

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

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

DIFFUSION PHARMACEUTICALS INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

2834
(Primary Standard Industrial
Classification Code Number)

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

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

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

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

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

With a Copy to:

**David S. Rosenthal, Esq.
Dechert LLP
1095 Avenue of the Americas
New York, New York 10036
(212) 698-3500**

**Robert F. Charron, Esq.
Ellenoff Grossman & Schole LLP
1345 Avenue of the Americas
New York, New York 10105
(212) 370-1300**

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

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

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

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

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

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

Large accelerated filer

Non-accelerated filer (Do not check if a smaller reporting company)

Accelerated filer

Smaller reporting company

Emerging growth company

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

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Proposed maximum aggregate offering price(1)	Amount of registration fee
Common Stock, \$0.001 par value per share (2)(3)	\$ 14,950,000	\$ 1,861.28

- (1) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(o) under the Securities Act. Includes the offering price of any additional securities that the underwriter has the option to purchase.
- (2) Includes \$1,950,000 of shares of common stock, as well as shares of common stock under any underwriter's option to purchase additional shares.
- (3) Pursuant to Rule 416 under the Securities Act, the securities being registered hereunder include such indeterminate number of additional securities as may be issued after the date hereof as a result of stock splits, stock dividends or similar transactions.

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

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

Subject to completion, dated December 20, 2017

PRELIMINARY PROSPECTUS

Diffusio₂n

Pharmaceuticals Inc.

Shares of Common Stock

We are offering _____ shares of our common stock. Our common stock is listed on the Nasdaq Capital Market under the symbol “DFFN.” On _____, 2017, the last reported sale price of our common stock on the Nasdaq Capital Market was \$ _____ per share. The public offering price per share will be determined between us and the underwriter at the time of pricing, and may be at a discount to the current market price.

Investing in our securities involves a high degree of risk. See the section entitled “Risk Factors” beginning on page 4 of this prospectus and in the documents incorporated by reference into this prospectus for a discussion of risks that should be considered in connection with an investment in our securities.

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

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

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

The offering is being underwritten on a firm commitment basis. We have granted the underwriter an option for a period of 30 days from the date of this prospectus to purchase up to an amount of additional shares of our common stock equal to 15% of the number of shares issued in this offering at a price per share equal to the public offering price, less the underwriting discounts and commissions.

The underwriter expects to deliver the shares of common stock to purchasers on or about _____, 2017.

Sole Book-Running Manager

H.C. Wainwright & Co.

The date of this prospectus is _____, 2017

TABLE OF CONTENTS

	Page
Prospectus Summary	6
The Offering	9
Risk Factors	10
Special Note Regarding Forward-Looking Statements	13
Use of Proceeds	15
Capitalization	16
Dilution	18
Description of Capital Stock	20
Market Price of our Common Stock	23
Underwriting	25
Legal Matters	28
Experts	28
Where You Can Find Additional Information	28
Incorporation of Certain Information by Reference	28

ABOUT THIS PROSPECTUS

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

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

PROSPECTUS SUMMARY

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

Diffusion Pharmaceuticals Inc.

