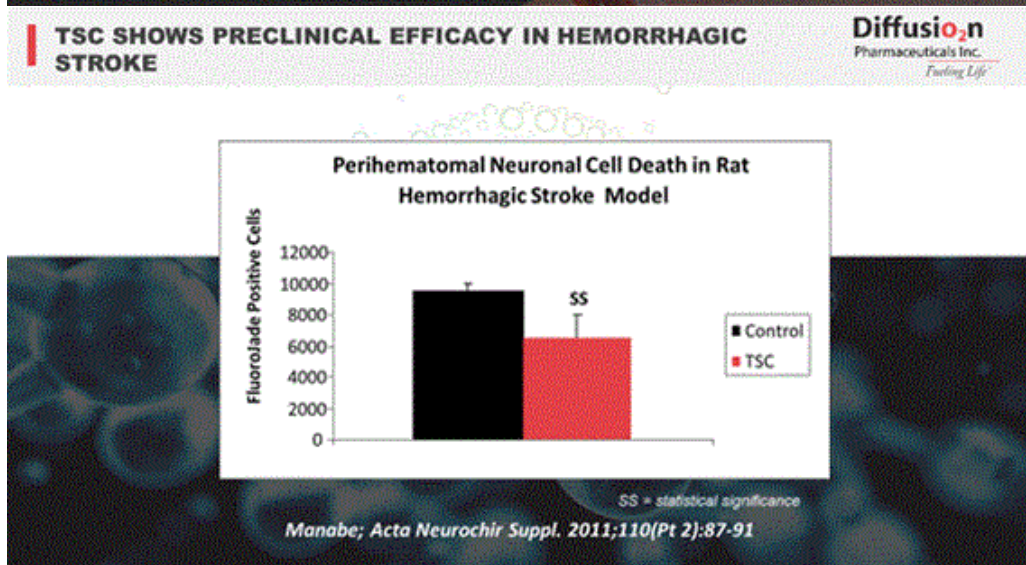
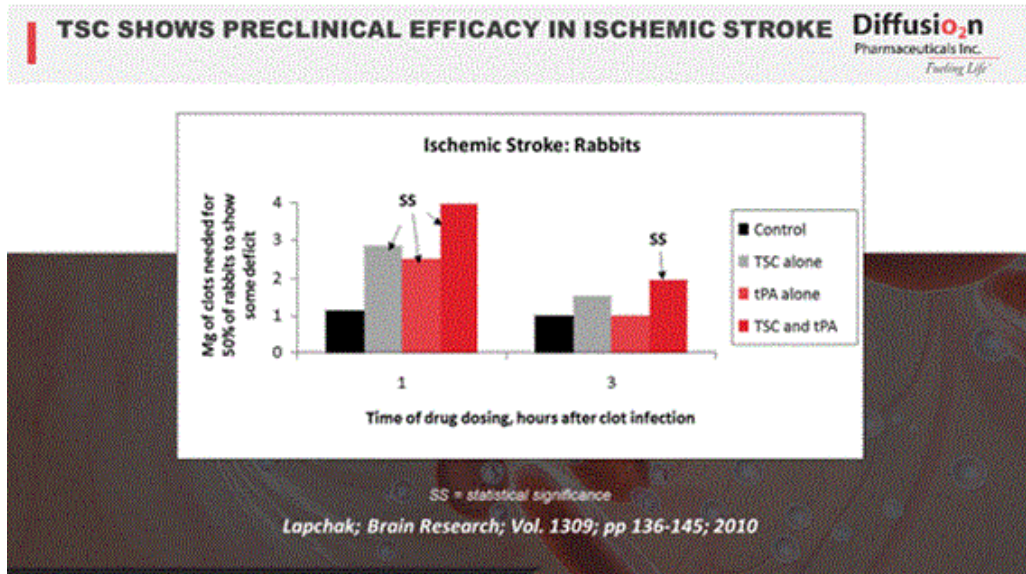


TSC Stroke Program

We believe that TSC has potential application as a treatment for stroke. Approximately 800,000 strokes occur in the United States each year, with an estimated annual cost of \$43.0 billion. The damage from a stroke begins immediately upon onset: brain cell death begins immediately at the onset of a stroke. A stroke can take a significant toll on its victims. Among long-term stroke survivors, approximately 66% of stroke patients end up needing mental or physical rehabilitation, approximately 40% are classified as moderately to severely disabled after the initial few days of recovery, and approximately 10% of stroke patients require long-term care.

We believe in-ambulance dosing of TSC could significantly cut the time in which the stroke-related oxygen deprivation to brain cells goes untreated, potentially leading to a better outcome for stroke victims treated in this manner. Half of all stroke patients are transported to hospitals by emergency medical services (EMS), such as ambulances, with estimates of up to 80% of all patients in urban and suburban areas being transported by EMS.

TSC has shown pre-clinical efficacy as a potential treatment for ischemic and hemorrhagic stroke in laboratory testing. Rabbits receiving TSC alone at one hour after developing a clot have shown a statistically significant positive response to treatment. Additionally, rabbits receiving TSC in conjunction with Tissue Plasminogen Activator (tPA) at three hours after developing a clot have shown a statistically significant positive response to treatment. Additionally, rats dosed with TSC in a hemorrhagic stroke showed a statistically significant decrease in damaged brain cells. The following charts provide additional detail on these animal studies:



Corporate Information

We are a Delaware corporation that was incorporated in June 2015. Prior to June 2015, we were a Nevada corporation. We maintain our principal executive offices at 1317 Carlton Avenue, Suite 200, Charlottesville, VA 22902. Our telephone number there is (434) 220-0718. The address of our website is www.diffusionpharma.com. The information set forth on, or connected to, our website is expressly not incorporated by reference into, and does not constitute a part of, this prospectus.

We are a “smaller reporting company” as defined in Rule 12b-2 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and have elected to take advantage of certain of the scaled disclosure available for smaller reporting companies in this prospectus as well as our filings under the Exchange Act.

THE OFFERING

Common stock offered by us in this offering

shares.

Pre-funded warrants offered by us in this offering

We are also offering to certain purchasers whose purchase of shares of common stock in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% (or, at the election of the purchaser, 9.99%) of our outstanding common stock immediately following the closing of this offering, the opportunity to purchase, if such purchasers so choose, pre-funded warrants to purchase shares of common stock, in lieu of shares of common stock that would otherwise result in any such purchaser's beneficial ownership exceeding 4.99% (or, at the election of the purchaser, 9.99%) of our outstanding common stock. Each pre-funded warrant will be exercisable for one share of our common stock. The purchase price of each pre-funded warrant and accompanying common warrant (as described below) will be equal to the price at which a share of common stock and accompanying common warrant is being sold to the public in this offering, minus \$0.001, and the exercise price of each pre-funded warrant will be \$0.001 per share. The pre-funded warrants will be exercisable immediately and may be exercised at any time until all of the pre-funded warrants are exercised in full. This offering also relates to the shares of common stock issuable upon exercise of any pre-funded warrants sold in this offering. For each pre-funded warrant we sell, the number of shares of common stock we are offering will be decreased on a one-for-one basis. Because we will issue a common warrant for each share of our common stock and for each pre-funded warrant to purchase one share of our common stock sold in this offering, the number of common warrants sold in this offering will not change as a result of a change in the mix of the shares of our common stock and pre-funded warrants sold.

For more information, see the section entitled "Description of Capital Stock" on page 16 of this prospectus.

Common warrants offered by us in this offering

Warrants to purchase up to _____ shares, which may be exercised beginning on their date of issuance. The warrants are exercisable until the five year anniversary of the original issuance date. The warrants have an exercise price of \$ _____ per share of common stock, subject to adjustment.

For more information, see the section entitled "Description of Capital Stock" on page 16 of this prospectus.

Option to purchase additional shares and warrants

The underwriter has a 30-day option to purchase up to an amount of additional shares of our common stock and/or an amount of additional common warrants to purchase our common stock equal to 15% of the number of shares (including shares underlying the pre-funded warrants) and/or 15% of the number of common warrants issued in this offering, at a price equal to the combined public offering price, less the underwriting discounts and commissions.

Common stock to be outstanding after this offering	shares (or shares of common stock if the underwriters exercise their option to purchase additional shares in full) in each case assuming no sales of pre-funded warrants, which, if sold, would reduce the number of shares of common stock that we are offering on a one-for-one basis and assuming no exercise of any common warrants issued in this offering.
Use of proceeds	We intend to use the net proceeds from this offering to fund research and development of our lead product candidate, TSC, including clinical trial activities, and for general corporate purposes. See “Use of Proceeds.”
Risk factors	You should read the “Risk Factors” section of this prospectus as well as all other information included in this prospectus, including the information in the documents incorporated by reference into this prospectus, for a discussion of certain of the factors to consider carefully before deciding to purchase any securities in this offering.
National Securities Exchange Listing	Our common stock is listed on the Nasdaq Capital Market under the symbol “DFFN.”
The number of shares of our common stock to be outstanding after this offering is based on 4,693,290 shares of common stock outstanding as of June 30, 2019 and excludes as of that date:	
	<ul style="list-style-type: none"> • 309,276 shares of common stock issuable upon the exercise of outstanding stock options under the Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan, as amended (the “2015 Equity Plan”), at a weighted-average exercise price of \$55.78 per share; • 3,469,925 shares of common stock issuable upon the exercise of outstanding warrants, at a weighted-average exercise price of \$15.11 per share; and • 19,740 shares of common stock reserved for future issuance under the 2015 Equity Plan.

