

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

Form S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Diffusion Pharmaceuticals Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State of Incorporation)

2020 Avon Court, #4
Charlottesville, VA 22902
(434) 220-0718
(Address, including zip code, and telephone number, including area code, of
registrant's principal executive offices)

30-0645032
(I.R.S. Employer
Identification No.)

David G. Kalergis
Chief Executive Officer
2020 Avon Court, #4
Charlottesville, VA 22902
(434) 220-0718

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

With a Copy to:
David S. Rosenthal, Esq.
Dechert LLP
1095 Avenue of the Americas
New York, New York 10036
(212) 698-3500

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

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, other than securities offered only in connection with dividend or interest reinvestment plans, 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 registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Accelerated Filer

Non-Accelerated Filer

Smaller Reporting Company

Emerging Growth Company

(Do not check if a smaller reporting company)

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered ⁽¹⁾	Proposed Maximum Offering Price per Security ⁽²⁾	Proposed Maximum Aggregate Offering Price ⁽²⁾	Amount of Registration Fee
Common Stock, \$0.001 par value per share	26,467,801	\$ 2.90	\$ 76,756,622.90	\$ 8,896.10

(1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), the shares being registered hereunder include such indeterminate number of shares of the Common Stock of the Company as may be issuable with respect to the shares being registered hereunder as may be issuable as a result of any stock dividend, stock split, recapitalization or other similar transaction.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) under the Securities Act. The offering price per share and aggregate offering price are based upon the average of the high and low prices per share of the Company's common stock, \$0.001 par value per share, as reported on the NASDAQ Capital Market, on May 11, 2017, a date within five business days prior to the filing of this registration statement.

- (3) Includes (i) 12,376,329 shares issued or issuable upon conversion of the Company's Series A Convertible Preferred Stock, (ii) 13,555,887 shares issued or issuable upon exercise of the Company's warrants issued in connection with its private placement of Series A Convertible Preferred Stock and (iii) an estimated 535,585 shares issuable as payment of dividends accruing through October 1, 2017 with respect to the Company's Series A Convertible Preferred Stock.

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 which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 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 prospectus is not complete and may be changed. The Selling Stockholders 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 is not soliciting an offer to buy or sell these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MAY 17, 2017

Diffusio₂n

Pharmaceuticals Inc.
Diffusion Pharmaceuticals Inc.

Common Stock
Up to 26,467,801 Shares of Common Stock
Offered by the Selling Stockholders

This prospectus relates to the resale or other disposition from time to time by the selling stockholders identified herein (including, except as the context may otherwise require, their donees, pledgees, transferees or other successors-in-interest, the "Selling Stockholders"), of, subject to adjustment, up to 26,467,801 shares of the common stock, \$0.001 par value per share (the "Common Stock"), of Diffusion Pharmaceuticals Inc. (the "Company"). Of these shares, (a) 12,376,329 are issued and outstanding as a result of, or issuable upon, the conversion of the Company's outstanding shares of Series A convertible preferred stock, \$0.001 par value per share (the "Series A Preferred Stock"), (b) 13,555,887 are issued and outstanding as a result of, or issuable upon, the exercise of warrants to purchase shares of Common Stock (the "Warrants") and (c) an estimated 535,585 are issuable as payment of dividends accruing through October 1, 2017 with respect to the Series A Preferred Stock. The Selling Stockholders acquired all of the securities covered by this prospectus in connection with a private placement transaction in which we sold the Series A Preferred Stock and Warrants to accredited investors in closings conducted on March 14, 2017 and March 31, 2017 (or, as applicable, a subsequent donation, pledge or transfer thereof). We are registering the resale or other disposition of the shares of Common Stock to satisfy registration rights we have granted to the Selling Stockholders.

Our registration of the shares of Common Stock covered by this prospectus does not mean that the Selling Stockholders will offer or sell any of the shares. The Selling Stockholders (including their donees, pledgees, transferees or other successors-in-interest) may, from time to time, resell or otherwise dispose of any or all of the shares of Common Stock described in this prospectus on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices, and may be to or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions. The Selling Stockholders will pay all underwriting discounts, commissions and any similar expenses it incurs, if any, in connection with the sale of the shares of Common Stock, and any related legal expenses incurred by it. We have agreed to pay certain expenses in connection with this registration statement and to indemnify the Selling Stockholders against certain liabilities. None of our shares of Common Stock may be sold without delivery of the applicable prospectus supplement describing the method and terms of the offering of the Common Stock. See "Plan of Distribution" beginning on page 19 for more information regarding the manners in which Selling Stockholders may sell or dispose of the securities registered hereby.

We are not selling any shares of Common Stock under this prospectus and will not receive any of the proceeds from the sale of shares of Common Stock by the Selling Stockholders. To the extent Warrants are exercised for cash, if at all, we will receive the exercise price thereof.

You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus carefully before you invest.

Our Common Stock is traded on the NASDAQ Capital Market under the symbol "DFFN." On May 16, 2017, the last reported sale price of our Common Stock was \$2.95 per share.

Investing in our Common Stock involves significant risks. See "Risk Factors" on page 7 of this prospectus, in our most recent Annual Report on Form 10-K, any of our other filings with the Securities and Exchange Commission and in any applicable prospectus supplement. You should read this prospectus, any accompanying prospectus supplement, and the documents incorporated by reference herein and therein carefully before you make your investment decision.

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

This prospectus is dated May 17, 2017

TABLE OF CONTENTS

	Page
ABOUT THIS PROSPECTUS	1
PROSPECTUS SUMMARY	2
THE OFFERING	6
RISK FACTORS	7
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS	8
USE OF PROCEEDS	9
THE SELLING STOCKHOLDERS	10
PLAN OF DISTRIBUTION	19
WHERE YOU CAN FIND MORE INFORMATION	22
LEGAL MATTERS	24
EXPERTS	24
PART II Information Not Required in Prospectus	25

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the U.S. Securities and Exchange Commission, or the Commission, using a “shelf” registration process. Under this process, the Selling Stockholders may from time to time, in one or more offerings, sell the Common Stock described in this prospectus.

You should rely only on the information provided in this prospectus, the related prospectus supplement, including any information incorporated by reference, and any pricing supplement. No one is authorized to provide you with information different from that which is contained, or deemed to be contained, in the prospectus, the related prospectus supplement and any pricing supplement. The Selling Stockholders are not making offers to sell Common Stock in any jurisdiction in which an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should not assume that the information in this prospectus, any prospectus supplement or any document incorporated by reference is accurate as of any date other than the date of the document in which the information is contained or other date referred to in that document, regardless of the time of sale or issuance of the Common Stock.

This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the Common Stock, you should refer to the registration statement including the exhibits. This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading “Where You Can Find Additional Information.” We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus were made solely for the benefit of the parties to such agreement, including in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless otherwise specified or unless the context requires otherwise, all references in this prospectus to “Diffusion,” the “Company,” “we,” “us,” “our” or similar references mean Diffusion Pharmaceuticals Inc. and its subsidiaries on a consolidated basis.

We have registered trademarks for RestorGenex and Diffusion. All other trade names, trademarks and service marks appearing in this prospectus are the property of their respective owners. Use or display by us of other parties’ trademarks, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owner.

PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our common stock under this prospectus. This summary does not contain all of the information that should be considered before investing in our common stock. Investors should read the entire prospectus carefully, including the risks related to our business and purchasing our common stock discussed under “Risk Factors” beginning on page 7 of this prospectus, “Special Notes Regarding Forward Looking Statements” and our financial statements and the notes to those financial statements incorporated by reference in this prospectus.

Diffusion Pharmaceuticals Inc.

Business Overview

We are a clinical stage biotechnology company focused on extending the life expectancy of cancer patients by improving the effectiveness of current standard-of-care treatments, including radiation therapy and chemotherapy. We are developing our lead product candidate, *transcrocetin sodium*, also known as *trans sodium crocetin* (“TSC”), for use in the many cancer types in which tumor oxygen deprivation (“hypoxia”) is known to diminish the effectiveness of current treatments. TSC is designed to target the cancer’s hypoxic micro-environment, re-oxygenating treatment-resistant tissue and making the cancer cells more susceptible to the therapeutic effects of standard-of-care radiation therapy and chemotherapy.