Business Overview

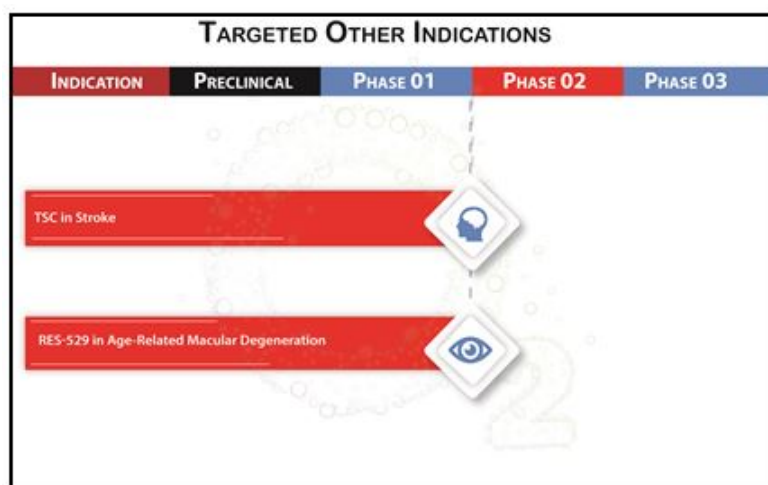
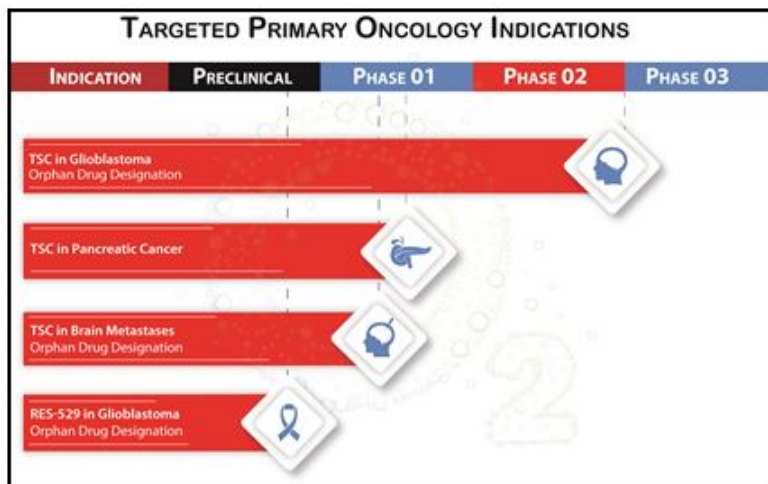
We are a clinical stage biotechnology company focused on extending the life expectancy of cancer patients by improving the effectiveness of current standard-of-care treatments, including radiation therapy and chemotherapy. We are developing our lead product candidate, transcrocetinate sodium, also known as trans sodium crocetininate (“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-oxygenate treatment-resistant tissue and make 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, with a focus on brain cancers. A Phase 2 clinical program, completed in the fourth quarter of 2015, evaluated 59 patients with newly diagnosed glioblastoma multiforme (“GBM”), a particularly deadly form of primary brain cancer. This open label, historically controlled study demonstrated a favorable safety and efficacy profile for TSC combined with standard of care, including a 36% improvement in overall survival over the control group at two years. A strong efficacy signal was seen in the inoperable patients, where survival of TSC-treated patients at two years was increased by almost four-fold over the controls. The U.S. Food and Drug Administration, or FDA, has provided Diffusion with final protocol guidance for a Phase 3 trial of TSC in this newly diagnosed inoperable GBM patient population. The Company has responded to all outstanding points raised by the FDA and plans to begin the trial under the protocol permitted by the FDA by the end of 2017. The trial will enroll 236 patients in total, 118 in each arm. 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 one specific tumor type, thereby making it potentially useful to improve standard-of-care treatments of other life-threatening cancers. Given TSC’s safety profile and animal data, we can, with appropriate funding, move directly into Phase 2 studies in other cancers. We also believe that TSC has potential application in other indications involving hypoxia, such as neurodegenerative diseases and emergency medicine. For example, a stroke program is now under discussion 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. Planning for such a trial is on-going.

In addition to the TSC programs, we are exploring alternatives regarding how best to capitalize upon our product candidate RES-529, which may include possible out-licensing and other options. RES-529 is a novel PI3K/Akt/mTOR pathway inhibitor which has completed two Phase 1 clinical trials for age-related macular degeneration and is 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.

Summary of Current Product Candidate Pipeline

The following tables, as of September 30, 2017, summarizes the targeted clinical indications for Diffusion’s lead molecule, TSC:



TSC eligible for Phase 2 studies based on preclinical and clinical data from prior Phase 1 and Phase 2 clinical trials, including GBM and Peripheral Artery Disease.

Potential Conversion of Series A Preferred Stock

If we sell at least \$10 million in gross proceeds of securities in this offering, substantially concurrently with the completion of this offering, our Series A Preferred Stock will automatically convert into the applicable number of shares of our common stock pursuant to the terms set forth in our Certificate of Incorporation, as amended. Unless otherwise indicated, all information contained in this prospectus assumes the automatic conversion of all outstanding shares of Series A Preferred Stock into _____ shares (the “Conversion Shares”) of common stock (including accrued dividends paid in kind and the “make-whole” adjustment feature thereof) pursuant to the terms thereof, which will occur substantially concurrently with the consummation of this offering provided that we sell at least \$10 million in gross proceeds of securities in this offering. See “Description of Capital Stock.”

For purposes of calculating an assumed number of Conversion Shares we have assumed a public offering price of \$ _____ per share (the last reported sale price of our common stock on the Nasdaq Capital Market on _____, 2017) and that this offering is completed on _____, 2017.

There is no assurance that we will sell \$10 million of securities in this offering, in which case the Series A Preferred Stock would not automatically convert into shares of common stock. See “Risk Factors -- If we do not sell at least \$10 million of securities in this offering, the Series A Preferred Stock will remain outstanding.”

Corporate Information

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

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

THE OFFERING

Common stock offered by us in this offering	shares.
Common stock to be outstanding after this offering	shares.
Option to purchase additional shares	The underwriter has a 30-day option to purchase up to an amount of additional shares of our common stock equal to 15% of the number of shares issued in this offering at a price per share equal to the public offering price, less the underwriting discounts and commissions.
Use of proceeds	We intend to use the net proceeds from this offering to fund research and development of our lead product candidate, TSC, including clinical trial activities, and for general corporate purposes. See “Use of Proceeds.”
Risk factors	You should read the “Risk Factors” section of this prospectus for a discussion of certain of the factors to consider carefully before deciding to purchase any shares of our common stock in this offering.
National Securities Exchange Listing	Our common stock is listed on the Nasdaq Capital Market under the symbol “DFFN.”