Unless otherwise indicated, all information contained in this prospectus assumes no exercise by the underwriter of its option to purchase additional shares of common stock and/or common warrants, and no sale of pre-funded warrants, which, if sold, would reduce the number of shares of common stock that we are offering on a one-for-one basis and no exercise of any common warrants issued in this offering. Additionally, unless otherwise indicated, all share information contained in this prospectus reflects the completion on December 13, 2018, of a 1-to-15 reverse stock split (the “Reverse Stock Split”) of our common stock. No fractional shares were issued in connection with the Reverse Stock Split. Stockholders who otherwise would have been entitled to receive fractional shares of common stock had their holdings rounded up to the next whole share. Proportional adjustments were made to the Company’s outstanding warrants, stock options and other equity securities and to the 2015 Equity Incentive Plan, as amended, to reflect the Reverse Stock Split, in each case, in accordance with the terms thereof.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks described below, together with the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus, before making your 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. In addition, you should also carefully consider the other risks described under the heading “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2018, which is incorporated herein by reference, as updated by annual, quarterly and other reports and documents we file with the SEC after the date of this prospectus and that are incorporated by reference herein.

Risks Related to this Offering

We have significant discretion over the use of the net proceeds from this offering.

Our net proceeds from this offering are expected to be approximately \$ _____, assuming no pre-funded warrants are sold in place of shares of common stock. We intend to use the net proceeds of this offering to fund research and development of our lead product candidate, TSC, including clinical trial activities, and for general corporate purposes. Accordingly, our management will have broad discretion as to the application of such proceeds. The proceeds shall be used to carry out our business plan, pay salaries to our employees, and satisfy all our expenses, foreseeable and unforeseeable. As is the case with any business, it should be expected that certain expenses unforeseeable to management at this juncture will arise in the future. There can be no assurance that management’s use of proceeds generated through this offering will prove optimal or translate into revenue or profitability for the Company. Investors are urged to consult with their attorneys, accountants and personal investment advisors prior to making any decision to invest in the Company.

Even if this offering is successful, we will need to raise additional capital in the future to continue operations, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

To date, we have not sold, or received approval to sell, any pharmaceutical products. We do not expect to sell any pharmaceutical products for at least the next several years, if at all. Our net losses were approximately \$18.4 million and \$1.4 million for the years ended December 31, 2018 and 2017, respectively, and our net losses attributable to common stockholders were approximately \$26.6 million and \$2.6 million for the years ended December 31, 2018 and 2017, respectively. As of June 30, 2019 and December 31, 2018, we had incurred cumulative net losses totaling approximately \$85.2 million and \$79.9 million, respectively. Moreover, we expect that our net losses will continue and may increase for the foreseeable future. We may never generate sufficient product revenue (if any) to become profitable. We also expect to have quarter-to-quarter fluctuations in revenues, expenses, and losses, some of which could be significant.

We estimate that we will receive net proceeds of approximately \$ _____ million from the sale of the securities offered by us in this offering, based on the assumed public offering price of \$ _____ per share of common stock and \$ _____ per common warrant (the last reported sale price of our common stock on the NASDAQ Capital Market on _____, 2019), assuming no pre-funded warrants are sold in place of shares of common stock, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. In the event of a decrease in the net proceeds to us from this offering as a result of a decrease in the assumed combined public offering price or the number of shares offered by us, we may need to raise additional capital sooner than we anticipate or may need to scale back or eliminate certain of our development programs.

We will need to raise more money to complete our planned clinical trials, continue the research and development necessary to bring our products to market and to establish marketing and additional manufacturing capabilities. Notably, the proceeds raised in this offering will not be enough to complete our planned Phase 2 clinical trial of TSC for stroke or our Phase 3 clinical trial of TSC for treatment of glioblastoma multiforme. Additionally, we do not intend to commence our Phase 3 clinical trial of TSC for treatment of GBM prior to engaging in a strategic partnership. We may seek additional funds through public and private stock offerings, government contracts and grants, arrangements with corporate collaborators, borrowings under lines of credit or other sources. However, we may not be able to raise additional funds on acceptable terms, or at all. Conditions in the capital markets and the financial services industry may make equity and debt financing more difficult to obtain, and may negatively impact our ability to complete financing transactions. Any debt financing, if available, may involve restrictive covenants, such as limitations on our ability to incur additional indebtedness and other operating restrictions that could adversely impact our ability to conduct our business.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates or one or more of our research and development initiatives, reduce our workforce, license to others products or technologies that we otherwise would seek to commercialize ourselves or, ultimately, cease operations. The amount of money we may need would depend on many factors, including:

- The costs and progress of our research and development programs;
- The scope and results of our preclinical studies and clinical trials; and
- The time and costs involved in: obtaining necessary regulatory approvals; filing, prosecuting and enforcing patent claims; scaling up our manufacturing capabilities; and the commercial arrangements we may establish.

An investment in our securities is speculative and there can be no assurance of any return on any such investment.

An investment in our securities is speculative and there is no assurance that investors will obtain any return on their investment. Investors will be subject to substantial risks involved in an investment in the Company, including the risk of losing their entire investment.

If you purchase our common stock, pre-funded warrants and common warrants in this offering, you will incur immediate and substantial dilution in the book value of your shares.

The combined public offering price in this offering is substantially higher than the net tangible book value per share of our common stock. Investors purchasing common stock and warrants in this offering will pay a price per share that substantially exceeds the book value of our tangible assets after subtracting our liabilities. As a result, investors purchasing common stock and warrants in this offering will incur immediate dilution of \$ per share, based on the assumed combined public offering price of \$ per share.

As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. For a further description of the dilution that you will incur as a result of purchasing shares in this offering, see “Dilution.”

There will likely be future sales of our securities or other dilution of our equity, which may adversely affect the market price of our common stock.

We are generally not restricted from issuing additional common stock, including any securities that are convertible into or exchangeable for, or that represent the right to receive, common stock. The market price of our common stock could decline as a result of sales of common stock or securities that are convertible into or exchangeable for, or that represent the right to receive, common stock after this offering or the perception that such sales could occur. To the extent that we raise additional funds by issuing equity securities, our stockholders may experience significant dilution.

If we cannot continue to satisfy the Nasdaq Capital Market continued listing standards and other Nasdaq rules, our common stock could be delisted, which would harm our business, the trading price of our common stock, our ability to raise additional capital and the liquidity of the market for our common stock.

Our common stock is currently listed on the Nasdaq Capital Market. To maintain the listing of our common stock on the Nasdaq Capital Market, we are required to meet certain listing requirements, including, among others, either: (i) a minimum closing bid price of \$1.00 per share, a market value of publicly held shares (excluding shares held by our executive officers, directors and 10% or more stockholders) of at least \$1 million and stockholders’ equity of at least \$2.5 million; or (ii) a minimum closing bid price of \$1.00 per share, a market value of publicly held shares (excluding shares held by our executive officers, directors and 10% or more stockholders) of at least \$1 million and a total market value of listed securities of at least \$35 million.

There is no assurance that we will continue to meet the minimum closing price requirement and other listing requirements. In the event that our common stock is delisted from Nasdaq and is not eligible for quotation or listing on another market or exchange, trading of our common stock could be conducted only in the over-the-counter market or on an electronic bulletin board established for unlisted securities such as the Pink Sheets or the OTC Bulletin Board. In such event, it could become more difficult to dispose of, or obtain accurate price quotations for, our common stock, and there would likely also be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further.

The pre-funded warrants and common warrants are speculative in nature.

Neither the pre-funded warrants nor the common warrants offered hereby confer any rights of common stock ownership on their holders, such as voting rights or the right to receive dividends, but rather merely represent the right to acquire shares of common stock at a fixed price. Specifically, commencing on the date of issuance, holders of the pre-funded warrants may acquire the common stock issuable upon exercise of such warrants at an exercise price of \$0.001 per share of common stock and holders of the common warrants may acquire the common stock issuable upon exercise of such warrants at an exercise price of \$ _____ per share. Moreover, following this offering, the market value of the pre-funded warrants and common warrants is uncertain and there can be no assurance that the market value of the pre-funded warrants or the common warrants will equal or exceed their public offering price. There can be no assurance that the market price of the common stock will ever equal or exceed the exercise price of the pre-funded warrants or common warrants, and consequently, whether it will ever be profitable for holders of the pre-funded warrants to exercise the pre-funded warrants or the holders of the common warrants to exercise the common warrants.

Holders of the pre-funded warrants and common warrants will have no voting rights as common stockholders until they acquire our common stock.

Until you acquire shares of our common stock upon exercise of the pre-funded warrants and common warrants, you will have no voting rights with respect to our common stock issuable upon exercise of the pre-funded warrants or common warrants. Upon exercise of your pre-funded warrants or common warrants, you will be entitled to exercise all the voting rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

Significant holders or beneficial holders of our common stock may not be permitted to exercise pre-funded warrants or common warrants that they hold.

The pre-funded warrants and common warrants being offered hereby will prohibit a holder from exercising its pre-funded warrants or common warrants if doing so would result in such holder (together with such holder's affiliates and any other persons acting as a group together with such holder or any of such holder's affiliates) beneficially owning more than 4.99% of our common stock outstanding immediately after giving effect to the exercise, provided that, at the election of a holder and notice to us, such beneficial ownership limitation shall be 9.99% of our common stock outstanding immediately after giving effect to the exercise. As a result, if you hold a significant amount of our securities, you may not be able to exercise your pre-funded warrants or common warrants for shares of our common stock, in whole or in part, at a time when it would be financially beneficial for you to do so.

There is no public market for the pre-funded warrants or common warrants to purchase shares of common stock being offered in this offering.

There is no established public trading market for the pre-funded warrants or common warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the pre-funded warrants or common warrants on any national securities exchange or other trading system, including the Nasdaq Capital Market. Without an active market, the liquidity of the pre-funded warrants or common warrants will be limited.

We may be limited in our ability to utilize, or may not be able to utilize, net operating loss carryforwards to reduce our future tax liability as a result of this offering.