Our lead development programs target TSC against cancers known to be inherently treatment-resistant, including brain cancers and pancreatic cancer. A Phase 2 clinical program, completed in the second quarter of 2015, evaluated 59 patients with newly diagnosed glioblastoma multiforme (“GBM”). This open label, historically controlled study demonstrated a favorable safety and efficacy profile for TSC combined with 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 380% over the controls. At an End-Of-Phase 2 Meeting, the U.S. Food and Drug Administration provided Diffusion with extensive guidance on the design for a Phase 3 trial of TSC in newly diagnosed, inoperable GBM patients. We believe focusing on the inoperable patient group in Phase 3 should reduce the needed number of patients from over 400 to around 230, which is expected to provide real cost savings, while the strength of the Phase 2 efficacy signal should make the showing of significant clinical gain in Phase 3 more likely. Assuming FDA sign-off on our final protocol design, focusing on the inoperable patients, the study is planned to initiate by the end of 2017. Due to its novel mechanism of action, TSC has safely re-oxygenated a range of tumor types in our preclinical and clinical studies. Diffusion believes its therapeutic potential is not limited to specific tumors, thereby making it potentially useful to improve standard-of-care treatments of other life-threatening cancers. Additional planned studies include a Phase 2 trial in pancreatic cancer and a study in brain metastases, with a study initiation subject to receipt of additional funding or collaborative partnering. We also believe that TSC has potential application in other indications involving hypoxia, such as neurodegenerative diseases and emergency medicine. For example, our stroke program is now in advanced discussions with doctors from UCLA and the University of Virginia, with whom we have established a joint team dedicated to developing a program to test TSC in the treatment of stroke, with an in-ambulance trial of TSC in stroke under consideration.

In addition to the TSC programs, we are exploring alternatives regarding how best to capitalize upon the legacy RestorGenex product candidate, RES-529, a novel PI3K/Akt/mTOR pathway inhibitor which has completed two Phase I clinical trials for age-related macular degeneration and was in preclinical development in oncology, specifically GBM. RES-529 has shown activity in both in vitro and in vivo glioblastoma animal models and has been demonstrated to be orally bioavailable and can cross the blood brain barrier.

Corporate Information

We are a Delaware corporation. We maintain our principal executive offices at 2020 Avon Court, Suite #4, 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.

Summary of Private Placement

In March 2017, we conducted a private placement (the “Private Placement”), pursuant to which we issued 12,376,329 shares of the Series A Preferred Stock, initially convertible into one share of Common Stock, and 5-year warrants to purchase 12,376,329 shares of Common Stock at an exercise price equal to \$2.22 per share (the “Investor 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 (who are included as Selling Stockholders) 5-year warrants, to purchase of 1,179,558 shares of Common Stock at an exercise price equal to \$2.22 per share, with such warrants containing a cashless exercise provision (the “Maxim Warrants” and, together with the Investor Warrants, the “Warrants”). The securities were issued to accredited investors in reliance upon an exemption pursuant to Section 4(a)(2) of the Securities Act of 1933, as amended (the “Securities Act”), and the rules and regulations promulgated thereunder. Please see “Description of Capital Stock” for a description of our Common Stock, Series A Preferred Stock and Warrants.

As part of the Private Placement, we entered into registration rights agreements with the investors in the Private Placement and Maxim (the “Registration Rights Agreement”), 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. We are required to use our commercially reasonable best efforts to cause the registration statement to be declared effective under the Securities Act, as soon as practicable, but in no event later than 120 days after the final closing of the Private Placement, which occurred on March 31, 2017 (the “Final Closing”). We agreed to keep the registration statement effective until the earlier of (i) 66 months after the Final Closing or (ii) all registrable securities may be sold pursuant to Rule 144 under the Securities Act or another similar exemption under the Securities Act. We also agreed, among other things, to indemnify the investors under the registration statement from certain liabilities and to pay all fees and expenses incident to our performance of or compliance with the Registration Rights Agreement.

Series A Convertible Preferred Stock

Voting. The holders of the Series A Preferred Stock will be entitled to vote with the holders of Common Stock (and any other class or series that may similarly be entitled to vote with the holders of Common Stock as the Board may authorize and issue) and not as a separate class, at any annual or special meeting of stockholders of the Company, and may act by written consent in the same manner as the holders of Common Stock. In the event of any such vote or action by written consent, each holder of shares of Series A Preferred Stock shall be entitled to that number of votes equal to the whole number of shares of Common Stock into which the aggregate number of shares of Series A Preferred Stock held of record by such holder are convertible as of the close of business on the record date fixed for such vote or such written consent based on a conversion price, solely for such purpose, equal to the closing price of our Common Stock on the date such Series A Preferred Stock was issued. In addition, for as long as 50% of the shares of Series A Preferred Stock outstanding immediately after the final closing remain outstanding, without the consent of holders of at least a majority of the then outstanding shares of Series A Preferred Stock, we may not (a) amend our amended and restated certificate of incorporation (the “Certificate of Incorporation”) and amended and restated bylaws (the “Bylaws”) so as to materially and adversely affect any rights of the holders of the Series A Preferred Stock, (b) increase or decrease (other than by conversion of the Series A Preferred Stock) the authorized number of Series A Preferred Stock to be in excess of the number of shares required to satisfy the maximum offering amount of the Private Placement, (c) amend the Certificate of Designation of Preferences, Rights and Limitations of the Series A Convertible Preferred Stock of Diffusion Pharmaceuticals Inc. (the “Certificate of Designation”), (d) repay, repurchase or offer to repay, repurchase or otherwise acquire more than a *de minimis* number of shares of Common Stock or Common Stock equivalents or (e) enter into any agreement or understanding with respect to (a) through (d).

Dividends. The Series A Preferred Stock will be entitled to an 8.0% cumulative preferred dividend payable semi-annually in shares of Common Stock that will begin accruing on the issue date of the Series A Preferred Stock. The dividend will begin to accrue and be cumulative on the first day of each applicable dividend period and shall remain accumulated dividends with respect to such Series A Preferred Stock until paid; provided, that the first dividend payable with respect to any share of Series A Preferred Stock shall not begin to accrue until the date of original issuance of such share of Series A Preferred Stock. Dividends shall accrue whether or not there are profits, surplus or other funds of the Company legally available for the payment of dividends but shall not be payable until legally permissible, as applicable.

Liquidation. The Series A Preferred Stock will rank senior to the Common Stock and each other class of capital stock of the Company or series of Series A Preferred Stock of the Company authorized by the Board in the future that does not expressly provide that such class or series ranks senior to, or on parity with, the Series A Preferred Stock (“Junior Securities”). In the event of a Liquidation Event (as defined in the Certificate of Designation), the holders of the Series A Preferred Stock shall be entitled to receive, out of the assets of the Company or proceeds thereof legally available therefor, an amount in cash equal to 100% of the stated value of the Series A Preferred Stock before any payment or distribution of the assets of the Company is made or set apart for the holders of Junior Securities. In addition, prior to such Liquidation Event, the holders of Series A Preferred Stock shall be entitled to notice so that they may exercise their conversion rights prior to such event. If, upon the occurrence of any Liquidation Event, the assets of the Company, or proceeds thereof, distributable after payment in full of our creditors and any securities senior to the Series A Preferred Stock shall be insufficient to pay in full the aggregate amount of 100% of the stated value to the holders of the Series A Preferred Stock, the assets of the Company, or the proceeds thereof, shall be distributed ratably among the holders of any Series A Preferred Stock and the holders of any security ranked equally with the Series A Preferred Stock.

Conversion Rate: Each share of Series A Preferred Stock is convertible into a share of Common Stock at a conversion price equal to the \$2.02, subject to adjustment as provided in the Certificate of Designation and summarized herein (the “Conversion Price”), at any time after the final closing date at the holder’s sole and absolute discretion. Holders may immediately convert their Series A Preferred Stock prior to the occurrence of certain Liquidation Events. Each share of Series A Preferred Stock will automatically convert, initially, into a share of Common Stock (a) on any date that is more than thirty (30) trading days after the original issued date of such share Series A Preferred Stock that the 30 day moving average of the closing price of the Common Stock on the NASDAQ Capital Market (or any other exchange where the Common Stock is traded) exceeds \$8.00 per share (subject to adjustment in the event of a stock dividend or split), (b) upon a financing of at least \$10 million or (c) upon the majority vote of the voting power of the then outstanding shares of Series A Preferred Stock. We are not required to issue any fractional shares of Series A Preferred Stock or Common Stock in connection with the conversion of Series A Preferred Stock and may, in each case, at our discretion, pay the holder such amount in cash or deliver an additional whole share in lieu thereof.

Limitations of Conversion: The number of shares of Common Stock issuable upon a conversion of the Series A Preferred Stock that may be acquired by a holder shall be limited to the extent necessary to ensure that, following such conversion (or other issuance), the total number of shares of Common Stock then beneficially owned by such holder and its affiliates and any other persons whose beneficial ownership of Common Stock would be aggregated with the Holder’s for purposes of Section 13(d) of the Exchange Act, does not exceed 4.99% of the total number of issued and outstanding shares of Common Stock (including for such purpose the shares of Common Stock issuable upon such conversion). However, any holder may increase or decrease such percentage to any other percentage not in excess of 9.99% of the total number of shares of Common Stock then issued and outstanding provided that such increase in percentage shall not be effective until sixty-one (61) days after notice to the Company.