The number of shares of our common stock to be outstanding after this offering is based on 14,503,976 shares of common stock outstanding as of September 30, 2017 and excludes as of that date:

- 213,879 shares issuable upon conversion of convertible promissory notes in an aggregate principal amount of \$0.6 million;
- 2,545,989 shares of common stock issuable upon the exercise of outstanding stock options under the Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan, as amended (the “2015 Equity Plan”), at a weighted-average exercise price of \$7.34 per share;
- 13,555,887 shares of common stock issuable upon the exercise of outstanding warrants issued in connection with the Series A Preferred Stock private placement, at a weighted-average exercise price of \$2.22 per share;
- 447,721 shares of common stock issuable upon the exercise of other outstanding warrants, at a weighted-average exercise price of \$44.52 per share; and
- 114,291 shares of common stock reserved for future issuance under the 2015 Equity Plan.

Unless otherwise indicated, all information contained in this prospectus assumes (i) no exercise by the underwriter of its option to purchase additional shares of common stock and (ii) the automatic conversion of all outstanding Series A Preferred Stock (including accrued dividends paid in kind and the “make-whole” adjustment feature thereof), which will occur substantially concurrently with the consummation of this offering provided that we sell at least \$10 million of securities in this offering. See “Description of Capital Stock.”

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, together with the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus, before making your decision to invest in shares of our common stock. We cannot assure you that any of the events discussed in the risk factors below will not occur. These risks could have a material and adverse impact on our business, results of operations, financial condition and cash flows, and our future prospects would likely be materially and adversely affected. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment. In addition, you should also carefully consider the other risks described under the heading “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2016 and our Quarterly Reports on Form 10-Q for the periods ended March 31, 2017, June 30, 2017 and September 30, 2017, which are incorporated herein by reference.

Risks Related to this Offering

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

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

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

To date, we have not sold, or received approval to sell, any pharmaceutical products. We do not expect to sell any pharmaceutical products for at least the next several years, if at all. Our net losses were approximately \$18.0 million, and \$6.7 million for the years ended December 31, 2016 and 2015, respectively. As of September 30, 2017 and December 31, 2016, we had incurred cumulative net losses totaling approximately \$63.3 million and \$60.2 million, respectively. Moreover, we expect that our net losses will continue and may increase for the foreseeable future. We may not be able to achieve projected results if we generate lower revenues (if any) or receive lower investment income than expected, or we incur greater expenses than expected, or all of the above. We may never generate sufficient product revenue (if any) to become profitable. We also expect to have quarter-to-quarter fluctuations in revenues, expenses, and losses, some of which could be significant.

We estimate that we will receive net proceeds of approximately \$ million from the sale of the securities offered by us in this offering, based on the assumed public offering price of \$ per share (the last reported sale price of our common stock on the NASDAQ Capital Market on , 2017), and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. In the event of a decrease in the proceeds to us from this offering as a result of a decrease in the assumed public offering price or the number of shares offered by us, we may need to raise additional capital sooner than we anticipate or may need to scale back or eliminate certain of our development programs.

We will need to raise more money to complete our planned clinical trials, continue the research and development necessary to bring our products to market and to establish marketing and additional manufacturing capabilities. We may seek additional funds through public and private stock offerings, government contracts and grants, arrangements with corporate collaborators, borrowings under lines of credit or other sources. However, we may not be able to raise additional funds on favorable terms, or at all. Conditions in the credit markets and the financial services industry may make equity and debt financing more difficult to obtain, and may negatively impact our ability to complete financing transactions. To the extent that we raise additional funds by issuing equity securities, our stockholders may experience significant dilution. Any debt financing, if available, may involve restrictive covenants, such as limitations on our ability to incur additional indebtedness and other operating restrictions that could adversely impact our ability to conduct our business.

If we are unable to obtain additional funds, we may have to scale back our development of new products, reduce our workforce, license to others products or technologies that we otherwise would seek to commercialize ourselves or, ultimately, cease operations. The amount of money we may need would depend on many factors, including:

- The costs and progress of our research and development programs;
- The scope and results of our preclinical studies and clinical trials;
- The amount of our legal expenses and any settlement or damages payments associated with litigation; and
- The time and costs involved in: obtaining necessary regulatory approvals; filing, prosecuting and enforcing patent claims; scaling up our manufacturing capabilities; and the commercial arrangements we may establish.

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

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

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares, including as a result of the “make-whole” feature of the Series A Preferred Stock.

The public offering price in this offering is substantially higher than the net tangible book value per share of our common stock. Investors purchasing common stock in this offering will pay a price per share that substantially exceeds the book value of our tangible assets after subtracting our liabilities. As a result, investors purchasing common stock in this offering will incur immediate dilution of \$ _____ per share, based on the assumed public offering price of \$ _____ per share. This dilution also reflects the reclassification of \$16.3 million common stock warrant liability to stockholders' equity as a result of the amendment of our certificate of incorporation on November 1, 2017 with respect to the dividend feature of the Series A Preferred Stock and the issuance of additional shares to the holders of our Series A Preferred Stock pursuant to the “make-whole” feature thereof (assuming the public offering price is less than \$2.02 per share). See “Description of Capital Stock.”

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

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

We are generally not restricted from issuing additional common stock, including any securities that are convertible into or exchangeable for, or that represent the right to receive, common stock. The market price of our common stock could decline as a result of sales of common stock or securities that are convertible into or exchangeable for, or that represent the right to receive, common stock after this offering or the perception that such sales could occur.