As disclosed in our most recent Annual Report on Form 10-K, under Section 382 of Internal Revenue Code of 1986, as amended (the “Code”), if a corporation undergoes an “ownership change,” generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation’s ability to use its pre-change net operating loss (“NOL”) carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited.

We believe that our reverse merger in January 2016 and other transactions that have occurred triggered an “ownership change” limitation that significantly limited our ability to utilize our NOL carryforwards. Our 2017, 2018 and 2019 financing transactions may have also triggered an ownership change, which could further limit our ability to utilize our NOL carryforwards. We have yet to determine this potential limitation. This offering may, alone or in conjunction with other changes in our stock ownership that we cannot control, result in an additional ownership change for purposes of Section 382. We may also experience ownership changes in the future as a result of strategic transactions or partnerships, equity offerings and other shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards and other deferred tax assets to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, similar limitations may apply at the state level and there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

An investment in the pre-funded warrants, common warrants and our common stock has numerous tax consequences.

There are numerous tax consequences to investors as a result of their investment in the Company. We encourage investors to seek advice from competent tax advisors as to the consequences of an investment in our pre-funded warrants, common warrants and common stock (See “Material U.S. Federal Income Tax Considerations”).

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 (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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the other information and documents incorporated by reference herein include forward-looking statements. 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 appear in and are incorporated by reference into a number of places throughout this prospectus and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, our intellectual property position, the degree of clinical utility of our products, particularly in specific patient populations, expectations regarding clinical trial data, our ability to commercialize our product candidates, our results of operations, cash needs, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us.

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 in or incorporated by reference into this prospectus, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in and incorporated by reference into this prospectus. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in and incorporated by reference into this prospectus, they may not be predictive of results or developments in future periods.

Actual results could differ materially from our forward-looking statements due to a number of factors, including risks related to:

- our ability to obtain additional financing;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- the success and timing of our preclinical studies and clinical trials;
- the difficulties in obtaining and maintaining regulatory approval of our products and product candidates, and the labeling under any approval we may obtain;
- our plans and ability to develop and commercialize our product candidates;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the accuracy of our estimates of the size and characteristics of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;
- the rate and degree of market acceptance of any of our product candidates;
- 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;
- recently enacted and future legislation regarding the healthcare system;
- our ability to satisfy the continued listing requirements of the Nasdaq Capital Market or any other exchange that our securities may trade on in the future;

- our ability to continue as a going concern;
- the success of competing products that are or may become available; and
- the performance of third parties, including contract research organizations and manufacturers.

You should also read carefully the factors described in the “Risk Factors” section contained in this prospectus and incorporated by reference herein from our Annual Report on Form 10-K for the fiscal year ended December 31, 2018 as updated by annual, quarterly and other reports and documents we file with the SEC after the date of this prospectus and that are incorporated by reference herein to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements contained in or incorporated by reference into this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of 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.

Any forward-looking statements that we make in or incorporate by reference into this prospectus speak only as of the date of such statement, and, except as required by applicable law, we undertake no obligation to update such statements to reflect events or circumstances after the date of this prospectus or to reflect the occurrence of unanticipated events. Comparisons of results for current and any prior periods are not intended to express any future trends or indications of future performance, unless expressed as such, and should only be viewed as historical data.

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.

USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately \$ (or approximately \$ if the underwriter's option to purchase additional shares of common stock and/or common warrants is exercised in full) from the sale of the securities offered by us in this offering, based on the assumed combined public offering price of \$ per share of common stock and common warrant (the last reported sale price of our common stock on the Nasdaq Capital Market on , 2019), assuming no sales of pre-funded warrants, which, if sold, would reduce the number of shares of common stock that we are offering on a one-for-one basis, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

A \$0.10 increase (decrease) in the assumed combined public offering price of \$ per share of common stock and common warrant would increase (decrease) the net proceeds to us from this offering by approximately \$, assuming that the number of shares of common stock and common warrants offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Similarly, a one hundred thousand share increase (decrease) in the number of shares of common stock and accompanying common warrants offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the net proceeds to us by approximately \$ and \$, respectively, assuming the assumed combined public offering price of \$ per share of common stock and common warrant remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We currently intend to use the net proceeds from this offering to fund research and development of our lead product candidate, TSC, including clinical trial activities, and for general corporate purposes. See "Risk Factors" in this prospectus and in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, incorporated by reference herein, as updated by annual, quarterly and other reports and documents we file with the SEC after the date of this prospectus and that are incorporated by reference herein, for a discussion of certain risks that may affect our intended use of the net proceeds from this offering, including that we will need to raise additional capital in the future to complete the development of TSC and our other product candidates.

Our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus, we cannot currently allocate specific percentages of the net proceeds that we may use for the purposes specified above, and we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering, or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual use of the net proceeds will vary depending on numerous factors, including our ability to obtain additional financing, the progress, cost and results of our preclinical and clinical development programs, and whether we are able to enter into future licensing or collaboration arrangements. We may find it necessary or advisable to use the net proceeds for other purposes, and our management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds from this offering.

Pending the use of the net proceeds from this offering, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing securities or certificates of deposit.

CAPITALIZATION

The following table sets forth cash and capitalization as of June 30, 2019:

- on an actual basis;
- on an as adjusted basis to give effect to the assumed issuance and sale of shares of common stock and warrants in this offering at the assumed combined public offering price of \$ per share of common stock and common warrant (but excluding shares of common stock to be issued and any proceeds received upon exercise of the common warrants) (the last reported sale price of our common stock on the Nasdaq Capital Market on , 2019), assuming no sales of pre-funded warrants, which, if sold, would reduce the number of shares of common stock that we are offering on a one-for-one basis, after deducting estimated underwriting discounts and commissions, and estimated offering expenses payable by us.

(unaudited)	Actual as of June 30, 2019	As Adjusted as of June 30, 2019
Cash and cash equivalents	\$ 8,372,741	\$
Stockholders' equity:		
Common stock, par value \$0.001 per share; 1,000,000,000 shares authorized, 4,693,290 shares issued and outstanding actual; 1,000,000,000 shares authorized, shares issued and outstanding as adjusted	4,694	
Additional paid-in capital	\$ 101,340,798	\$
Accumulated deficit	\$ (85,167,906)	\$
Total stockholders' equity	\$ 16,177,586	\$
Total capitalization	\$ 16,177,586	\$

The number of shares of our common stock to be outstanding after this offering is based on 4,693,290 shares of common stock outstanding as of June 30, 2019 and excludes as of that date:

- 309,276 shares of common stock issuable upon the exercise of outstanding stock options under the 2015 Equity Plan at a weighted-average exercise price of \$55.78 per share;
- 3,469,925 shares of common stock issuable upon the exercise of outstanding warrants, at a weighted-average exercise price of \$15.11 per share; and
- 19,740 shares of common stock reserved for future issuance under the 2015 Equity Plan.

The amounts set forth in the table above also assume no exercise by the underwriter of its option to purchase additional shares of common stock and/or common warrants.

DILUTION

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the combined public offering price per share of our common stock and accompanying common warrant and the net tangible book value per share of our common stock upon consummation of this offering. Dilution results from the fact that the combined public offering price is substantially in excess of the book value per share attributable to the existing stockholders for the presently outstanding stock.

The historical net tangible book value of our common stock as of June 30, 2019 was approximately \$7.5 million, or approximately \$1.61 per share of common stock. Historical net tangible book value (deficit) per share is determined by dividing the number of outstanding shares of common stock into its total tangible assets (total assets less intangible assets) less total liabilities and preferred shares, if any.

Investors purchasing securities in this offering will incur immediate and substantial dilution. After giving effect to the sale of securities offered in this offering assuming a combined public offering price of \$ _____ per share of common stock and common warrant, the closing price of our common stock on the Nasdaq Capital Market on _____, 2019 (but excluding any shares of common stock to be issued and any proceeds to be received upon exercise of the common warrants), and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us, our as adjusted net tangible book value as of June 30, 2019 would have been approximately \$ _____, or approximately \$ _____ per share of common stock. This represents an immediate decrease in net tangible book value of \$ _____ per share to existing stockholders, and an immediate dilution in the as adjusted net tangible book value of \$ _____ per share to investors purchasing shares of our common stock and common warrants in this offering.

The following table illustrates this per share dilution:

Assumed combined public offering price per share of common stock and common warrant		\$ _____
Historical net tangible book value per share as of June 30, 2019	\$ 1.61	
Decrease in net tangible book value per share attributable to this offering		_____
As adjusted net tangible book value as of June 30, 2019 (giving effect to this offering)		_____
Dilution per share to investors		\$ _____

The dilution information discussed above is illustrative only and will change based on the actual combined public offering price and other terms of this offering determined at pricing. A \$0.10 increase or decrease in the assumed combined public offering price of \$ _____ per share of common stock and common warrant would increase or decrease the as adjusted net tangible book value per share by \$ _____, or approximately \$ _____ per share, and the dilution per share to investors participating in this offering by approximately \$ _____ per share, assuming the number of shares of common stock and common warrants offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The discussion and table above assume (i) no sales of pre-funded warrants, which, if sold, would reduce the number of shares of common stock that we are offering on a one-for-one basis, (ii) no exercise of the underwriter's option to purchase additional shares of common stock and/or common warrants, and (iii) no exercise of common warrants accompanying the shares of common stock and pre-funded warrants, if any, sold in this offering. If the underwriter fully exercises its option to purchase _____ additional shares of common stock and additional common warrants in the offering (but excluding any shares of common stock to be issued and any proceeds to be received upon exercise of the common warrants), our as adjusted net tangible book value after this offering, calculated in the manner set forth above, would be approximately \$ _____ million, our as adjusted net tangible book value per share after this offering would be \$ _____ per share, the increase in our as adjusted net tangible book value per share attributable to investors participating in this offering would be \$ _____ per share and the as adjusted dilution per share to new investors in this offering would be \$ _____ per share.