Dilution Protection. In the event we, at any time after the first date of issue of the Series A Preferred Stock and while at least one share of Series A Preferred Stock is outstanding: (a) pay a dividend or otherwise make a distribution or distributions on shares of its Common Stock or any other equity or equity equivalent securities payable in shares of Common Stock (which, for avoidance of doubt, shall not include any shares of Common Stock issued by the Company upon conversion of the Series A Preferred Stock or any debt securities), (b) subdivide outstanding shares of Common Stock into a larger number of shares, (c) combine (including by way of reverse stock split) outstanding shares of Common Stock into a smaller number of shares or (d) issue by reclassification of shares of Common Stock any shares of capital stock of the Company, then in each case the conversion price shall be multiplied by a fraction of which (x) the numerator shall be the number of shares of Common Stock (excluding treasury shares, if any) outstanding immediately before such event and (y) the denominator shall be the number of shares of Common Stock outstanding immediately after such event. Any adjustment made pursuant to this section shall become effective immediately after the effective date of the applicable event described in subsections (a) through (d) above.

Make-Whole Adjustment. In the event we, during the three years immediately following the Initial Closing, subject to certain exceptions, issue in an offering at least \$10 million of Common Stock or securities convertible into or exercisable for Common Stock at a per share price less than \$2.02 (the “Make-Whole Price”), we will be required to issue to the holders of Series A Preferred Stock a number of shares of Common Stock equal to the additional number of shares of Common Stock that such shares of Series A Preferred Stock would be convertible into if the conversion price of the Series A Preferred Stock was equal to 105% of the Make-Whole Price (the “Make-Whole Adjustment”). We are only obligated to issue shares with respect to a Make-Whole Adjustment in the first such subsequent offering, if any, following the Private Placement.

Warrants Issued in the Private Placement

As of May 5, 2017 there were 13,555,887 Warrants issued and outstanding. The Warrants have an exercise price \$2.22 per share, are immediately exercisable and are subject to customary anti-dilution adjustments. The Warrants are exercisable until March 31, 2022. The Warrants are subject to a provision prohibiting the exercise of such Warrants to the extent that, after giving effect to such exercise, the holder of such Warrant (together with the holder’s affiliates, and any other persons acting as a group together with the holder or any of the holder’s affiliates), would beneficially own in excess of 19.99% of the outstanding Common Stock. In addition, the Maxim Warrants contain a cashless exercise provision.

THE OFFERING

Selling Stockholders	Accredited investors who purchased shares of Series A Preferred Stock and Warrants the Private Placement conducted in March 2017, the placement agent for the Private Placement, Maxim, and its designees, and their respective donees, pledges, transferees and other successors-in-interest.
Common Stock offered by the Selling Stockholders	Subject to adjustment, up to 26,467,801 shares of Common Stock, which includes (a) 12,376,329 shares issued and outstanding as a result of, or issuable upon, the conversion of the Series A Preferred Stock, (b) 13,555,887 shares issued and outstanding as a result of, or issuable upon, the exercise of the Warrants and (c) an estimated 535,585 issuable as payment of dividends accruing through October 1, 2017 with respect to the Series A Preferred Stock.
Use of proceeds	We are not selling any shares of Common Stock under this prospectus and will not receive any of the proceeds from the sale of shares of Common Stock by the Selling Stockholders. To the extent Warrants are exercised for cash, we will receive the exercise price thereof.
Risk factors	Investing in our Common Stock involves a high degree of risk. See “Risk Factors” beginning on page 7 of this prospectus, and any other risk factors described in the documents incorporated by reference in this prospectus or in any accompanying prospectus supplement, for a discussion of factors that you should carefully consider before deciding to invest in our Common Stock.
NASDAQ Capital Market symbol	DFFN

RISK FACTORS

Investing in our Common Stock involves a high degree of risk. Prior to making any decision to invest in our securities, you should carefully consider the information contained or incorporated by reference in this prospectus or in any accompanying prospectus supplement, including, without limitation, the risks described in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, which is incorporated herein by reference, the risk factors described under the caption “Risk Factors” in any applicable prospectus supplement and any risk factors set forth in our other filings with the Commission, pursuant to Sections 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, before making an investment decision. The occurrence of any of these risks might cause you to lose all or a part of your investment in the offered securities. See “Where You Can Find More Information.”

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any applicable prospectus supplement and the documents incorporated by reference herein contain forward-looking statements within the meaning of Section 21E of the Exchange Act and Section 27A of the Securities Act, and are subject to the safe harbor created by those sections. We have identified some of these forward-looking statements with words like “believe,” “may,” “could,” “would,” “might,” “possible,” “potential,” “will,” “should,” “expect,” “intend,” “plan,” “predict,” “anticipate,” “estimate” and “continue”, the negative of these words, other words and terms of similar meaning and the use of future dates. Forward-looking statements involve risks and uncertainties. These uncertainties include factors that affect all businesses as well as matters specific to us. Forward-looking statements by their nature address matters that are, to different degrees, uncertain. Uncertainties and risks may cause our actual results to be materially different than those expressed in or implied by our forward-looking statements. For us, particular uncertainties and risks include, among others, our history of operating losses and negative cash flow, uncertainties regarding clinical testing, the difficulty of developing pharmaceutical products, obtaining regulatory and other approvals and achieving market acceptance and other risks and uncertainties described in our filings with the Commission, including:

- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- our ability to continue as a going concern;
- 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;
- our ability to obtain additional financing;
- 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;
- the success of competing products that are or become available; and
- the performance of third parties, including contract research organizations and manufacturers.

All forward-looking statements in this prospectus, any applicable prospectus supplement and the documents incorporated by reference herein speak only as of the date of this prospectus or any applicable prospectus supplement and are based on our current beliefs and expectations. We undertake no obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as otherwise required by law.

USE OF PROCEEDS

We will receive no proceeds from the sale of the Common Stock by the Selling Stockholders. To the extent Warrants are exercised for cash, we will receive the exercise price thereof.

The Selling Stockholders will pay any underwriting discounts and commissions and any similar expenses they incur in disposing of the Common Stock, if any, and any related legal expenses incurred by them. We will bear all other costs, fees and expenses incurred in effecting the registration of the Common Stock covered by this prospectus, including all registration and filing fees, fees and expenses of compliance with securities or “blue sky” laws, listing application fees, printing expenses, transfer agent’s and registrar’s fees, costs of distributing prospectuses in preliminary and final form as well as any supplements thereto, and fees and disbursements of counsel for the Company and all independent certified public accountants and other persons retained by the Company.

THE SELLING STOCKHOLDERS

This prospectus relates to the resale or other disposition from time to time by the Selling Stockholders identified herein (including their donees, pledgees, transferees or other successors-in-interest) of, subject to adjustment, up to 26,467,801 shares of Common Stock. Of these shares, (a) 12,376,329 are issued and outstanding as a result of, or issuable upon, the conversion of the Series A Preferred Stock, (b) 13,555,887 are issued and outstanding as a result of, or issuable upon, the exercise of the Warrants (including the Maxim Warrants) and (c) an estimated 535,585 are issuable as payment of dividends accruing through October 1, 2017 with respect to the Series A Preferred Stock. We entered into subscription agreements on March 14, 2017 and March 31, 2017 for the sale of an aggregate of 12,376,329 shares of the Series A Preferred Stock for aggregate gross proceeds of approximately \$25.0 million in the Private Placement to the investors therein. In addition, each such investor received a Warrant to purchase one share of Common Stock for each share of Series A Preferred Stock purchased by such investor in the Private Placement. In connection with the Private Placement, we entered into the Registration Rights Agreement with such investors. The filing of the registration statement of which this prospectus is a part is pursuant to our obligations to register the shares of Common Stock on behalf of the Selling Stockholders under the Registration Rights Agreement. All expenses incurred with the registration of the Common Stock owned by the Selling Stockholders will be borne by us. This prospectus will not cover subsequent sales of Common Stock purchased from a Selling Stockholder named in this prospectus.

We cannot predict when or whether any of the Selling Stockholders will convert their Series A Preferred Stock or exercise their Warrants and even if they do, we do not know how long the Selling Stockholders will hold the shares of Common Stock acquired upon conversion or exercise, as applicable, before selling them, and we currently have no agreements, arrangements or understandings with the Selling Stockholders regarding the sale or other disposition of any of the shares. The shares of Common Stock covered hereby may be offered from time to time by the Selling Stockholders.

Furthermore, we do not know when or in what amounts the Selling Stockholders may sell or otherwise dispose of the shares covered hereby. The Selling Stockholders might not sell any or all of the shares covered by this prospectus or may sell or dispose of some or all of the shares other than pursuant to this prospectus. Because the Selling Stockholders may not sell or otherwise dispose of some or all of the shares covered by this prospectus and because there are currently no agreements, arrangements or understandings with respect to the sale or other disposition of any of the shares, we cannot estimate the number of the shares that will be held by the Selling Stockholders after completion of the offering. For purposes of the table below, we have assumed that the Selling Stockholders will have sold all of the shares covered by this prospectus upon completion of the applicable offering.