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

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

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

If we do not sell at least \$10 million of securities in this offering, the Series A Preferred Stock will remain outstanding.

If we sell at least \$10 million of securities in this offering, substantially concurrently with the completion of this offering, the Series A Preferred Stock will automatically convert into the applicable number of shares of our common stock pursuant to the terms set forth in our Certificate of Incorporation, as amended ("Certificate of Incorporation"). See "Description of Capital Stock." However, if at least \$10 million of securities are not sold in this offering, and the Series A Preferred Stock will not automatically convert into shares of our common stock and the outstanding shares of Series A Preferred Stock will rank senior to the shares of common stock in the event of a liquidation, dissolution or winding up of the Company. In the event of a Liquidation Event (as defined in the Certificate of Incorporation), 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 the common stock.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the other information and documents incorporated by reference herein include forward-looking statements. We may, in some cases, use terms such as “believes,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “will,” “should,” “approximately” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements appear in and are incorporated by reference into a number of places throughout this prospectus and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, our intellectual property position, the degree of clinical utility of our products, particularly in specific patient populations, our ability to develop commercial functions, expectations regarding clinical trial data, our results of operations, cash needs, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics and industry change, and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in or incorporated by reference into this prospectus, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in and incorporated by reference into this prospectus. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in and incorporated by reference into this prospectus, they may not be predictive of results or developments in future periods.

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

- our ability to obtain additional financing, including the overhang and restrictive provisions of the Series A convertible preferred stock and related warrants;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- our ability to continue as a going concern;
- obtaining and maintaining intellectual property protection for our product candidates and our proprietary technology;
- 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 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;
- our ability to operate our business without infringing the intellectual property rights of others;
- recently enacted and future legislation regarding the healthcare system;
- our ability to satisfy the continued listing requirements of the Nasdaq Capital Market or any other exchange that our securities may trade on in the future;

- our plans and ability to develop and commercialize our product candidates;
- the rate and degree of market acceptance of any of our product candidates;
- the success of competing products that are or may become available; and
- the performance of third parties, including contract research organizations and manufacturers.

You should also read carefully the factors described in the “Risk Factors” section contained in this prospectus and incorporated by reference herein from our Annual Report on Form 10-K filed with the SEC on March 31, 2017, as amended, our Quarterly Reports on Form 10-Q and our other public filings to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements contained in or incorporated by reference into this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

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

For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately \$ million (or approximately \$ million if the underwriter's option to purchase additional shares is exercised in full) from the sale of the securities offered by us in this offering, based on the assumed public offering price of \$ per share (the last reported sale price of our common stock on the Nasdaq Capital Market on , 2017), and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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

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

We currently intend to use the net proceeds from this offering to fund research and development of our lead product candidate, TSC, including clinical trial activities, and for general corporate purposes. See "Risk Factors" for a discussion of certain risks that may affect our intended use of the net proceeds from this offering, including that we will need to raise additional capital in the future to complete the development of TSC and our other product candidates.

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

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

CAPITALIZATION

The following table sets forth cash and capitalization as of September 30, 2017:

- on an actual historical basis for Diffusion;
- on a pro forma basis to give effect to the reclassification of \$16.3 million common stock warrant liability to stockholders' equity as a result of the amendment of our certificate of incorporation on November 1, 2017 with respect to the dividend feature of the Series A Preferred Stock and resulting accounting adjustments;
- on a pro forma, as adjusted basis to give effect to:
 - o the assumed issuance and sale of shares of common stock in this offering at the assumed public offering price of \$ per share (the last reported sale price of our common stock on the Nasdaq Capital Market on , 2017), after deducting estimated placement agent fees and commissions, and estimated offering expenses payable by us; and
 - o the automatic conversion of all outstanding shares of Series A Preferred Stock into shares (the "Conversion Shares") of common stock (including accrued dividends paid in kind and the "make-whole" adjustment feature thereof) pursuant to the terms thereof, which will occur substantially concurrently with the consummation of this offering, assuming a public offering price of \$ per share (the last reported sale price of our common stock on the Nasdaq Capital Market on , 2017) and that this offering is completed on , 2017.

	Actual as of September 30, 2017	Pro Forma	Pro Forma as Adjusted
Cash, cash equivalents and certificate of deposit	\$ 11,236,164	\$ 11,236,164	\$
Common Stock warrant liability	\$ 16,316,054	\$ —	\$ —
Convertible debt	\$ 550,000	\$ 550,000	\$
Series A - 13,750,000 shares authorized, 8,324,032 issued and outstanding, actual; 13,750,000 shares authorized, no shares issued or outstanding, as adjusted	—	—	
Stockholders' equity:			
Common stock, par value \$0.001 per share; 1,000,000,000 authorized, 14,503,976 shares issued and outstanding actual; 1,000,000,000 shares authorized, [] shares issued and outstanding pro forma as adjusted	14,504	14,504	
Additional paid-in capital	\$ 69,686,744	\$ 82,840,268	\$
Accumulated deficit	\$ (63,344,552)	\$ (60,182,022)	\$
Total stockholders' equity	\$ 6,356,696	\$ 22,672,750	\$
Total capitalization	\$ 23,222,750	\$ 23,222,750	\$