DESCRIPTION OF CAPITAL STOCK

Company Capitalization

Our authorized capital stock consists of 1,000,000,000 shares of common stock and 30,000,000 shares of preferred stock, \$0.001 par value, all of which remains undesignated. The following summary is qualified in its entirety by reference to our Certificate of Incorporation, as amended, a copy of which is filed as an exhibit to our previous filings with the SEC and incorporated herein by reference.

Common Stock

Authorized. We are authorized to issue 1,000,000,000 shares of common stock, of which 4,693,290 shares were issued and outstanding as of June 30, 2019. We may amend from time to time our Certificate of Incorporation to increase the number of authorized shares of common stock. Any such amendment would require the approval of the holders of a majority of the voting power of the shares entitled to vote thereon.

Voting Rights. For all matters submitted to a vote of stockholders, each holder of common stock is entitled to one vote for each share registered in the holder's name on our books. Our common stock does not have cumulative voting rights. At all meetings of the stockholders, except where otherwise provided by law, the Certificate of Incorporation or Bylaws, the presence, in person or by proxy duly authorized, of the holders of a majority of the outstanding shares of common stock entitled to vote constitutes a quorum for the transaction of business. Except as otherwise provided by law or by the Certificate of Incorporation or Bylaws, in all matters other than the election of directors, the affirmative vote of the majority of shares of common stock present in person or represented by proxy at the meeting and entitled to vote generally on the subject matter shall be the act of the stockholders. Except as otherwise provided by law, the Certificate of Incorporation or Bylaws, directors are elected by a plurality of the votes of the shares of common stock present in person or represented by proxy at the meeting and entitled to vote generally on the election of directors.

Dividends. Subject to limitations under Delaware law and any preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared by our Board out of legally available funds.

Liquidation. Upon our liquidation, dissolution or winding up, the holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities of our company, subject to any prior rights of any preferred stock then outstanding.

Fully Paid and Non-assessable. All shares of our outstanding common stock are fully paid and non-assessable and any additional shares of common stock that we issue will be fully paid and non-assessable.

Other Rights and Restrictions. Holders of common stock do not have preemptive or subscription rights, and they have no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to common stock. The rights, preferences and privileges of common stockholders are subject to the rights of the stockholders of any series of preferred stock which we may designate in the future. Our Certificate of Incorporation and Bylaws do not restrict the ability of a holder of common stock to transfer the holder's shares of common stock.

Listing. Our common stock is quoted on the Nasdaq Capital Market under the symbol "DDFN." As of October 11, 2019, there were 515 record holders of our common stock.

Transfer Agent and Registrar. The transfer agent and registrar for common stock is Computershare Investor Services, LLC, 250 Royall Street, Canton, Massachusetts, telephone number: 1-800-942-5909.

Pre-Funded Warrants

The material terms and provisions of the pre-funded warrants being issued in this offering are summarized below. The following description is subject to, and qualified in its entirety by, the form of pre-funded warrant which is filed herewith as an exhibit. You should review the form of pre-funded warrant for a complete description of the terms and conditions applicable to the pre-funded warrants. See "Information Incorporated by Reference and Available Information" below.

Duration and Exercise Price. Each pre-funded warrant offered hereby will have an initial exercise price per share equal to \$0.001. The pre-funded warrants will be immediately exercisable and may be exercised at any time until the pre-funded warrants are exercised in full. The exercise price and number of shares of common stock issuable upon exercise is subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock and the exercise price.

Exercisability. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of our common stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of the pre-funded warrant to the extent that the holder would own more than 4.99% of the outstanding common stock immediately after exercise, except that upon at least 61 days' prior notice from the holder to us, the holder may increase the amount of ownership of outstanding stock after exercising the holder's pre-funded warrants up to 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. Purchasers of pre-funded warrants in this offering may also elect prior to the issuance of the pre-funded warrants to have the initial exercise limitation set at 9.99% of our outstanding common stock.

Transferability. Subject to applicable laws, the pre-funded warrants are separately tradeable immediately after issuance at the option of the holders and may be transferred at the option of the holders upon surrender of the pre-funded warrant to us together with the appropriate instruments of transfer.

No Listing. There is no established public trading market for the pre-funded warrants and we do not expect a market to develop. In addition, we do not intend to apply for listing of the pre-funded warrants on any securities exchange or trading system. Without an active market, the liquidity of the pre-funded warrants will be limited.

Fundamental Transactions. In the event of a "fundamental transaction," as defined in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction.

Cashless Exercise. If, at the time a holder exercises its pre-funded warrants, a registration statement registering the issuance of the shares of common stock underlying the pre-funded warrants under the Securities Act is not then effective or available, then in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the pre-funded warrants.

Rights as a Stockholder. Except as otherwise provided in the pre-funded warrant or by virtue of a holder's ownership of shares of our common stock, the holders of the pre-funded warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until they exercise their pre-funded warrants.

Amendments. Amendments and waivers of the terms of the pre-funded warrants require the written consent of the holders of pre-funded warrants representing not less than a majority of the shares issuable upon exercise of the pre-funded warrants then outstanding and us, as well as any pre-funded warrant holder that would be disproportionately and materially adversely impacted by the amendment.

No Fractional Shares. No fractional shares or scrip representing fractional shares shall be issued upon the exercise of the pre-funded warrants. As to any fraction of a share which the holder would otherwise be entitled to purchase upon such exercise, we shall or shall cause, at our option, the payment of a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the exercise price of the pre-funded warrant per whole share or round such fractional share up to the nearest whole share.

Common Warrants

The material terms and provisions of the common warrants being issued in this offering are summarized below. The following description is subject to, and qualified in its entirety by, the form of common warrant which is filed herewith as an exhibit. You should review the form of common warrant for a complete description of the terms and conditions applicable to the common warrants. See “Information Incorporated by Reference and Available Information” below.

General. Each purchaser of shares will receive a common warrant to purchase one share of common stock for each share purchased in the offering.

Exercisability. The common warrants may be exercised at any time on or after their date of issuance, will have an exercise price of \$ per share and are exercisable until the fifth year anniversary of the date of issuance. The common warrants will be exercisable, at the option of each holder, in whole or in part by delivering a duly executed exercise notice to us accompanied by payment in full for the number of shares of our common stock purchased upon such exercise. The exercise price of the common warrant is subject to adjustment in the event of stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock.

Exercise Limitations. A holder of a common warrant will not have the right to exercise any portion of the common warrant if the holder (together with its affiliates) would beneficially own in excess of 4.99% (or, at election of holder, 9.99%) of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the common warrants. However, any holder may increase or decrease such percentage to any other percentage not in excess of 9.99% upon notice to us provided that any increase shall not be effective until 61 days following notice to us.

Transferability. Subject to applicable laws, the common warrants are separately tradeable immediately after issuance at the option of the holders and may be transferred at the option of the holders upon surrender of the common warrant to us together with the appropriate instruments of transfer.

No Listing. There is no established public trading market for the common warrants and we do not expect a market to develop. In addition, we do not intend to apply for listing of the common warrants on any securities exchange or trading system. Without an active market, the liquidity of the common warrants will be limited.

Fundamental Transactions. In the event of a “fundamental transaction,” as defined in the warrant agreement and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, the holders of the common warrants will be entitled to receive upon exercise of the common warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the common warrants immediately prior to such fundamental transaction.

In addition, in the event of a fundamental transaction (subject to certain exceptions), we or any successor entity shall, at the holder’s option, purchase the holder’s common warrants for an amount of cash equal to the value of the common warrants as determined in accordance with the Black-Scholes option pricing model.

Cashless Exercise. If, at the time a holder exercises its common warrant, there is no effective registration statement registering, or the prospectus contained therein is not available for an issuance of the shares underlying the common warrant to the holder, and the holder is not able to sell the shares issuable upon exercise of the common warrant without limitations on volume pursuant to Rule 144, then in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of our common stock determined according to a formula set forth in the common warrant. In the event of a cashless exercise, if we fail to timely deliver the shares underlying the common warrants, we will be subject to certain buy-in provisions.

Rights as a Stockholder. Except as otherwise provided in the common warrant or by virtue of a holder's ownership of shares of our common stock, the holders of the common warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until they exercise their common warrants.

Amendments. Amendments and waivers of the terms of the common warrants require the written consent of the holders of common warrants representing not less than a majority of the shares issuable upon exercise of the common warrants then outstanding and us, as well as any common warrant holder that would be disproportionately and materially adversely impacted by the amendment.

No Fractional Shares. No fractional shares or scrip representing fractional shares shall be issued upon the exercise of the common warrants. As to any fraction of a share which the holder would otherwise be entitled to purchase upon such exercise, we shall or shall cause, at our option, the payment of a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the exercise price of the common warrant per whole share or round such fractional share up to the nearest whole share.

Undesignated Preferred Stock

As of June 30, 2019, no shares of preferred stock of the Company were issued or outstanding. Our Certificate of Incorporation authorizes our board of directors to provide for the issuance of up to 30,000,000 shares of preferred stock in one or more series and to fix the preferences, powers and relative, participating, optional or other special rights, and qualifications, limitations or restrictions thereof, including the dividend rate, conversion rights, voting rights, redemption rights and liquidation preference, and to fix the number of shares to be included in any such series without any further vote or action by our stockholders. Any preferred stock so issued may rank senior to our common stock with respect to the payment of dividends or amounts upon liquidation, dissolution or winding up, or both. The issuance of preferred stock may have the effect of delaying, deferring or preventing a change in control of our company without further action by the stockholders and may adversely affect the voting and other rights of the holders of common stock. The issuance of preferred stock with voting and conversion rights may adversely affect the voting power of the holders of common stock, including the loss of voting control to others. At present, we have no plans to issue any preferred stock.