The table below presents information regarding the Selling Stockholders and the shares of our Common Stock that they may sell or otherwise dispose of from time to time under this prospectus. The percentage of beneficial ownership is based upon 10,345,637 shares of Common Stock issued and outstanding as of May 5, 2017. Beneficial ownership is determined under Section 13(d) of the Exchange Act and generally includes voting or investment power with respect to securities and includes any securities that grant the Selling Stockholders the right to acquire Common Stock within 60 days of May 5, 2017. Information in the table below is based on information provided by or on behalf of the Selling Stockholders. Since the date on which they provided us with the information below, the Selling Stockholders may have sold, transferred or otherwise disposed of some or all of the shares in transactions exempt from the registration requirements of the Securities Act.

Name of Selling Stockholders ⁽¹⁾	Shares of Common Stock Beneficially Owned Before this Offering ⁽²⁾		Estimated Shares of Common Stock to be Issuable as Dividends on the Series A Preferred Stock at 10/1/2017	Number of Shares of Common Stock Being Offered Pursuant to this Prospectus ⁽³⁾	Shares of Common Stock Beneficially To Be Owned Upon Completion of this Offering ⁽⁴⁾	
	Number	Percentage ⁽⁵⁾	Number	Number	Number	Percentage ⁽⁵⁾
	ABG – USL1 Limited ⁽⁶⁾	1,127,182	9.9%	21,210	970,892	177,500
ACNYC, LLC	607,550	4.6%	11,056	506,106	112,500	1.1%
Adam Lipson	99,010	*	2,211	101,221	—	—
Adam T Drobot & Lucy S. Drobot JT Ten	27,254	*	553	25,307	2,500	*
Adolfo Carmona & Donna Carmona JT TEN	93,170	*	1,857	85,027	10,000	*
Advanced Ambulatory ANES LLC Defined Benefit Plan	272,526	2.6%	5,528	253,054	25,000	*
Albert Gentile & Heidi Lyn Gentile JT TEN	41,604	*	884	40,488	2,000	*
Alva Terry Staples	24,952	*	557	25,509	—	—
Alyson D. Schlosser	37,154	*	774	35,428	2,500	*
Andrew Schwartzberg	455,446	4.2%	9,311	464,757	—	—
Andy Entertainment Limited	49,506	*	1,106	50,612	—	—
Angelo Moesslang & Monika Moesslang JT TEN	69,308	*	1,548	70,856	—	—
Anthony Daulerio	49,506	*	1,106	50,612	—	—
AR Properties C/O Dennis Repp	300,196	2.9%	3,354	153,550	150,000	1.4%
Arnold E. Spangler	101,510	*	2,211	101,221	2,500	*
Arnold T Hagler Separate Trust U/A/D 9/17/97 Arnold T Hagler TTEE	27,754	*	553	25,307	3,000	*
Barclay Armitage	89,160	*	1,880	86,040	5,000	*
Ben Crown	208,020	1.3%	4,422	202,442	10,000	*
Benjamin King	24,754	*	506	25,260	—	—
Benjamin L. Padnos	160,398	1.5%	3,279	163,677	—	—
Benjamin R. Hasty	27,254	*	506	25,260	2,500	*
BES Investments, LLC	133,812	1.3%	2,653	121,465	15,000	*
Bigger Capital Fund, L.P.	247,600	2.3%	5,062	252,662	—	—
Bowling Family Trust	55,446	*	1,238	56,684	—	—
Bradley Cuvelier	99,010	*	2,211	101,221	—	—
Brian Potiker Revocable Trust UAD 8/7/96 Brian Potiker TTEE	62,006	*	1,012	50,518	12,500	*

Bruce D. Goethe & Laura K. Goethe COMM PROP WROS	30,224	*	619	28,343	2,500	*
Bruce Inglis & Nancy Inglis JT TEN	27,254	*	553	25,307	2,500	*
Bryan Ezralow 1994 Trust UTD 12/22/1994 U/A/D 12/22/94 Bryan Ezralow TTEE AMD 12/01/12	198,020	1.9%	4,422	202,442	—	—
C. Barnes Darwin II	99,110	*	1,990	91,100	10,000	*
Carleen Tufo DTD 2/21/2017	27,254	*	553	25,307	2,500	*
Charles Brinkley	27,254	*	506	25,260	2,500	*
Chitayat Holdings, LLC	99,010	*	2,211	101,221	—	—
Ciro Giuseppe Randazzo	49,506	*	1,012	50,518	—	—
CJ Biotech II, LLC	222,774	2.1%	4,554	227,328	—	—
Clay Struve	109,010	1.0%	2,211	101,221	10,000	*
Craig Geers	38,154	*	708	35,362	3,500	*
Daniel P. Petro	32,254	*	553	25,307	7,500	*
David Abel	29,704	*	663	30,367	—	—
David Abraham & Joann Abraham JT TEN	133,714	1.2%	2,875	131,589	5,000	*
David D. Shively Rev Wealth Preservation Trust UAD 7/21/04						
David D. Shively TTEE	99,010	*	2,211	101,221	—	—
David E. Schwartz	83,708	*	1,548	70,856	14,400	*
David E.I. Pyott Revocable Living Trust U/A/D 4/18/14 David E.I. Pyott TTEE	495,050	4.6%	10,121	505,171	—	—
David Frydrych	505,546	4.7%	9,109	454,655	60,000	*
David G. Schmidt	1,169,643	10.6%	14,373	657,939	526,077	4.9%
David Pouland	99,010	*	2,211	101,221	—	—
David R. Victor Revocable Trust UAD 3/29/00 David R. Victor TTEE	54,506	*	1,106	50,612	5,000	*
David S. Nagelberg 2003 Rev TR U/A/D 07/02/03 David S. Nagelberg TTEE A/M/D 12/11/07	247,526	2.3%	5,528	253,054	—	—
David Schneider	218,020	2.1%	4,422	202,442	20,000	*
David Y. Norton	49,704	*	663	30,367	20,000	*
David Young & Karen Plaisance JT TEN	49,506	*	1,106	50,612	—	—
Dennis Shasha	114,010	1.1%	2,211	101,221	15,000	*
DJ&J, LLC	218,020	2.1%	4,422	202,442	20,000	*
Dominick Abel TOD	38,154	*	774	35,428	3,500	*
Donald E. Hinkle	32,664	*	662	30,326	3,000	*
Donald Sesterhenn	24,754	*	553	25,307	—	—
Douglas J. Gold	24,754	*	506	25,260	—	—
Dyke Rogers	207,920	2.0%	4,422	202,442	9,900	*

E.L. Property Trust UAD 7/01/83						
Robert C. Kopple TTEE	990,100	8.7%	22,112	1,012,212	—	—
Edgar D. Jannotta JR Exempt Family Trust U/A/D 10/02/1998						
Erika Pearsall TTEE	247,526	2.3%	5,061	252,587	—	—
Eldar Investments, LLC	24,754	*	506	25,260	—	—
Elevado Investments Company, LLC	208,020	2.0%	4,422	202,442	10,000	*
Eric Prescott Campbell	44,556	*	911	45,467	—	—
Erick Richardson	148,516	1.4%	3,036	151,552	—	—
Ernest W. Moody Revocable Trust U/A/D 01/14/09 Ernest W. Moody TTEE	1,215,100	10.7%	20,242	1,010,342	225,000	2.1%
EZ Colony Partners, LLC	208,020	2.0%	4,422	202,442	10,000	*
EZ MM & B Holdings, LLC	208,020	2.0%	4,422	202,442	10,000	*
G. Jan Van Heek	27,254	*	553	25,307	2,500	*
Garfinkle Revocable Trust UAD 5/15/08 Morris Garfinkle & Stephanie Garfinkle TTEES	106,510	1.0%	2,211	101,221	7,500	*
Gary M. Ferman	35,625	*	613	30,613	5,625	*
Gary W. Jaster	55,446	*	1,238	56,684	—	—
Graham Burton	990,100	8.7%	20,242	1,010,342	—	—
Graham R. Smith	54,506	*	1,106	50,612	5,000	*
Greenway Capital, L.P.	198,020	1.9%	4,048	202,068	—	—
Gregory L. Storm	123,764	1.2%	2,530	126,294	—	—
Henry Herzing Revocable Living Trust U/A/D 10/27/93 Henry Herzing TTEE AMD 05/22/00	475,842	4.4%	9,287	425,129	60,000	*
Howard J. Worman	27,254	*	553	25,307	2,500	*
IRA FBO Kristian Weinman Pershing LLC as Custodian Roth	20,000	*	409	20,409	—	—
IRA FBO Marhsall S Ezralow Pershing LLC as Custodian Roth Account	208,020	2.0%	4,422	202,442	10,000	
IRA FBO Robin J. Steele Pershing LLC as Custodian Rollover Account	99,010	*	2,024	101,034	—	—
IRA FBO Stephen R. Meyer Pershing LLC as Custodian Rollover Account	98,110	*	1,990	91,100	9,000	*
IRA FBO Steven Yost Pershing LLC as Custodian Roth Conversion Account #2	29,664	*	662	30,326	—	—