The number of shares of common stock outstanding in the table excludes the following, outstanding as of September 30, 2017:

- o 213,879 shares issuable upon conversion of convertible promissory notes in an aggregate principal amount of \$0.6 million;

- o 2,545,989 shares of common stock issuable upon the exercise of outstanding stock options under the 2015 Equity Plan, at a weighted-average exercise price of \$7.34 per share;
- o 13,555,887 shares of common stock issuable upon the exercise of outstanding warrants issued in connection with the Series A private placement, at a weighted-average exercise price of \$2.22 per share;
- o 447,721 shares of common stock issuable upon the exercise of other outstanding warrants, at a weighted-average exercise price of \$44.52 per share; and
- o 114,291 shares of common stock reserved for future issuance under the 2015 Equity Plan.

The amounts set forth in the table above also assume no exercise by the underwriter of its option to purchase additional shares.

DILUTION

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

The historical net tangible book value (deficit) of our common stock as of September 30, 2017 was approximately \$(9.2) million, or approximately \$(0.64) per share of common stock. Historical net tangible book value (deficit) per share is determined by dividing the number of outstanding shares of common stock into its total tangible assets (total assets less intangible assets) less total liabilities and preferred shares.

On a pro forma basis, after giving effect to the reclassification of our \$16.3 million common stock warrant liability to stockholders' equity as a result of the amendment of our certificate of incorporation on November 1, 2017 with respect to the dividend feature of the Series A Preferred Stock and resulting accounting adjustments, pro forma net tangible book value (deficit) of our common stock as of September 30, 2017 was approximately \$7.1 million, or approximately \$0.48 per share of common stock. This represents an immediate increase in pro forma net tangible book value of \$1.12 per share.

In addition, assuming the aggregate gross proceeds of this offering are at least \$10 million, all of the outstanding shares of our Series A Preferred Stock will automatically convert into shares of common stock on a one-for-one basis. Further, each holder of Series A Preferred Stock will also receive additional shares of common stock representing (i) paid-in-kind dividends accrued through the date of conversion and (ii) assuming that the public offering price in this offering is less than \$2.02 per share, payment in respect of the "make-whole" feature of the Series A Preferred Stock. For purposes of calculating an assumed number of Conversion Shares, we have assumed a public offering price of \$ _____ per share (the last reported sale price of our common stock on the Nasdaq Capital Market on _____, 2017) and that this offering is completed on _____, 2017, which would result in the issuance of, in the aggregate, _____ shares of common stock in respect of the conversion of our Series A Preferred Stock.

On a pro forma as adjusted basis, after giving effect to the conversion of the outstanding shares of Series A Preferred Stock, assuming the public offering price in this offering is \$ _____ per share, the closing price of our common stock on the Nasdaq Capital Market on [____], 2017, and assuming that this offering is closed on _____, 2017, our net tangible book value at September 30, 2017 would have been approximately \$ _____ million, or approximately \$ _____ per share of common stock.

Investors purchasing securities in this offering will incur immediate and substantial dilution. After giving effect to the sale of common stock offered in this offering assuming a public offering price of \$ _____ per share, the closing price of our common stock on the Nasdaq Capital Market on _____, 2017, and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us, our as adjusted net tangible book value as of September 30, 2017 would have been approximately \$ _____ million, or approximately \$ _____ per share of common stock. This represents an immediate increase in pro forma as adjusted net tangible book value of \$ _____ per share to existing stockholders, and an immediate dilution in the pro forma as adjusted net tangible book value of \$ _____ per share to investors purchasing shares of our common stock in this offering.

The following table illustrates this per share dilution:

Assumed public offering price per share	
Historical net tangible book value (deficit) per share	(0.64)
Increase per share attributable to pro forma adjustments	1.12
Pro forma net tangible book value (deficit) per share at September 30, 2017	0.48
Increase in net tangible book value per share attributable to this offering and automatic conversion of Series A preferred stock	
Pro forma as adjusted net tangible book value after this offering	
Dilution per share to investors	

The dilution information discussed above is illustrative only and will change based on the actual public offering price and other terms of this offering determined at pricing. A \$1.00 increase or decrease in the assumed public offering price of \$ _____ per share would increase or decrease the as adjusted net tangible book value per share by \$ _____ million, or approximately \$ _____ per share, and the dilution per share to investors participating in this offering by approximately \$ _____ per share, assuming the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The discussion and table above assume no exercise of the underwriter's option to purchase additional shares of common stock. If the underwriter fully exercises its option to purchase _____ additional shares of common stock in the offering, our as adjusted net tangible book value after this offering, calculated in the manner set forth above, would be approximately \$ _____ million, our as adjusted net tangible book value per share after this offering would be \$ _____ per share, the increase in our as adjusted net tangible book value per share attributable to investors participating in this offering would be \$ _____ per share and the as adjusted dilution per share to new investors in this offering would be \$ _____ per share.