Anti-Takeover Provisions

Delaware Anti-Takeover Law

We are subject to Section 203 of the DGCL. Section 203 generally prohibits a public Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years after the date of the transaction in which the person became an interested stockholder, unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (a) shares owned by persons who are directors and also officers of the corporation and (b) shares issued under employee stock plans under which employee participants do not have the right to determine whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of its stock owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Warrants and Stock Options Issued and Outstanding

As of June 30, 2019, the Company had the following warrants outstanding to acquire shares of its common stock:

	Outstanding	Range of exercise price per share	Expiration dates
Common stock warrants issued prior to 2016	1,767	\$562.50 - \$735.00	2019
Common stock warrants issued in 2017	903,870	\$33.30	March 2022
Common stock warrants issued in 2018	1,181,375	\$12.00 - \$15.00	January 2023
Common stock warrants issued in 2019	1,382,913	\$5.00 - \$6.11875	2024
	<u>3,469,925</u>		

Additionally, as of June 30, 2019, we had 309,276 shares of common stock issuable upon the exercise of outstanding stock options under the 2015 Equity Plan at a weighted-average exercise price of \$55.78 per share.

UNDERWRITING

We have entered into an underwriting agreement dated _____, 2019, with H.C. Wainwright & Co., LLC as the sole book-running manager of this offering. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriter and the underwriter has agreed to purchase from us, at the combined public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, _____ shares of common stock and pre-funded warrants and accompanying common warrants to purchase _____ shares of common stock.

A copy of the underwriting agreement has been filed as an exhibit to the registration statement of which this prospectus is a part. The shares of common stock and pre-funded warrants and accompanying common warrants we are offering are being offered by the underwriter subject to certain conditions specified in the underwriting agreement.

We have been advised by the underwriter that it proposes to offer the shares of common stock and pre-funded warrants and accompanying common warrants directly to the public at the public offering prices set forth on the cover page of this prospectus. Any shares of common stock and pre-funded warrants and accompanying common warrants sold by the underwriter to securities dealers will be sold at the combined public offering price less a selling concession not in excess of \$ _____ per share of common stock and pre-funded warrant and accompanying common warrant.

The underwriting agreement provides that the underwriter's obligation to purchase the shares of common stock and pre-funded warrants and accompanying common warrants we are offering is subject to conditions contained in the underwriting agreement. The underwriter is obligated to purchase and pay for all of the shares of common stock and pre-funded warrants and accompanying common warrants offered by this prospectus, other than those shares covered by the option to purchase additional securities described below.

None of the securities included in this offering may be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sales of any of the securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons who receive this prospectus are advised to inform themselves about and to observe any restrictions relating to this offering of the securities and the distribution of this prospectus. This prospectus is neither an offer to sell nor a solicitation of any offer to buy the securities in any jurisdiction where that would not be permitted or legal.

The underwriter has advised us that it does not intend to confirm sales to any accounts over which it exercises discretionary authority.

Underwriting Discounts, Commissions and Expenses

We have agreed to pay an underwriter discount equal to 8.0% of the aggregate gross proceeds raised in this offering.

The following table shows the combined public offering price, underwriting discounts and commissions and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriter's option to purchase shares of common stock and/or common warrants.

The following table shows underwriting discounts and commissions payable to the underwriters by us in connection with this offering:

	Per Share and Common Warrant	Per Pre-Funded Warrant and Common Warrant	Total	
			Without Option Exercise	With Full Option Exercise
Public offering price	\$	\$	\$	\$
Underwriting discounts and commissions payable by us	\$	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$	\$

We estimate the total expenses payable by us for this offering to be approximately \$, which amount includes (i) an underwriting discount of \$ (\$ if the underwriter's option to purchase additional shares of common stock and/or common warrants is exercised in full), (ii) a management fee equal to 1% of the aggregate gross proceeds raised in this offering, (iii) a \$25,000 non-accountable expense allowance payable to the underwriter, (iv) reimbursement of the accountable expenses of the underwriter equal to \$100,000 including the legal fees of the underwriter being paid by us (none of which has been paid in advance), (v) the underwriter's clearing expenses in the amount of \$10,000 in connection with this offering and (vi) other estimated expenses of approximately \$ which include legal, accounting, printing costs and various fees associated with the registration and listing of our shares. The table also no sales of pre-funded warrants, which, if sold, would reduce the number of shares of common stock that we are offering on a one-for-one basis. In addition, we have agreed to issue the Underwriter Warrants to the underwriter. See "Underwriter Warrants" below for additional detail.

Option to Purchase Additional Securities

We have granted the underwriter an option for a period of 30 days from the date of this prospectus to purchase up to additional shares of our common stock and/or up to additional common warrants (15% of the shares and pre-funded warrants and accompanying common warrants issued in the offering) at a price per share equal to the combined public offering price, less the underwriting discounts and commissions. The underwriter may exercise its option at any time, and from time to time, within 30 days from the date of this prospectus. If any additional shares of common stock and/or common warrants are purchased pursuant to the option to purchase additional securities, the underwriter will purchase these shares on the same terms as those on which the securities are being offered hereby.

Underwriter Warrants

We have agreed to issue to the Underwriter Warrants to purchase shares of our common stock which represent 5% of the number of shares of common stock and pre-funded warrants being sold in this offering (including the shares of common stock and pre-funded warrants issued pursuant to the underwriter's exercise of its over-allotment option). The Underwriter Warrants will have a term of five years from the effective date of this prospectus and an exercise price per share equal to \$ per share, which represents 125% of the public offering price for the shares of common stock sold in this offering. Pursuant to FINRA Rule 5110(g), the Underwriter Warrants and any shares issued upon exercise of the Underwriter Warrants shall not be sold, transferred, assigned, pledged, or hypothecated, or be the subject of any hedging, short sale, derivative, put or call transaction that would result in the effective economic disposition of the securities by any person for a period of 180 days immediately following the date of effectiveness or commencement of sales of this offering, except the transfer of any security: (i) by operation of law or by reason of our reorganization; (ii) to any FINRA member firm participating in the offering and the officers or partners thereof, if all securities so transferred remain subject to the lock-up restriction set forth above for the remainder of the time period; (iii) if the aggregate amount of our securities held by the underwriter or related persons does not exceed 1% of the securities being offered; (iv) that is beneficially owned on a pro rata basis by all equity owners of an investment fund, provided that no participating member manages or otherwise directs investments by the fund and the participating members in the aggregate do not own more than 10% of the equity in the fund; or (v) the exercise or conversion of any security, if all securities remain subject to the lock-up restriction set forth above for the remainder of the time period.

Right of First Refusal

We have also granted the underwriter, for a period of 12 months from the closing date of this offering, a right of first refusal to act as sole book-running manager for a public offering or a private placement or any other capital-raising financing of equity (other than an at-the-market offering), equity-linked or debt securities using an underwriter or placement agent by us or any of our successors or subsidiaries. We have also agreed to a tail fee equal to the cash and warrant compensation in this offering if any investor to which the underwriter introduced us with respect to this offering during the term of its engagement provides us with further capital in a public or private offering or capital raising transaction during the 12-month period following termination of our engagement of the underwriter.

Nasdaq Capital Market Listing

Our stock is currently traded on the Nasdaq Capital Market under the symbol “DFFN.” On October 11, 2019, the last reported sale price of our common stock was \$1.78 per share. We do not plan to list the pre-funded warrants, common warrants or the Underwriter’s Warrants on the Nasdaq Capital Market or any other securities exchange or trading market.

Lock-up Agreements

Our officers and directors have agreed with the underwriter to be subject to a lock-up period of 90 days following the date of this prospectus. This means that, during the applicable lock-up period, such persons may not offer for sale, contract to sell, sell, distribute, grant any option, right or warrant to purchase, pledge, hypothecate or otherwise dispose of, directly or indirectly, any shares of our common stock or any securities convertible into, or exercisable or exchangeable for, shares of our common stock. We have also agreed in the underwriting agreement, subject to certain exceptions, to similar lock-up restrictions on the issuance and sale of our securities for 90 days following the closing of this offering, and to not issue any securities that are subject to a price reset based on trading prices of our common stock or upon a specified or contingent event in the future, or enter into an agreement to issue securities at a future determined price, for one year following the closing of this offering. The underwriter may, in its sole discretion and without notice, waive the terms of any of these lock-up agreements.

Stabilization, Short Positions and Penalty Bids

The underwriter may engage in syndicate covering transactions, stabilizing transactions and penalty bids or purchases for the purpose of pegging, fixing or maintaining the price of our common stock:

- Syndicate covering transactions involve purchases of shares in the open market after the distribution has been completed in order to cover syndicate short positions. Such a naked short position would be closed out by buying shares in the open market. A naked short position is more likely to be created if the underwriter is concerned that there could be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.
- Stabilizing transactions permit bids to purchase the shares so long as the stabilizing bids do not exceed a specific maximum.
- Penalty bids permit the underwriter to reclaim a selling concession from a syndicate member when the shares originally sold by the syndicate member are purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

These syndicate covering transactions, stabilizing transactions and penalty bids may have the effect of raising or maintaining the market prices of our shares or preventing or retarding a decline in the market prices of our shares. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. Neither we nor the underwriter make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on the Nasdaq Capital Market, in the over-the-counter market or on any other trading market and, if commenced, may be discontinued at any time.

In connection with this offering, the underwriter also may engage in passive market making transactions in our common stock in accordance with Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of the distribution. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for that security. However, if all independent bids are lowered below the passive market maker's bid that bid must then be lowered when specific purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

Neither we nor the underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the prices of our securities. In addition, neither we nor the underwriter make any representation that the underwriter will engage in these transactions or that any transactions, once commenced, will not be discontinued without notice.