IRA FBO: Peter J. Spengler Pershing LLC as Custodian	99,010	*	2,211	101,221	—	—
IRA FBO: Roger L. Hawley Pershing LLC as Custodian	198,020	1.9%	4,422	202,442	—	—
Irrevocable Aloha Trust UAD 5/1/02 Marianne Schmitt Hellauer TTEE	198,020	1.9%	4,422	202,442	—	—
Irwin Blitt Revocable Trust UAD 1/28/78 Irwin Blitt TTEE AMD 1/11/07	54,506	*	1,106	50,612	5,000	*
Isymax Corp	22,000	*	491	22,491	—	—
Jack Cavin Holland 1979 Trust U/A/D 2/14/79 Jack Cavin Holland TTEE	49,506	*	1,012	50,518	—	—
Jack R. Frank II	27,254	*	506	25,260	2,500	*
Jacob D. Wiznitzer	34,654	*	708	35,362	—	—
James A. Kluge	31,754	*	553	25,307	7,000	*
James B. and Karen A Glavin Family Trust U/A/D 10/30/98 James B. and Karen A. Glavin TTEES	54,506	*	1,106	50,612	5,000	*
James Diasio	33,724	*	619	28,343	6,000	*
James F. Winschel, JR	49,506	*	1,106	50,612	—	—
James L. Dritz	36,496	*	681	31,177	6,000	*
James L. Payne & Arlene H. Payne TEN COMM	247,526	2.3%	5,528	253,054	—	—
James R. Hollingshead and Amita Hollingshead Revocable Living Trust 5/30/08 James and Amita Hollingshead TTEES	49,506	*	1,012	50,518	—	—
James W. Thomas	11,402	*	202	10,104	1,500	*
Jason Schmidt	49,506	*	1,106	50,612	—	—
Jay & Jennifer Ferguson JT TEN	99,010	*	2,024	101,034	—	—
Jayant Aphale	99,010	*	2,024	101,034	—	—
Jeff Kurtz	27,254	*	553	25,307	2,500	*
Jeffrey & Margaret Padnos 2010 Generation Trust F/B/O Benjamin Padnos	50,000	*	1,022	51,022	—	—
Jeffrey Bacha	24,750	*	506	25,256	—	—
Jeffrey S. Padnos & Margaret Mais Padnos JT TEN	100,000	*	2,044	102,044	—	—
Jeffrey Wren & Shannon Wren TEN COMM	24,754	*	506	25,260	—	—
Joel L. Hochman Revocable Trust UAD 12/08/94 Joel L. Hochman TTEE	81,758	*	1,658	75,916	7,500	*
Joel Yanowitz	19,802	*	405	20,207	—	—

John Florsheim	24,754	*	553	25,307	—	—
John Ford	24,754	*	506	25,260	—	—
John V. Wagner	54,506	*	1,106	50,612	5,000	*
Jonathan Gilliland	29,802	*	405	20,207	10,000	*
Jonathan Patronik	25,600	*	470	23,470	2,600	*
Joshua Gregg Berkowitz	148,516	1.4%	3,317	151,833	—	—
Juan Carlos Alzate Tejada	49,506	*	1,106	50,612	—	—
Juli-Ann Cialone	15,248	*	341	15,589	—	—
Karen Shasha	24,754	*	553	25,307	—	—
Keith Gelles	163,516	1.6%	3,317	151,833	15,000	*
Keller Enterprises, LLC	695,050	6.4%	10,121	505,171	200,000	1.9%
Kenmont Capital Private Equity Partners III	148,516	1.4%	3,317	151,833	—	—
Kenneth F. Buechler Trust 9/24/2007 UAD 9/24/07 Kenneth F. Buechler TTEE	24,754	*	506	25,260	—	—
Kevin Gabrik	19,802	*	405	20,207	—	—
Lambda IV, LLC	247,526	2.3%	5,528	253,054	—	—
Leonite Capital, LLC	74,258	*	1,518	75,776	—	—
Leslie Rudes Grandchildren Trust UAD 2/27/03 Lis Rudes Sandel TTEE	260,026	2.5%	5,061	252,587	12,500	*
Leipman Trust UAD 5/08/1984 Holger A Liepmann & Loraine Liepmann TTEES AMD 4/22/12	44,556	*	957	45,513	—	—
Lisa Rudes Grandchildren Trust UAD 2/13/03 Lis Rudes Sandel TTEE	260,026	2.5%	5,060	252,586	12,500	*
Loeb Holding Corporation	99,010	*	2,211	101,221	—	—
Louis Vigden	109,010	*	2,024	101,034	10,000	*
Lundring Family Trust U/A/D 2/13/02 Eric Lundring and Lori Yost Lundring TTEES	29,704	*	663	30,367	—	—
Mai 2, LLC	346,536	3.2%	7,739	354,275	—	—
Marc Cohen	39,904	*	774	35,428	5,250	*
Marc R. Jalbert	49,506	*	1,106	50,612	—	—
Mark Grinbaum and Tatyana Grinbaum JT TEN	74,308	*	1,548	70,856	5,000	*
Mark H. Rubin	64,358	*	1,316	65,674	—	—
Mark Ravich	24,754	*	506	25,260	—	—
Marsha K. Ederer	74,258	*	1,518	75,776	—	—
Mayhar Eidgah	24,754	*	553	25,307	—	—
Maxim Merchant Capital(7)	1,377,695	4.9%	—	1,179,558	198,137	1.9%
Michael Cohn & Paula Cohn JT TEN	27,452	*	557	25,509	2,500	*
Michael P. Ross	203,020	1.9%	4,422	202,442	5,000	*

Monte D. Anglin & Janet S.						
Anglin JT TEN	27,254	*	553	25,307	2,500	*
Neil H. Wasserman	29,704	*	663	30,367	—	—
OSI Holdings, LLC	29,754	*	553	25,307	5,000	*
OSPREY I, LLC	81,758	*	1,658	75,916	7,500	*
Panella Living Trust U/A/D 05/11/04 Joseph Panella and Pan						
Panella TTEES	14,144	*	260	11,904	2,500	*
Patrick Lin	49,506	*	1,012	50,518	—	—
Peter B. Rauenbuehler & Mary L. Mines Living Trust U/A/D 09/26/05 Peter B. Rauenbuehler & Mary MinesTTEES	99,802	*	2,229	102,031	—	—
Peter D. Schiffrin	49,506	*	1,106	50,612	—	—
Peter john Freix	24,754	*	506	25,260	—	—
Pura Vida Master Fund, LTD	165,632	1.6%	3,386	169,018	—	—
Rande R Willison	29,754	*	506	25,260	5,000	*
Richard D. Cohen	150,892	1.4%	2,477	113,369	40,000	*
Richard Dvorak	29,324	*	619	28,343	1,600	*
Richard F. Braun	115,010	1.1%	2,211	101,221	16,000	*
Richard Martin Reiter	27,254	*	553	25,307	2,500	*
Richman Trust DTD 6/02/1983 UAD 6/02/83 Douglas Richman & Eva Richman TTEES AMD 1/6/14	29,704	*	663	30,367	—	—
Rick D. Mace & Karen Mace JT TEN	34,654	*	774	35,428	—	—
Robert C. Monks	26,000	*	409	20,409	6,000	*
Robert Charles Bourge	109,010	1.0%	2,211	101,221	10,000	*
Robert Giesen	13,402	*	221	10,123	3,500	*
Robert Kantor	54,506	*	1,106	50,612	5,000	*
Robert N Garff	57,050	*	1,166	58,216	—	—
Robin J. Steele Trust DTD 1/30/2015 Robin J. Steele TTEE AMD 05/04/15	99,010	*	2,211	101,221	—	—
Robin Rothstein & Jeffery Rothstein COMM PROP WROS	49,506	*	1,106	50,612	—	—
Ron Eller & Beth Eller JT TEN	32,724	*	619	28,343	5,000	*
RP Capital, LLC	455,446	4.2%	9,311	464,757	—	—
Russell Nowak	49,506	*	1,012	50,518	—	—
Russell S. Dritz	9,518	*	186	8,504	1,200	*
Ryan Miller & Gail Miller	29,704	*	663	30,367	—	—
Sean Janzer	24,754	*	553	25,307	—	—
Shamus, LLC	489,132	4.6%	5,765	263,897	231,000	2.2%
Sherry Casali	24,754	*	506	25,260	—	—
Shiloh Produce, Inc.	191,388	1.8%	3,913	195,301	—	—
Stanley M. Marks	54,506	*	1,106	50,612	5,000	*
Stephen Bender	109,010	1.0%	2,211	101,221	10,000	*