DESCRIPTION OF CAPITAL STOCK

Company Capitalization

Our authorized capital stock consists of 1,000,000,000 shares of common stock and 30,000,000 shares of preferred stock, \$0.001 par value, 13,750,000 of which have been designated as Series A Preferred Stock and the remainder of which remain undesignated. The following summary is qualified in its entirety by reference to our Certificate of Incorporation, as amended, a copy of which is filed as an exhibit to our previous filings with the SEC and incorporated herein by reference.

Common Stock

Authorized. We are authorized to issue 1,000,000,000 shares of common stock, of which 14,503,976 shares were issued and outstanding as of September 30, 2017. We may amend from time to time our Certificate of Incorporation to increase the number of authorized shares of common stock. Any such amendment would require the approval of the holders of a majority of the voting power of the shares entitled to vote thereon.

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

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

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

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

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

Listing. Our common stock is quoted on the Nasdaq Capital Market under the symbol "DFFN."

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

Series A Convertible Preferred Stock

As of September 30, 2017, there were 8,324,032 shares of the Series A Preferred Stock issued and outstanding. The following is a summary of the rights, privileges and preferences of the Series A Preferred Stock, which such summary is qualified in its entirety by the Certificate of Designation of Preferences, Rights and Limitations of the Series A Convertible Preferred Stock (the "Series A Certificate of Designation").

Voting. The holders of the Series A Preferred Stock are 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 is 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, the Company may not (a) amend the Certificate of Incorporation or 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, (c) amend the Series A 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 are entitled to an 8.0% cumulative preferred dividend payable semi-annually in shares of common stock or cash (in the Company's sole discretion) that began 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 ranks senior to the common stock and will rank senior to each other class of capital stock of the Company or series of 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 ("Series A Junior Securities"). In the event of a Liquidation Event (as defined in the Series A Certificate of Designation), the holders of the Series A Preferred Stock are 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 Series A Junior Securities. In addition, prior to such Liquidation Event, the holders of Series A Preferred Stock are 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 the Company's creditors and any securities senior to the Series A Preferred Stock are 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 Purchase Price, subject to adjustment as provided in the Certificate of Designation and summarized herein (the "Series A 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. The Company is 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 the Company's discretion, pay the holder such amount in cash or deliver an additional whole share in lieu thereof. If the Company sells at least \$10 million of securities in this offering, the Series A Preferred Stock will automatically convert into the applicable number of shares of our common stock.

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 Securities and 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 the Company, 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) pays 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) subdivides outstanding shares of common stock into a larger number of shares, (c) combines (including by way of reverse stock split) outstanding shares of common stock into a smaller number of shares or (d) issues by reclassification of shares of common stock any shares of capital stock of the Company, then in each case the Series A 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 the Company, during the three years immediately following the Initial Closing, subject to certain exceptions, issues 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 per share (the "Make-Whole Price"), the Company 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 Series A Conversion Price of the Series A Preferred Stock was equal to 105% of the Make-Whole Price (the "Make-Whole Adjustment"). The Company will only be obligated to issue shares with respect to a Make-Whole Adjustment in the first such subsequent offering, if any, following the final closing of the Series A Preferred Stock.

Warrants and Stock Options Issued and Outstanding

In connection with the Series A Preferred Stock private placement, we issued 5-year warrants to purchase 12,376,329 shares of common stock at an exercise price equal to \$2.22 per share to the holders of the Series A Preferred stock and we issued 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 to our placement agent in the Series A private placement. As of September 30, 2017, all 13,555,887 warrants issued in connection with the Series A private placement were outstanding and exercisable.

In addition, as of September 30, 2017, other warrants to purchase an aggregate of 447,721 shares of common stock were outstanding and exercisable with per share exercise prices ranging from \$20.00 to \$750.00 per share, a weighted average exercise price of \$44.52 and expiration dates ranging from March 27, 2018 to December 8, 2019.

MARKET PRICE FOR OUR COMMON STOCK

Our common stock trades publicly on the Nasdaq Capital Market under the symbol “DFFN.” Prior to November 9, 2016, our common stock traded on the OTCQX over-the-counter bulletin board. The following table sets forth the high and low daily sale prices for our common stock, as reported or quoted by the Nasdaq Capital Market or the OTCQX, as applicable, for each calendar quarter during 2017, 2016 and 2015, after giving effect to the 1-for-10 reverse stock split of our common stock on August 17, 2016. The over-the-counter market quotations reflect inter-dealer prices, without retail mark-up, mark-down or commission and may not necessarily represent actual transactions.