Indemnification

We have agreed to indemnify the underwriter against certain liabilities, including certain liabilities arising under the Securities Act, or to contribute to payments that the underwriter may be required to make for these liabilities.

Other Relationships

The underwriter and its respective affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. The underwriter has received, or may in the future receive, customary fees and commissions for these transactions.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS

The following is a general discussion of the material U.S. federal income considerations applicable to the ownership and disposition of shares of our common stock and warrants acquired in this offering. This discussion is for general information only and is not tax advice. Accordingly, all prospective holders of our common stock and warrants should consult their own tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock and warrants. This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences described in this prospectus. We assume in this discussion that each holder holds shares of our common stock and warrants as capital assets within the meaning of Section 1221 of the Code (generally property held for investment).

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular holder in light of that holder's individual circumstances, does not address the alternative minimum or Medicare contribution taxes, and does not address any aspects of U.S. state, local or non-U.S. taxes or any U.S. federal taxes other than income tax. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address aspects of U.S. federal income taxation that may be applicable to investors that are subject to special tax rules, including without limitation:

- insurance companies;
- tax-exempt organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- real estate investment trusts;
- pension plans, individual retirement accounts and other tax deferred accounts;
- persons that mark their securities to market;
- controlled foreign corporations;
- passive foreign investment companies;
- "dual resident" corporations;
- persons that receive our common stock or warrants as compensation for the performance of services;
- owners that hold our common stock or warrants as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- owners that own, or are deemed to own, more than 5% of our capital stock (except to the extent specifically set forth below);
- persons that have a functional currency other than the U.S. dollar; and
- certain U.S. expatriates.

In addition, this discussion does not address the tax treatment of partnerships or other pass-through entities for U.S. federal income tax purposes, or persons who hold our common stock or warrants through partnerships or other pass-through entities for U.S. federal income tax purposes. A partner in a partnership or other pass-through entity that will hold our common stock or warrants should consult his, her or its own tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock or warrants through a partnership or other pass-through entity, as applicable.

There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We have not obtained, nor do we intend to obtain, a ruling from the IRS with respect to the U.S. federal income tax consequences of the purchase, ownership or disposition of our common stock or warrants.

Allocation of Purchase Price Between Common Stock or Pre-Funded Warrant and Accompanying Common Warrant to Purchase Our Common Stock

Each share of common stock or pre-funded warrant will be issued together with a common warrant, and each holder of our common stock and pre-funded warrants and common warrants must allocate the purchase price paid by such holder for our common stock or pre-funded warrant and an accompanying common warrant between the share of common stock or pre-funded warrant and the accompanying common warrant based on the relative fair market value of each. This allocation will establish a holder's initial tax basis for U.S. federal income tax purposes in their shares of common stock and pre-funded warrants and common warrants. We will not be providing holders with such allocation, and it is possible that different holders will reach different determinations regarding such allocation. A holder's allocation of purchase price between common stock and pre-funded warrants and common warrants is not binding on the IRS or the courts, and no assurance can be given that the IRS or the courts will agree with a holder's allocation.

Accordingly, each prospective holder should consult their own tax advisor with respect to the risks associated with an allocation of the purchase price between our common stock and pre-funded warrants and common warrants.

Treatment of Pre-Funded Warrants

Although it is not entirely free from doubt, a pre-funded warrant should be treated as a share of our common stock for U.S. federal income tax purposes and a holder of pre-funded warrants should generally be taxed in the same manner as a holder of common stock, as described below. Accordingly, no gain or loss should be recognized upon the exercise of a pre-funded warrant and, upon exercise, the holding period of a pre-funded warrant should carry over to the share of common stock received. Similarly, the tax basis of the pre-funded warrant should carry over to the share of common stock received upon exercise, increased by the exercise price of \$0.001 per share. Each holder should consult his, her or its own tax advisor regarding the risks associated with the acquisition of pre-funded warrants pursuant to this offering (including potential alternative characterizations). The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes.

U.S. Holders

This section applies to you if you are a "U.S. holder." For purposes of this discussion, a "U.S. holder" means a beneficial owner of our common stock and warrants who is for U.S. federal income tax purposes: (i) an individual who is a citizen or resident of the United States; (ii) a corporation, or any other organization taxable as a corporation for U.S. federal income tax purposes, created or organized in the United States or under the laws of the United States or of any state thereof or the District of Columbia; (iii) an estate, the income of which is subject to U.S. federal income tax regardless of its source; or (iv) a trust if (1) a U.S. court is able to exercise primary supervision over the trust's administration and one or more U.S. persons have the authority to control all of the trust's substantial decisions or (2) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

Distributions on Our Common Stock and Warrants

Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the U.S. holder's investment, up to such U.S. holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "—Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock." Dividends paid by us will generally be eligible for the reduced rates of tax for qualified dividend income allowed to individual U.S. holders and for the dividends received deduction allowed to corporate U.S. holders, in each case assuming that certain holding period and other requirements are satisfied.

Conversion of Common Warrants into Our Common Stock

Except as discussed below with respect to the cashless exercise of a common warrant, a U.S. holder will not recognize gain or loss on the conversion of common warrants into our common stock. A U.S. holder's tax basis in the common stock received upon a conversion will equal the sum of (i) the initial tax basis of the common warrants converted and (ii) price paid upon exercise. The U.S. holder's holding period for the common stock received upon exercise of the common warrants will begin on the date following the date of exercise of the common warrants and will not include the period during which the U.S. holder held the common warrants.

The tax consequences of a cashless exercise of a common warrant are not clear under current U.S. tax law. A cashless exercise may be tax-free, either because the exercise is not a realization event or because the exercise is treated as a recapitalization for U.S. federal income tax purposes. In this case, a U.S. holder's basis in the common stock received would equal the U.S. holder's basis in the common warrant. If the cashless exercise were treated as a recapitalization, the holding period of the common stock would include the holding period of the common warrant.

It is possible that a cashless exercise could be treated in part as a taxable exchange in which gain or loss would be recognized with respect to the common warrants surrendered to pay the exercise price for common warrants converted into common stock. In that event, a U.S. holder could be deemed to have surrendered only those common warrants used to satisfy the exercise price for an amount equal to the aggregate fair market value of the exercise price of the total number of common warrants to be exercised. The U.S. holder would recognize capital gain or loss in an amount equal to the difference between the amount deemed realized and the U.S. holder's tax basis in the common warrants surrendered to pay the exercise price. In this case, a U.S. holder's tax basis in the common stock received would equal the sum of the U.S. holder's initial investment in the converted common warrants (i.e., the portion of the U.S. holder's purchase price for the shares of common stock that is allocated to the common warrants, as described above under "—Allocation of Purchase Price between Common Stock and Warrants") and the exercise price of the common warrants converted. A U.S. holder's holding period for the common stock would commence on the date following the date of exercise.

Due to the absence of authority on the U.S. federal income tax treatment of a cashless exercise, there can be no assurance which, if any, of the alternative tax consequences and holding periods described above would be adopted by the IRS or a court of law. Accordingly, U.S. holders should consult their own tax advisors regarding the tax consequences of a cashless exercise.

If a common warrant is allowed to lapse unexercised, a U.S. holder generally will recognize a capital loss equal to such holder's tax basis in the common warrant.

Sale, Exchange or Other Taxable Disposition of Our Common Stock or Warrants

Upon the sale, exchange, or other taxable disposition of our common stock or warrants, a U.S. holder will recognize gain or loss equal to the difference between the amount realized upon the disposition and the U.S. holder's tax basis in the common stock or warrants sold or exchanged. Any gain or loss generally will be capital gain or loss, and will be long-term capital gain or loss if the U.S. holder's holding period for the common stock or warrants exceeded one year at the time of the disposition. Certain U.S. holders (including individuals) are currently eligible for preferential rates of U.S. federal income taxation in respect of long-term capital gains. The deductibility of capital losses is subject to significant limitations.

Information Reporting and Backup Withholding

In general, information reporting requirements may apply to dividends paid to a U.S. holder on our common stock, and to the proceeds of the sale, exchange or other disposition of our common stock and warrants, unless the U.S. holder is an exempt recipient. Backup withholding may apply to such payments if the U.S. holder fails to provide a taxpayer identification number, a certification of exempt status or has been notified by the IRS that it is subject to backup withholding (and such notification has not been withdrawn). Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules will be allowed as a refund or a credit against a U.S. holder's U.S. federal income tax liability provided the required information is timely furnished to the IRS.

Non-U.S. Holders

This section applies to you if you are a "non-U.S. holder". For purposes of this discussion, a "non-U.S. holder" means a person who is not a U.S. holder (as defined above under "U.S. Holders").

Distributions on Our Common Stock

Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such non-U.S. holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock."

Subject to the discussions below regarding backup withholding and the Foreign Account Tax Compliance Act, or FATCA, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a rate of 30% of the gross amount or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence, unless such dividends are effectively connected with a trade or business conducted by a non U.S. holder within the U.S (as discussed below). A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form), as applicable, and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may be able to obtain a refund or credit of any excess amounts withheld by timely filing the required information with the IRS.

Subject to the discussions below regarding backup withholding and FATCA, dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a "permanent establishment" or a "fixed base" maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. U.S. effectively connected income, net of specified deductions and credits, is generally taxed at the same graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

Conversion of Common Warrants into Our Common Stock

The U.S. federal income tax treatment of a non-U.S. holder's exercise of a common warrant, or the lapse of a common warrant held by a Non-U.S. Holder, generally will correspond to the U.S. federal income tax treatment of the exercise or lapse of a common warrant by a U.S. Holder, as described under "U.S. Holders—Conversion of Common Warrants into Common Stock" above.

Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock or Warrants

Subject to the discussions below regarding backup withholding and FATCA, in general, a non-U.S. holder will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale, exchange or other taxable disposition of shares of our common stock or warrants unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a "permanent establishment" or a "fixed base" maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on such gain at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Non-U.S. Holders—Distributions on Our Common Stock" also may apply to such gain;
- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the taxable disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the taxable disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any; or
- we are, or have been, at any time during the five-year period preceding such taxable disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation," unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the 5-year period ending on the date of the taxable disposition or the period that the non-U.S. holder held our common stock. If we are determined to be a U.S. real property holding corporation and the foregoing exception does not apply, then a purchaser may withhold 15% of the proceeds payable to a non-U.S. holder from a sale of our common stock or warrants, and the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions paid on our common stock to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock or warrants. Dividends paid to non-U.S. holders subject to the U.S. withholding tax, as described above in "Non-U.S. Holders—Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock and warrants by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS.

Withholding and Information Reporting Requirements—FATCA

FATCA may impose a U.S. federal withholding tax at a rate of 30% on payments of dividends on our common stock paid to certain foreign entities, unless (i) if the foreign entity is a “foreign financial institution,” such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a “foreign financial institution,” such foreign entity either certifies that it does not have any “substantial United States owners” (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (iii) the foreign entity otherwise qualifies from an exemption these rules. Under applicable U.S. Treasury Regulations, withholding under FATCA currently applies to payments of dividends paid on our common stock. A Non-U.S. holder that is not subject to FATCA withholding generally may certify its exempt status by furnishing a properly executed IRS Form W-8BEN or Form W-8BEN-E (or successor form), as applicable. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of the tax. Certain intergovernmental agreements between the United States and other countries may modify these rules. Non-U.S. holders should consult their own tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon for us by Dechert LLP. The underwriter is being represented by Ellenoff Grossman & Schole LLP, New York, New York.

EXPERTS

The consolidated financial statements of Diffusion Pharmaceuticals Inc. as of and for the years ended December 31, 2018 and 2017, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing. The audit report covering the December 31, 2018 consolidated financial statements contains an explanatory paragraph that states that the Company has suffered recurring losses from operations, has limited resources available to fund current research and development activities, and will require substantial additional financing to continue to fund its research and development activities that raise substantial doubt about its ability to continue as a going concern. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act, with respect to the securities being offered by this prospectus. This prospectus does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the securities offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

We file electronically with the SEC annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy statements and other information and amendments to those reports filed or furnished pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. The SEC maintains an Internet site (www.sec.gov) that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. Copies of these reports, proxy and information statements and other information may be obtained by electronic request at the following e-mail address: publicinfo@sec.gov.

We make available, free of charge and through our Internet web site at www.diffusionpharma.com, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendments to any such reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. We also make available, free of charge and through our Internet web site, to any stockholder who requests, the charters of our board committees, our Corporate Governance Guidelines and our Code of Business Conduct and Ethics. Requests for copies can be directed to Investor Relations at (434) 220-0718. The information set forth on, or connected to, our website is expressly not incorporated by reference into, and does not constitute a part of, this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information into this prospectus. This means we can disclose information to you by referring you to another document we filed with the SEC. We will make those documents available to you without charge upon your oral or written request. Requests for those documents should be directed to Investor Relations Department, Diffusion Pharmaceuticals Inc., 1317 Carlton Avenue, Suite 200, Charlottesville, Virginia 22902, Attention: Secretary, telephone: (434) 220-0718. This prospectus incorporates by reference the following documents (other than any portion of the respective filings furnished, rather than filed, under the applicable SEC rules) that we have filed with the SEC but have not included or delivered with this prospectus:

- our Annual Report on [Form 10-K for the fiscal year ended December 31, 2018, filed with the SEC on March 19, 2019](#);

- our Quarterly Reports on Form 10-Q for the fiscal quarters ended [March 31, 2019](#) and [June 30, 2019](#), filed with the SEC on May 9, 2019 and August 8, 2019, respectively;
- our Current Reports on Form 8-K filed with the SEC on [January 18, 2019](#), [May 28, 2019](#) and [June 13, 2019](#);
- our Definitive Proxy Statement on [Schedule 14A filed with the SEC on April 30, 2019](#); and
- the description of our common stock included in our amended registration statement on [Form 8-A filed on November 8, 2016](#) under the Exchange Act, and any amendment or report we may file with the SEC for the purpose of updating such description.

In addition, all documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, prior to the termination of the offering shall be deemed to be incorporated by reference into this prospectus (other than current reports or portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K).

You may request a free copy of any or all of the documents incorporated by reference in this prospectus by writing or telephoning us at the following address:

Diffusion Pharmaceuticals Inc.
1317 Carlton Avenue, Suite 200
Charlottesville, Virginia 22902
(434) 220-0718
Attention: Investor Relations

In accordance with Rule 412 of the Securities Act, any statement contained in a document incorporated by reference herein shall be deemed modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement.

Diffusion₂n

Pharmaceuticals Inc.

Shares of Common Stock

Pre-Funded Warrants to Purchase Shares of Common Stock

Warrants to Purchase up to Shares of Common Stock

PROSPECTUS

Sole Book-Running Manager

H.C. Wainwright & Co.

, 2019

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth all costs and expenses, other than underwriting discounts and commissions, paid or payable by us, in connection with the sale of the securities being registered under this registration statement. All amounts shown are estimates except for the SEC registration fee and the Financial Industry Regulatory Authority, Inc., or FINRA, filing fee.

	Amount
SEC registration fee	\$ 2,462.96
FINRA filing fee	2,975
Blue-sky qualification fees and expenses	1,500
Legal fees and expenses	60,000
Accounting fees and expenses	100,000
Transfer agent and registrar fees and expenses	2,500
Miscellaneous expenses	140,562.04
Total	\$ 310,000

* To be filed by amendment.

Item 14. Indemnification of Directors and Officers.

We are incorporated under the laws of the State of Delaware. Section 145 of the Delaware General Corporation Law (“DGCL”), provides that a Delaware corporation may indemnify any persons who are, or are threatened to be made, parties to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of such corporation), by reason of the fact that such person was an officer, director, employee or agent of such corporation, or is or was serving at the request of such person as an officer, director, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys’ fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding, provided that such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the corporation’s best interests and, with respect to any criminal action or proceeding, had no reasonable cause to believe that his or her conduct was illegal. A Delaware corporation may indemnify any persons who are, or are threatened to be made, a party to any threatened, pending or completed action or suit by or in the right of the corporation by reason of the fact that such person was a director, officer, employee or agent of such corporation, or is or was serving at the request of such corporation as a director, officer, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys’ fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit provided such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the corporation’s best interests except that no indemnification is permitted without judicial approval if the officer or director is adjudged to be liable to the corporation. Where an officer or director is successful on the merits or otherwise in the defense of any action referred to above, the corporation must indemnify him or her against the expenses which such officer or director has actually and reasonably incurred. Article V of our restated certificate of incorporation provides for indemnification of our directors and officers, and Article X of our amended and restated bylaws provides for indemnification of our directors, officers, employees and other agents, to the maximum extent permitted by the DGCL. We have entered into indemnification agreements with our officers and directors. In addition, we maintain a policy providing directors’ and officers’ liability insurance.

Section 102 of the DGCL permits a corporation to provide in its certificate of incorporation that a director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duties as a director, except for liability:

- for any breach of the director’s duty of loyalty to the corporation or its stockholders;
- for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- for acts related to unlawful stock repurchases, redemptions or other distributions or payment of dividends; or
- for any transaction from which the director derived an improper personal benefit.

Our restated certificate of incorporation and amended and restated bylaws include such a provision. Expenses incurred by any officer or director in defending any such action, suit or proceeding in advance of its final disposition shall be paid by us upon delivery to us of an undertaking, by or on behalf of such director or officer, to repay all amounts so advanced if it shall ultimately be determined that such director or officer is not entitled to be indemnified by us.

The Underwriting Agreement filed as Exhibit 1.1 to this Registration Statement provides for indemnification by the underwriters of us and our directors and officers for certain liabilities under the Securities Act, or otherwise.

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding securities issued by us since January 1, 2016 that were not registered under the Securities Act of 1933, as amended, or the Securities Act. Also included is the consideration, if any, received by us, for such securities and information relating to the Securities Act, or rule of the SEC, under which exemption from registration was claimed.

Acorn Advisory Services

On May 21, 2018 and October 22, 2018, we issued 3,031 and 4,762 shares of Common Stock (each as adjusted for the Reverse Stock Split), respectively, to Acorn Management Partners, L.L.C. as consideration for advisory services provided to us. The securities were issued to an accredited investor in reliance upon an exemption pursuant to Section 4(a)(2) of the Securities Act and the rules and regulations promulgated thereunder.

March 2017 Private Placement

In March 2017, we conducted a private placement (the “Private Placement”), pursuant to which we issued 12,376,329 shares of Series A Preferred Stock and 5-year warrants to purchase 825,099 shares of our common stock at an exercise price equal to \$33.30 per share (the “Warrants”). The aggregate gross proceeds from the Private Placement were \$25.0 million, prior to deducting placement agent fees and expenses payable by us. Maxim Merchant Capital, a division of Maxim Group LLC (“Maxim”), acted as our sole placement agent in the Private Placement. We issued to Maxim and its designees 5-year warrants, to purchase 78,638 shares of common stock at an exercise price equal to \$33.30 per share, with such warrants containing a cashless exercise provision. The securities were issued to accredited investors in reliance upon an exemption pursuant to Section 4(a)(2) of the Securities Act and the rules and regulations promulgated thereunder.

As part of the Private Placement, we entered into registration rights agreements with the investors in the Private Placement and Maxim, pursuant to which we agreed to file a registration statement to register for resale the shares of common stock (i) issued and outstanding as a result of, or issuable upon, the conversion of the shares of Series A Preferred Stock, (ii) issued and outstanding as a result of, or issuable upon, the exercise of the Warrants sold in the Private Placement and (iii) issuable as payment of dividends accruing on the Series A Preferred Stock. Such registration statement was declared effective on June 1, 2017.