Stephen Dwayne Richards	49,506	*	1,106	50,612	—	—
Stephen J. Meringoff	495,050	4.6%	10,121	505,171	—	—
Stephen M. Payne	59,506	*	1,106	50,612	10,000	*
Stephen Mut	24,754	*	553	25,307	—	—
Steve Goodman & Helane Goodman JT TEN	39,604	*	884	40,488	—	—
Steven and Kaye Yost Family Trust U/A/D 02/07/92 AMD 6/04/97 Steven A. Yost and Kate Yost TTEES	59,902	*	1,114	51,016	10,000	*
Steven F. White	51,393	*	531	26,521	25,403	*
Steven Glassman	27,254	*	553	25,307	2,500	*
Steven H. Oram Revocable Trust UAD 5/17/06 Steven H. Oram & Terri Oram TTEES	54,506	*	1,106	50,612	5,000	*
Steven K. Luminais & Elizabeth Kindwall Luminais JT TEN	54,506	*	1,106	50,612	5,000	*
Steven M. Nelson	26,827	*	557	25,509	1,875	*
Swift Run Capital	990,100	8.7%	22,112	1,012,212	—	—
Terrence E. Troy	86,210	*	1,769	80,979	7,000	*
The A.C. Trust (Delaware) UAD 8/21/08 Seth Lapidow TTEE	495,050	4.6%	11,056	506,106	—	—
The Bahr Family Limited Partnership	119,912	1.1%	2,432	111,344	11,000	*
The Kentor Trust U/A/D 9/18/02 Eric Kentor and Adrienne Kentor TTEES	24,754	*	553	25,307	—	—
The Notas Family Trust UAD 8/13/1997 Bernard Notas & Eve Notas TTEES	69,308	*	1,548	70,856	—	—
The Oberkfell Living Trust U/A/D 12/18/02 HF Oberkfell & VA Oberkfell TTEES AMD 06/29/10	55,446	*	1,238	56,684	—	—
The R Scott Greer and Michelle Greer Revocable Trust U/A/D 10/01/00 R. Scott Greer and Michelle Greer TTEES	49,506	*	1,106	50,612	—	—
The Robert L. Bahr Revocable Trust UAD 3/14/85 Robert Bahr TTEE	89,110	*	1,990	91,100	—	—
The Stanford Baratz Revocable Trust U/A/D 09/07/94 Stanford Baratz & Amy Baratz TTEES	21,875	*	409	20,409	1,875	*
Thomas L. Eisenberg	28,754	*	553	25,307	4,000	*
Thomas L. Kempner	99,010	*	2,211	101,221	—	—
Thomas M Vertin	49,506	*	1,012	50,518	—	—
Timothy Michael Cicchese	99,010	*	2,211	101,221	—	—
Timothy P. Hanley & Monica Hanley JTWROS	99,010	*	2,211	101,221	—	—
Tom Sego	99,010	*	2,024	101,034	—	—
Trust of David Benaderet U/A/D 1/15/13 David Benaderet TTEE	54,506	*	1,106	50,612	5,000	*
Trust U/W Renee Weiss DTD 5/9/90 Peter H. Weiss TTEE	23,552	*	442	20,244	3,750	*
William Filon	21,802	*	442	20,244	2,000	*
William H. Costigan	24,754	*	506	25,260	—	—
William Huff	51,956	*	1,105	50,561	2,500	*
William Kadi & Sandra Marie Kadi JT TEN	24,754	*	506	25,260	—	—
William Krywicki & Nancie Krywicki JT TEN	49,506	*	1,106	50,612	—	—
William Strawbridge	24,754	*	553	25,307	—	—
Wilson Wilson & Wilson	44,556	*	910	45,466	—	—
Zhe Qiu	99,012	*	2,117	101,129	—	—

* Less than 1%

- (1) All information contained as of May 5, 2017.
- (2) Includes (a) shares of our Common Stock held by the applicable Selling Stockholder, (b) shares of Common Stock issuable upon exercise or conversion of convertible securities that are currently exercisable or convertible or are exercisable or convertible within 60 days of May 5, 2017 beneficially owned by the applicable Selling Stockholder outside of the Private Placement and (c) shares of Common Stock issuable to the applicable Selling Stockholder upon the conversion of the Series A Preferred Stock or the exercise of the Warrants sold in the Private Placement.
- (3) Consists only of (a) shares of Common Stock issuable to the applicable Selling Stockholder upon the conversion of the Series A Preferred Stock or the exercise of the Warrants sold in the Private Placement and (b) shares of Common Stock issuable to the applicable Selling Stockholder as dividends on the Series A Preferred Stock.
- (4) For purposes of this table, the Company assumes that all of the shares covered by this prospectus will be sold by the Selling Stockholders.
- (5) Based on a denominator equal to the sum of (a) 10,345,637 shares of our Common Stock outstanding on May 5, 2017, and (b) the number of shares of Common Stock issuable upon exercise or conversion of convertible securities that are currently exercisable or convertible or are exercisable or convertible within 60 days of May 5, 2017 beneficially owned by the applicable Selling Stockholder.
- (6) Shares beneficially owned is based solely on the Schedule 13G/A filed with the SEC on April 6, 2017 by Ally Bridge Group Capital Partners II, L.P. (“Ally Bridge”). The address of Ally Bridge is Unit 3002-3004, 30th Floor, Gloucester Tower, The Landmark, 15 Queen’s Road Central, Hong Kong. Amounts reported do not include 6,099 shares of Common Stock held by ABG II - SO Limited, as reported on the Schedule 13G/A filed with the SEC on April 6, 2017 by Ally Bridge. The conversion of the Series A Preferred Stock and the exercise of certain warrants held by this Selling Stockholder are subject to a 9.99% ownership blocker.
- (7) Maxim Merchant Capital, a division of Maxim Group LLC, a FINRA member broker-dealer, acted as our sole placement agent in the Private Placement. In connection with the Private Placement, we issued to Maxim and its designees 5-year warrants to purchase of 1,179,558 shares of Common Stock at an exercise price equal to \$2.22 per share, with such warrants containing a cashless exercise provision. The exercise of certain warrants held by this Selling Stockholder are subject to a 4.99% ownership blocker.

Each time the Selling Stockholders sell any shares of Common Stock offered by this prospectus, they are required to provide you with this prospectus and the related prospectus supplement, if any, containing specific information about the Selling Stockholders and the terms of the shares of Common Stock being offered in the manner required by the Securities Act.

No offer or sale may occur unless the registration statement that includes this prospectus has been declared effective by the Commission and remains effective at the time the Selling Stockholders offer or sell shares of Common Stock. We are required, under certain circumstances, to update, supplement or amend this prospectus to reflect material developments in our business, financial position and results of operations and may do so by an amendment to this prospectus, a prospectus supplement or a future filing with the Commission incorporated by reference in this prospectus.

This prospectus also covers any additional shares of Common Stock that become issuable in connection with the shares being registered by reason of any stock dividend, stock split, recapitalization or other similar transaction effected without the receipt of consideration which results in an increase in the number of our outstanding shares of Common Stock.

PLAN OF DISTRIBUTION

We are registering the shares of Common Stock issuable to the Selling Stockholders upon conversion of the Series A Preferred Stock or exercise of the Warrants issued to the Selling Stockholders to permit the resale of these shares of Common Stock by the holders thereof from time to time after the date of this prospectus, pursuant to the provisions of the Registration Rights Agreement. As used in this prospectus, "Selling Stockholders" includes donees, pledgees, transferees or other successors-in-interest selling shares received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other permitted transfer.

We will not receive any of the proceeds from the sale by the Selling Stockholders of the shares of Common Stock. We will bear all fees and expenses incident to our obligation to register the shares of Common Stock.

The Selling Stockholders may sell all or a portion of the shares of Common Stock beneficially owned by them and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of Common Stock are sold through underwriters or broker-dealers, the Selling Stockholders will be responsible for underwriting discounts, commissions or any similar expenses it incurs in disposing of the Common Stock, if any, and any related legal expenses incurred by it. The shares of Common Stock may be sold on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, in the over-the-counter market or in transactions otherwise than on these exchanges or systems or in the over-the-counter market and in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions. In addition, the Selling Stockholders may use any one or more of the following methods when selling shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;
- broker-dealers may agree with the Selling Stockholders to sell a specified number of such shares at a stipulated price per share;
- through the writing or settlement of options or other hedging transactions, whether such options are listed on an options exchange or otherwise;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The Selling Stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, as permitted by that rule, or Section 4(a)(1) under the Securities Act, if available, rather than under this prospectus, provided that they meet the criteria and conform to the requirements of those provisions.

Broker-dealers engaged by the Selling Stockholders may arrange for other broker-dealers to participate in sales. If the Selling Stockholders effect such transactions by selling shares of Common Stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the Selling Stockholders or commissions from purchasers of the shares of Common Stock for whom they may act as agent or to whom they may sell as principal. Such commissions will be in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with FINRA Rule 2121; and in the case of a principal transaction a markup or markdown in compliance with FINRA Rule 2121.01.