For the year ended December 31, 2017	High	Low
Fourth Quarter (through [December 18], 2017)	[\$2.97]	[\$1.27]
Third Quarter	\$3.04	\$1.34
Second Quarter	\$4.73	\$2.26
First Quarter	\$15.50	\$2.01

For the year ended December 31, 2016	High	Low
Fourth Quarter	\$7.00	\$1.94
Third Quarter	9.25	5.27
Second Quarter	11.50	8.00
First Quarter	17.00	8.50

For the year ended December 31, 2015	High	Low
Fourth Quarter	\$26.00	\$4.00
Third Quarter	17.50	8.00
Second Quarter	30.50	16.50
First Quarter	37.50	23.50

Anti-Takeover Provisions

Delaware Anti-Takeover Law

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

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

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;

- any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of its stock owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

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

UNDERWRITING

We have entered into an underwriting agreement dated _____, 2017, with H.C. Wainwright & Co., LLC as the sole book-running manager of this offering. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriter and the underwriter has agreed to purchase from us, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, _____ shares of common stock.

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

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

The underwriting agreement provides that the underwriter's obligation to purchase the shares we are offering is subject to conditions contained in the underwriting agreement. The underwriter is obligated to purchase and pay for all of the shares offered by this prospectus.

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

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

Underwriting Discounts, Commissions and Expenses

We have agreed to pay an underwriter discount equal to 8% of the aggregate gross proceeds raised in this offering.

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

		Total	
	Per Share	Without Option Exercise	With Full Option Exercise
Public offering price			
Underwriting discounts and commissions			
Proceeds, before expenses, to us			

We estimate the total expenses payable by us for this offering to be approximately \$ _____ million, which amount includes (i) an underwriting discount of \$ _____ million (\$ _____ million if the underwriter's option to purchase additional shares is exercised in full), (ii) a management fee equal to 1% of the aggregate gross proceeds raised in this offering, (iii) a \$35,000 non-accountable expense allowance payable to the underwriter, (iv) reimbursement of the accountable expenses of the underwriter equal to \$100,000 including the legal fees of the underwriter being paid by us (none of which has been paid in advance), and (v) other estimated expenses of approximately \$ _____ which include legal, accounting, printing costs and various fees associated with the registration and listing of our shares.

Option to Purchase Additional Securities

We have granted the underwriter the option to purchase up to _____ additional shares of common stock (15% of the shares issued in the offering) at the public offering price per share, less the underwriting discounts and commissions. The underwriter may exercise its option at any time, and from time to time, within 30 days from the date of this prospectus. If any additional shares are purchased pursuant to the option to purchase additional shares of common stock, the underwriter will purchase these shares on the same terms as those on which the shares are being offered hereby.

Underwriter Warrants

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

Right of First Refusal

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

Nasdaq Capital Market Listing

Our stock is currently traded on the Nasdaq Capital Market under the symbol "DFFN." On _____, 2017, the last reported sale price of our common stock was \$ per share.

Lock-up Agreements

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

Stabilization, Short Positions and Penalty Bids

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

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

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

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

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

Indemnification

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

Other Relationships

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

LEGAL MATTERS

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

EXPERTS

The consolidated financial statements of Diffusion Pharmaceuticals Inc. as of and for the years ended December 31, 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.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

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

We file 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.

INCORPORATION OF CERTAIN INFORMATION 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., 1317 Carlton Avenue, Suite 200, Charlottesville, Virginia 22902, Attention: Secretary, telephone: (434) 220-0718. This prospectus incorporates by reference the following documents (other than any portion of the respective filings furnished, rather than filed, under the applicable 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 SEC on March 31, 2017.
- our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2017, June 30, 2017 and September 30, 2017, filed with the SEC on May 15, 2017, August 14, 2017 and November 13, 2017, respectively.

- our Current Reports on Form 8-K filed with the SEC on January 9, 2017, January 26, 2017 (to the extent not furnished), March 15, 2017, April 3, 2017, April 11, 2017, May 26, 2017, June 16, 2017, July 6, 2017, November 2, 2017 and November 20, 2017;
- our Definitive Proxy Statement on Schedule 14A filed with the SEC on May 12, 2017; and
- 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.

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

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

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

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

Diffusi₂n

Pharmaceuticals Inc.

Shares of Common Stock

PROSPECTUS

Sole Book-Running Manager

H.C. Wainwright & Co.

, 2017

30

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

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

	Amount
SEC registration fee	\$ 1,861.28
FINRA filing fee	*
Blue-sky qualification fees and expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer agent and registrar fees and expenses	*
Miscellaneous expenses	*
Total	\$ *

* To be filed by amendment.

Item 14. Indemnification of Directors and Officers.

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

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

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

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

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding securities issued by us since January 1, 2014 that were not registered under the Securities Act of 1933, as amended, or the Securities Act. Also included is the consideration, if any, received by us, for such securities and information relating to the Securities Act, or rule of the SEC, under which exemption from registration was claimed.

Private Placement

In March 2017, we conducted a private placement (the “Private Placement”), pursuant to which we issued 12,376,329 shares of Series A Preferred Stock and 5-year warrants to purchase 12,376,329 shares of our common stock at an exercise price equal to \$2.22 per share (the “Warrants”). The aggregate gross proceeds from the Private Placement were \$25.0 million, prior to deducting placement agent fees and expenses payable by us. Maxim Merchant Capital, a division of Maxim Group LLC (“Maxim”), acted as our sole placement agent in the Private Placement. We issued to Maxim and its designees 5-year warrants, to purchase 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 securities were issued to accredited investors in reliance upon an exemption pursuant to Section 4(a)(2) of the Securities Act and the rules and regulations promulgated thereunder. 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, pursuant to which we agreed to file a registration statement to register for resale the shares of common stock (i) issued and outstanding as a result of, or issuable upon, the conversion of the shares of Series A Preferred Stock, (ii) issued and outstanding as a result of, or issuable upon, the exercise of the Warrants sold in the Private Placement and (iii) issuable as payment of dividends accruing on the Series A Preferred Stock. Such registration statement was declared effective on June 1, 2017.