On January 22, 2018, substantially concurrently with the completion our January 2018 public offering of common stock and warrants (the “January Offering”), all outstanding shares of Series A Preferred Stock mandatorily converted into an equivalent number of shares of our common stock. We were obligated to issue for no consideration to the holders of Series A Preferred Stock as of January 22, 2018 an aggregate of 553,752 shares of common stock upon conversion of the outstanding Series A Preferred Stock, 777,895 shares of common stock pursuant to a make-whole adjustment and an aggregate of 39,596 shares of common stock in respect of accrued but unpaid dividends on the Series A Preferred Stock. The dividend shares also include 7 shares of common stock issuable in respect of accrued but unpaid dividends on shares of Series A Preferred Stock converted into common stock voluntarily by the holder prior to the closing of the January Offering.

Warrant Private Placement

On May 23, 2019, we entered into a Securities Purchase Agreement with certain institutional and accredited investors (the “Securities Purchase Agreement”) providing for the sale in a registered direct offering by the Company of 1,317,060 shares of our common stock, par value \$0.001 per share at an offering price of \$4.77 for gross proceeds of approximately \$6,282,376 before the deduction of the placement agent fee and offering expenses. Concurrently with the closing of the transactions contemplated by the Securities Purchase Agreement, in a private placement transaction, we issued to the investors warrants to purchase an aggregate of 1,317,060 shares of our common stock at an initial exercise price equal to \$5.00 per share and to the placement agent warrants to purchase up to 65,853 shares of common stock at an initial exercise price equal to \$6.11875 per share. The warrants issued to the investors are exercisable for approximately five and one-half years beginning on the date of their issuance. The warrants issued to the placement agent have a term of approximately five years from the date of issuance and (other than the exercise price noted above) are otherwise substantially similar to the warrants issued to the investors. H.C. Wainwright & Co., LLC served as placement agent for the May 2019 private placement. The securities were issued to accredited investors in reliance upon an exemption pursuant to Section 4(a)(2) of the Securities Act and the rules and regulations promulgated thereunder. We registered the 1,382,913 shares of common stock underlying the investors’ warrants and the placement agent’s warrants on a registration statement on Form S-1 that was declared effective on October 8, 2019.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

See the Exhibit Index attached to this registration statement, which is incorporated by reference herein.

(b) Financial Statement Schedules.

No financial statement schedules are provided because the information called for is not required or is shown either in the financial statements or the notes thereto.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes:

- (1) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant’s annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan’s annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (2) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (3) That, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities, The undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser (i) any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424 promulgated under the Securities Act, (ii) any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant, (iii) the portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and (iv) any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

- (4) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (5) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (6) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

EXHIBIT INDEX

Exhibit No.	Description	Method of Filing
1.1	Underwriting Agreement, dated [____], by and between the Company and H.C. Wainwright & Co., LLC	To be filed by amendment
3.1	Certificate of Incorporation of Diffusion Pharmaceuticals Inc., as amended	Incorporated by reference to Exhibit 3.1 to the registrant's annual report on Form 10-K for the year ended December 31, 2018
3.2	Bylaws of Diffusion Pharmaceuticals Inc., as amended	Incorporated by reference to Exhibit 3.4 to the registrant's annual report on Form 10-K for the year ended December 31, 2015
4.1	Form of Warrant issued to Investors in the 2017 Private Placement by Diffusion Pharmaceuticals Inc.	Incorporated by reference to Exhibit 4.1 to the registrant's current report on Form 8-K filed on March 15, 2017
4.2	Form of 2018 Common Stock Warrant	Incorporated by reference to Exhibit 4.1 to the registrant's current report on Form 8-K filed on January 19, 2018
4.3	Form of 2018 Underwriters' Warrant	Incorporated by reference to Exhibit 4.2 to the registrant's current report on Form 8-K filed on January 22, 2018
4.4	Form of May 2019 Warrant	Incorporated by reference to Exhibit 4.1 to the registrant's current report on Form 8-K filed on May 28, 2019

4.5	<u>Form of May 2019 Placement Agent’s Warrant</u>	Incorporated by reference to Exhibit 4.2 to the registrant’s current report on Form 8-K filed on May 28, 2019
4.6	Form of Common Warrant	To be filed by amendment
4.7	Form of Pre-Funded Warrant	To be filed by amendment
4.8	Form of Underwriter’s Warrant	To be filed by amendment
5.1	Opinion of Dechert LLP	To be filed by amendment
10.1	<u>Employment Agreement, dated as of September 6, 2016, by and between David G. Kalergis and Diffusion Pharmaceuticals Inc.*</u>	Incorporated by reference to Exhibit 10.1 to the registrant’s current report on Form 8-K as filed on September 8, 2016
10.2	<u>Amended and Restated Employment Agreement, dated as of September 21, 2018, by and between William Karl Hornung and Diffusion Pharmaceuticals Inc.*</u>	Incorporated by reference to Exhibit 10.1 to the Company’s Current Report on Form 8-K filed September 27, 2018.
10.3	<u>Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan*</u>	Incorporated by reference to Exhibit 10.2 to the registrant’s current report on Form 8-K as filed on June 18, 2015
10.4	<u>Amendment No. 1 to Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan*</u>	Incorporated by reference to Appendix B to the registrant’s definitive proxy statement on Schedule 14A filed on June 10, 2016
10.5	<u>Form of Diffusion Pharmaceuticals Inc. Stock Option Award Agreement*</u>	Incorporated by reference to Exhibit 10.5 to the registrant’s annual report on Form 10-K for the year ended December 31, 2017
10.6	<u>Form of Diffusion Pharmaceuticals LLC Stock Option Award Agreement*</u>	Incorporated by reference to Exhibit 10.24 to the registrant’s annual report on Form 10-K for the year ended December 31, 2015

10.7	<u>Form of 2015 Incentive Stock Option Agreement under the Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan*</u>	Incorporated by reference to Exhibit 10.3 to the registrant's current report on Form 8-K filed on June 18, 2015
10.8	<u>Form of 2015 Non-Statutory Stock Option Agreement under the Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan*</u>	Incorporated by reference to Exhibit 10.4 to the registrant's current report on Form 8-K filed on June 18, 2015
10.9	<u>Form of Stock Option Agreement between the Company and certain former Executive Officers*</u>	Incorporated by reference to Exhibit 10.12 to the registrant's annual report on Form 10-K for the fiscal year ended December 31, 2014
10.10	<u>Form of Stock Option Agreement between the Company and certain former Directors*</u>	Incorporated by reference to Exhibit 10.13 to the registrant's annual report on Form 10-K for the fiscal year ended December 31, 2014
10.11	<u>Form of Indemnification Agreement between Diffusion Pharmaceuticals Inc. and each of its Directors and Officers*</u>	Incorporated by reference to Exhibit 10.3 to the registrant's annual report on Form 10-K for the year ended December 31, 2015
10.12	<u>Lease Agreement, dated March 31, 2017, by and between Diffusion Pharmaceuticals Inc. and One Carlton LLC</u>	Incorporated by reference to Exhibit 10.4 to the registrant's quarterly report on Form 10-Q for the quarter ended March 31, 2017
10.13	<u>Contingent Value Rights Agreement, dated as of January 8, 2016, by and between Diffusion Pharmaceuticals Inc. and Computershare, Inc., as Rights Agent</u>	Incorporated by reference to Exhibit 10.2 to the registrant's current report on Form 8-K filed on January 8, 2016

21.1	Subsidiaries of Diffusion Pharmaceuticals Inc.	Incorporated by reference to Exhibit 21.1 to the registrant's annual report on Form 10-K for the year ended December 31, 2018
23.1	Consent of KPMG LLP, independent registered public accounting firm	Filed herewith
23.2	Consent of Dechert LLP	Included in Exhibit 5.1 hereto
24.1	Powers of Attorney	Included on the signature pages hereto
*	A management contract or compensatory plan or arrangement.	

SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Charlottesville, Virginia, on the 16th day of October, 2019.

Diffusion Pharmaceuticals Inc.

By: /s/ David G. Kalergis

David G. Kalergis

Chief Executive Officer (Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints David G. Kalergis and William K. Hornung, and each of them, as his true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him and in his name, place or stead, in any and all capacities, to sign any and all amendments to this registration statement (including post-effective amendments), and to sign any registration statement for the same offering covered by this registration statement that is to be effective upon filing pursuant to Rule 462(b) promulgated under the Securities Act, and all post-effective amendments thereto, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
<u>/s/ David G. Kalergis</u> David G. Kalergis	Chief Executive Officer and Chairman of the Board <i>(Principal Executive Officer)</i>	October 16, 2019
<u>/s/ William K. Hornung</u> William K. Hornung	Chief Financial Officer <i>(Principal Financial & Accounting Officer)</i>	October 16, 2019
<u>/s/ Robert Adams</u> Robert Adams	Director	October 16, 2019
<u>/s/ John L. Gainer</u> John L. Gainer, Ph.D.	Director	October 16, 2019
<u>/s/ Mark T. Giles</u> Mark T. Giles	Director	October 16, 2019
<u>/s/ Alan Levin</u> Alan Levin	Director	October 16, 2019

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Diffusion Pharmaceuticals Inc.:

We consent to the use of our report incorporated by reference herein and to the reference to our firm under the heading “Experts” in the prospectus.

Our report dated March 19, 2019 contains an explanatory paragraph that states that the Company has suffered recurring losses from operations, has limited resources available to fund current research and development activities, and will require substantial additional financing to continue to fund its research and development activities that raise substantial doubt about its ability to continue as a going concern. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ KPMG LLP

McLean, Virginia
October 16, 2019