In connection with sales of the shares of Common Stock or otherwise, the Selling Stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the shares of Common Stock in the course of hedging in positions they assume. The Selling Stockholders may also sell shares of Common Stock short and if such short sale shall take place after the date that this Registration Statement is declared effective by the Commission, the Selling Stockholders may deliver shares of Common Stock covered by this prospectus to close out short positions and to return borrowed shares in connection with such short sales. The Selling Stockholders may also loan or pledge shares of Common Stock to broker-dealers that in turn may sell such shares, to the extent permitted by applicable law. The Selling Stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). Notwithstanding the foregoing, the Selling Stockholders have been advised that they may not use shares registered on this registration statement to cover short sales of our common stock made prior to the date the registration statement, of which this prospectus forms a part, has been declared effective by the Commission.

The Selling Stockholders may, from time to time, pledge or grant a security interest in some or all of the Warrants or shares of Series A Preferred Stock or Common Stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of Common Stock from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending, if necessary, the list of Selling Stockholders to include the pledgee, transferee or other successors in interest as Selling Stockholders under this prospectus. The Selling Stockholders also may transfer and donate the shares of Common Stock in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The Selling Stockholders and any broker-dealer or agents participating in the distribution of the shares of Common Stock may be deemed to be "underwriters" within the meaning of Section 2(a)(11) of the Securities Act in connection with such sales. In such event, any commissions paid, or any discounts or concessions allowed to, any such broker-dealer or agent and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Selling Stockholders who are "underwriters" within the meaning of Section 2(a)(11) of the Securities Act will be subject to the applicable prospectus delivery requirements of the Securities Act including Rule 172 thereunder and may be subject to certain statutory liabilities of, including but not limited to, Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Exchange Act.

Except as set forth herein, each Selling Stockholder has informed the Company that it is not a registered broker-dealer and does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the Common Stock. Upon the Company being notified in writing by a Selling Stockholder that any material arrangement has been entered into with a broker-dealer for the sale of common stock through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, a supplement to this prospectus will be filed, if required, pursuant to Rule 424(b) under the Securities Act, disclosing (i) the name of each such Selling Stockholder and of the participating broker-dealer(s), (ii) the number of shares of Common Stock involved, (iii) the price at which such the shares of Common Stock were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable, (v) that such broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus, and (vi) other facts material to the transaction. In no event shall any broker-dealer receive fees, commissions and markups, in the aggregate, in excess of eight percent (8.0%) of any offering.

Under the securities laws of some states, the shares of Common Stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of Common Stock may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with. Subject to the terms of the Registration Rights Agreement, the Company has no obligation to qualify the resale of any shares in any particular state.

There can be no assurance that any Selling Stockholder will sell any or all of the shares of Common Stock registered pursuant to the shelf registration statement, of which this prospectus forms a part.

Each Selling Stockholder and any other person participating in such distribution will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including, without limitation, to the extent applicable, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of Common Stock by the Selling Stockholder and any other participating person. To the extent applicable, Regulation M may also restrict the ability of any person engaged in the distribution of the shares of Common Stock to engage in market-making activities with respect to the shares of Common Stock. All of the foregoing may affect the marketability of the shares of Common Stock and the ability of any person or entity to engage in market-making activities with respect to the shares of Common Stock.

We will pay all expenses of the registration of the shares of Common Stock pursuant to the registration rights agreement, including, without limitation, Commission filing fees and expenses of initial compliance with state securities or “blue sky” laws; *provided, however*, that each selling stockholder will pay all underwriting discounts, commissions and any similar expenses it incurs in disposing of the Common Stock, if any, and any related legal expenses incurred by it. We will indemnify the Selling Stockholders against certain liabilities, including some liabilities under the Securities Act, in accordance with the Registration Rights Agreements, or the Selling Stockholders will be entitled to contribution. We may be indemnified by the Selling Stockholders against civil liabilities, including liabilities under the Securities Act that may arise from any written information furnished to us by the Selling Stockholders specifically for use in this prospectus, in accordance with the related Registration Rights Agreements or we may be entitled to contribution.

WHERE YOU CAN FIND MORE INFORMATION

Available Information

We file annual, quarterly and current reports, proxy statements and other information with the Commission. You may read and copy any of this information at the Commission's public reference room at 100 F Street, N.E., Washington, D.C. 20549. Please call the Commission at (800) SEC-0330 or (202) 942-8090 for further information on the public reference room. The Commission also maintains an Internet website that contains reports, proxy statements and other information regarding issuers, including us, who file electronically with the Commission. The address of that site is www.sec.gov.

We also maintain an Internet website at www.diffusionpharma.com, which can be used to access free of charge, through the investor relations section, our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, current reports on Form 8-K and any amendments to those reports, as soon as reasonably practicable after we electronically file such material with or furnish it to the Commission and all such reports of ours going forward. 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.

This prospectus is part of a registration statement on Form S-3 that we have filed with the Commission under the Securities Act, for the registration under the Securities Act of the securities offered hereby. This prospectus does not contain all the information set forth in the registration statement, parts of which are omitted in accordance with the rules and regulations of the Commission. Reference is hereby made to the registration statement which contains further information with respect to our company and our securities. Statements herein concerning the provisions of documents filed as exhibits to the registration statement are necessarily summaries of such documents, and each such statement is qualified by reference to the copy of the applicable document filed with the Commission.

Incorporation of Documents by Reference

The Commission 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 Commission. 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., 2020 Avon Court, Suite 4, 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 Commission rules) that we have filed with the Commission but have not included or delivered with this prospectus:

- Our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, as amended, filed with the Commission on March 31, 2017.
- Our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2017, filed with the Commission on May 15, 2017.
- Our Current Reports on Form 8-K filed on January 9, 2017, January 26, 2017 (to the extent not furnished), March 15, 2017, April 3, 2017 and April 11, 2017.
- Our Definitive Proxy Statement on Schedule 14A filed on May 12, 2016.
- The description of our Common Stock included in our amended registration statements on Form 8-A filed on November 8, 2016 under the Exchange Act, and any amendment or report we may file with the Commission for the purpose of updating such description.

We also incorporate by reference into this registration statement and prospectus any future filings we will make with the Commission under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of the offering of the securities covered by this prospectus (other than current reports or portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K). This additional information is a part of this prospectus from the date of filing of those documents.

Any statements made in this prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document, which is also incorporated or deemed to be incorporated into this prospectus, modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus. The information relating to us contained in this prospectus should be read together with the information in the documents incorporated by reference.

LEGAL MATTERS

The validity of the issuance of the Common Stock offered by this prospectus will be passed upon for us by Dechert LLP, New York, New York. Any underwriter or agent will be advised about other issues relating to any offering by its own legal counsel.

EXPERTS

The consolidated financial statements of Diffusion Pharmaceuticals Inc. as of and for the years ended December 31, 2016 and 2015, 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, 2016 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, which 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 that uncertainty.

PART II

Information Not Required in Prospectus

Item 14. Other Expenses of Issuance and Distribution

The following is a statement of the expenses (all of which are estimated) to be incurred by us in connection with a distribution of the Common Stock registered under this registration statement:

SEC registration fee	\$	8,896
Legal fees and expenses	\$	35,000
Accounting fees and expenses	\$	7,050
Printing fees		*
Miscellaneous		*
Total	\$	<u>50,946</u>

* The estimated expenses are presently indeterminable and will be set forth in the applicable prospectus supplement with respect to any offering of the Common Stock registered hereunder.

Item 15. Indemnification of Directors and Officers

The summary set forth below does not purport to be complete and is subject to and qualified in its entirety by reference to our Certificate of Incorporation and Bylaws, each of which is incorporated by reference as an exhibit to the registration statement of which this prospectus is a part, and the applicable provisions of the Delaware General Corporation Law.

We are incorporated under the laws of the State of Delaware. Section 145 of the Delaware General Corporation Law 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 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 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. Our certificate of incorporation and bylaws provide for the indemnification of our directors and officers to the fullest extent permitted under the Delaware General Corporation Law.

Section 102(b)(7) of the Delaware General Corporation Law 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:

- transaction from which the director derives an improper personal benefit;
- act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or redemption of shares; or
- breach of a director's duty of loyalty to the corporation or its stockholders.

Our certificate of incorporation includes 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 the Company.

As permitted by the Delaware General Corporation Law, we have entered into and intend to enter into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us to indemnify each director and officer to the fullest extent permitted by law and advance expenses to each indemnitee in connection with any proceeding in which indemnification is available.

We have an insurance policy covering our officers and directors with respect to certain liabilities, including liabilities arising under the Securities Act or otherwise.

Item 16. Exhibits

The exhibits to this registration statement are listed in the exhibit index that immediately precedes such exhibits and is incorporated herein by reference.

Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act;
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
 - (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i), (ii) and (iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Exchange Act that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment 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.
- (3) 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.
- (4) That, for the purpose of determining liability under the Securities Act to any purchaser:
- (i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.
- (b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to section 13(a) or section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Exchange Act) that is incorporated by reference in the 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.
- (c) Insofar as indemnification for liabilities arising under the Securities Act 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 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

SIGNATURES

Pursuant to the requirements of the Securities Act, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement on Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Charlottesville, Commonwealth of Virginia, on this 17th day of May, 2017.

DIFFUSION PHARMACEUTICALS INC.

By: /s/ David G. Kalergis
David G. Kalergis
Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

KNOWN TO ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints David G. Kalergis, Chief Executive Officer and Director of Diffusion Pharmaceuticals Inc., his true and lawful attorney-in-fact and agent, who may act alone, with full powers of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any or all amendments to this registration statement, including post-effective amendments to this registration statement and registration statements filed pursuant to Rule 429 under the Securities Act, and to file the same, with all exhibits thereto, and other documents and in connection therewith, with the Commission, granting unto said attorney-in-fact and agent the 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, and hereby ratifies and confirms all his said attorney-in-fact and agent or his substitute or substitutes may lawfully do or cause to be done by virtue hereof.

This Power of Attorney may be executed in multiple counterparts, each of which shall be deemed an original, but which taken together shall constitute one instrument. Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ David G. Kalergis</u> David G. Kalergis	Chief Executive Officer and Chairman	May 17, 2017
<u>/s/ Ben L. Shealy</u> Ben L. Shealy	Senior Vice President – Finance, Treasurer and Secretary (Principal Financial Officer)	May 17, 2017
<u>/s/ Isaac Blech</u> Isaac Blech	Vice Chairman, Board of Directors	May 17, 2017
<u>/s/ John L. Gainer</u> John L. Gainer, Ph.d.	Director	May 17, 2017
<u>/s/ Robert Adams</u> Robert Adams	Director	May 17, 2017
<u>/s/ Mark T. Giles</u> Mark T. Giles	Director	May 17, 2017
<u>/s/ Alan Levin</u> Alan Levin	Director	May 17, 2017

EXHIBIT INDEX

Exhibit No.	Description
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, 2016 (File No. 001-37942), filed March 31, 2017).
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 (File No. 001-24477), filed March 25, 2016).
3.3	Certificate of Designations for Series A Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37942), filed March 15, 2017).
3.4	Certificate of Conversion, as filed with the Secretary of State of the State of Delaware on June 18, 2015 (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-24477), filed June 18, 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 (File No. 001-37942), filed March 15, 2017).
4.2	Form of Registration Rights Agreement entered into by and among the Company and Investors in the 2017 Series A Private Placement (incorporated by reference to Exhibit 4.2 to the Registrant's Quarterly Report on Form 10-Q for the period ended March 31, 2017 (File No. 001-37942), filed May 15, 2017).
4.3	Form of Diffusion Pharmaceuticals Inc. Convertible Note Agreement (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-37942), filed October 3, 2016).
4.4	Form of Diffusion Pharmaceuticals LLC Convertible Note Agreement (incorporated by reference to Exhibit 4.7 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2015 (File No. 001-24477), filed March 25, 2016).
5.1	Opinion of Dechert LLP regarding validity
10.1	Placement Agency Agreement, dated January 27, 2017, by and between Diffusion Pharmaceuticals Inc. and Maxim Merchant Capital, a division of Maxim Group LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-37942), filed March 15, 2017).
10.2	Form of 2017 Private Placement Subscription Agreement (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-37942), filed March 15, 2017).
10.3	Amendment to the Placement Agency Agreement, dated March 14, 2017, by and between Diffusion Pharmaceuticals Inc. and Maxim Merchant Capital, a division of Maxim Group LLC (incorporated by reference to Exhibit 10.17 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2016 (File No. 001-37942), filed March 31, 2017).
23.1	Consent of KPMG LLP
23.2	Consent of Dechert LLP (included in Exhibit 5.1)
24.1	Powers of Attorney (included on signature page of the Registration Statement)



1095 Avenue of the Americas
 New York, NY 10036-6797
 +1 212 698 3500 Main
 +1 212 698 3599 Fax
 www.dechert.com

May 17, 2017

Diffusion Pharmaceuticals Inc.
2020 Avon Court, #4
Charlottesville, VA 22902

Re: Diffusion Pharmaceuticals Inc.

Dear Ladies and Gentlemen:

We have acted as counsel to Diffusion Pharmaceuticals Inc., a Delaware corporation (the "Company"), in connection with the preparation and filing by the Company of a Registration Statement on Form S-3 (the "Registration Statement"), including the prospectus constituting a part thereof (the "Prospectus"), with the U.S. Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended (the "Act"), on or about the date hereof, with respect to the resale from time to time by the selling stockholders set forth in the Registration Statement (the "Selling Stockholders"), of up to an aggregate of 26,467,801 shares of the Company's common stock, par value \$0.001 per share ("Common Stock") consisting of (a) 12,376,329 shares issued and outstanding as a result of, or issuable upon, the conversion of the Company's outstanding shares of Series A convertible preferred stock, \$0.001 par value per share (the "Series A Preferred Stock"), (b) 13,555,887 shares issued and outstanding as a result of, or issuable upon, the exercise of warrants to purchase shares of Common Stock (the "Warrants") and (c) an estimated 535,585 shares issuable as payment of dividends accruing through October 1, 2017 with respect to the Series A Preferred Stock. The Registration Statement provides that the Common Stock may be offered in amounts, at prices and on terms to be set forth in one or more supplements to the Prospectus (each, a "Prospectus Supplement"). This opinion letter is being furnished to the Company in accordance with the requirements of Item 601(b)(5) under Regulation S-K of the Act, and we express no opinion herein as to any matter other than as to the legality of the Common Stock.

In rendering the opinion expressed below, we have examined and relied on originals or copies, certified or otherwise identified to our satisfaction, of such agreements, corporate records and other instruments and such documents, certificates and receipts of public officials, certificates of officers and other representatives of the Company and others, and such other documents as we have deemed necessary or appropriate as a basis for rendering the opinion set forth below, including the following documents:

- (i) the Registration Statement;
- (ii) the Prospectus;

A Pennsylvania Limited Liability Partnership

US Austin Boston Charlotte Hartford New York Newport Beach Philadelphia Princeton San Francisco Silicon Valley Washington DC EUROPE Brussels
 London Luxembourg Moscow Munich Paris ASIA Beijing Hong Kong

- (iii) the Company's Certificate of Designations of Series A Convertible Preferred Stock, as filed with the Secretary of State of the State of Delaware on March 13, 2016 (the "Series A Certificate of Designations");
- (iv) the Company's Certificate of Incorporation, as filed with the Secretary of State of the State of Delaware on June 18, 2015 (as amended on January 8, 2016, August 17, 2016 and January 23, 2017, and together with the Series A Certificate of Designations, the "Certificate of Incorporation");
- (v) the Company's Amended and Restated Bylaws effective as of January 8, 2016 (the "Bylaws");
- (vi) the form of Warrant;
- (vii) a certificate of good standing with respect to the Company issued by the Secretary of State of the State of Delaware, dated May 15, 2017; and
- (viii) the resolutions of the board of directors of the Company (the "Board of Directors"), relating to, among other things, the authorization and approval of the preparation and filing of the Registration Statement, certified as of the date hereof by an officer of the Company.

As to the facts upon which this opinion is based, we have relied upon certificates of public officials and certificates and written statements of officers, directors, employees and representatives of, and accountants for, the Company and we have assumed in this regard the truthfulness of such certifications and statements. We have not independently established the facts so relied on.

In our examination, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as original documents, the conformity to original documents of all documents submitted to us as copies, the legal capacity of natural persons who are signatories to the documents examined by us and the legal power and authority of all persons signing on behalf of the parties to all documents (other than the Company). We have further assumed that there has been no oral modification of, or amendment or supplement (including any express or implied waiver, however arising) to, any of the agreements, documents or instruments used by us to form the basis of the opinion expressed below.

On the basis of the foregoing and such examination of law as we have deemed necessary, and subject to the assumptions and qualifications set forth in this letter, we are of the opinion that the shares of Common Stock, when issued upon conversion of the Series A Preferred Stock or upon exercise of the Warrants, in each case in accordance with their respective terms, or when issued as a dividend in accordance with the Certificate of Incorporation, as the case may be, are or will be validly issued, fully paid and non-assessable.



The opinion set forth in this letter relates only to the Federal laws of the United States of America, the laws of the State of New York, and, to the extent relevant, the General Corporation Law of the State of Delaware (the "DGCL"). We express no opinion concerning the laws of any other jurisdiction, and we express no opinion concerning any state securities or "blue sky" laws, rules or regulations, or any federal, state, local or foreign laws, rules or regulations relating to the offer and/or sale of the Common Stock.

The opinion expressed herein is based upon the law as in effect and the documentation and facts known to us on the date hereof. We have not undertaken to advise you of any subsequent changes in the law or of any facts that hereafter may come to our attention.

This opinion letter has been prepared for your use solely in connection with the Registration Statement. We assume no obligation to advise you of any changes in the foregoing subsequent to the effectiveness of the Registration Statement.

We hereby consent to the filing of this opinion as an exhibit to the Registration Statement and to the reference to this firm under the caption "Legal Matters" in the prospectus that forms a part of the Registration Statement. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission thereunder.

Very truly yours,

/s/ Dechert LLP

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 31, 2017 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. The conditions 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
May 17, 2017