Reverse Merger

On January 8, 2016, we completed our merger (the “Merger”) with Diffusion Pharmaceuticals LLC, a Virginia limited liability company (“Diffusion LLC”). In connection with the Merger, we issued to the former equity holders of Diffusion LLC an aggregate number of shares of our common stock such that, immediately following the Merger and on a fully-diluted basis, the former equity holders of Diffusion LLC owned approximately 84.1% of our common stock and our pre-Merger stockholders owned approximately 15.9% of our common stock. The issuance of common stock in connection with the Merger was exempt from registration pursuant to Section 4(a)(2) of the Securities Act and Regulation D promulgated thereunder.

Item 16. Exhibits and Financial Statement Schedules.*(a) Exhibits.*

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

(b) Financial Statement Schedules.

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

Item 17. Undertakings.

The undersigned Registrant hereby undertakes:

- (1) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (2) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (3) That, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities, The undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser (i) any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424 promulgated under the Securities Act, (ii) any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant, (iii) the portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and (iv) any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (4) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (5) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (6) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

EXHIBIT INDEX

Exhibit No.	Description	Method of Filing
1.1	Underwriting Agreement, dated [____], by and between the Company and H.C. Wainwright & Co., LLC	To be filed by amendment
2.1	<u>Plan of Conversion, dated June 18, 2015</u>	Incorporated by reference to Exhibit 2.1 to the registrant's current report on Form 8-K filed on June 18, 2015
2.2	<u>Agreement and Plan of Merger dated as of December 15, 2015 among the Company, Arco Merger Sub, LLC and Diffusion Pharmaceuticals LLC *</u>	Incorporated by reference to Exhibit 2.1 to the registrant's current report on Form 8-K filed on December 15, 2015
3.1	<u>Certificate of Incorporation of Diffusion Pharmaceuticals Inc., as amended</u>	Incorporated by reference to Exhibit 3.1 to the registrant's annual report on Form 10-K for the year ended December 31, 2016
3.2	<u>Bylaws of Diffusion Pharmaceuticals Inc., as amended</u>	Incorporated by reference to Exhibit 3.4 to the registrant's annual report on Form 10-K for the year ended December 31, 2015
3.3	<u>Certificate of Designation of Preferences, Rights and Limitations of the Series A Convertible Preferred Stock of Diffusion Pharmaceuticals Inc.</u>	Filed herewith
3.5	<u>Certificate of Conversion, as filed with the Secretary of State of the State of Delaware on June 18, 2015</u>	Incorporated by reference to Exhibit 3.2 to the registrant's current report on Form 8-K filed on June 18, 2015
4.1	<u>Form of Diffusion Pharmaceuticals Inc. Convertible Note Agreement</u>	Incorporated by reference to Exhibit 4.1 to the registrant's current report on Form 8-K filed on October 3, 2016
4.2	<u>Form of Diffusion Pharmaceuticals LLC Convertible Note Agreement</u>	Incorporated by reference to Exhibit 4.7 to the registrant's annual report on Form 10-K for the year ended December 31, 2015
4.3	<u>Form of Warrant issued to Investors in the 2017 Private Placement by Diffusion Pharmaceuticals Inc.</u>	Incorporated by reference to Exhibit 4.1 to the registrant's current report on Form 8-K filed on March 15, 2017

4.4	<u>Form of Warrant issued to Investors in the 2014 Private Placement by the Company</u>	Incorporated by reference to Exhibit 4.1 to the registrant's current report on Form 8-K filed on April 29, 2014
4.5	<u>Warrant, dated October 21, 2014, issued by the Company to Isaac Blech</u>	Incorporated by reference to Exhibit 4.5 to the registrant's annual report on Form 10-K for the fiscal year ended December 31, 2014
4.6	<u>Warrant, dated April 29, 2014, issued by the Company to Sol J. Barer, Ph.D.</u>	Incorporated by reference to Exhibit 4.4 to the registrant's annual report on Form 10-K for the fiscal year ended December 31, 2014
4.7	<u>Form of Registration Rights Agreement entered into by and among the Company and Investors in the 2017 Private Placement</u>	Incorporated by reference to Exhibit 4.2 to the registrant's current report on Form 10-Q for the fiscal quarter ended March 31, 2017
4.8	<u>Form of Registration Rights Agreement entered into by and among the Company and Investors in the 2014 Private Placement</u>	Incorporated by reference to Exhibit 10.2 to the registrant's current report on Form 8-K filed on April 29, 2014
4.9	<u>Registration Rights Agreement dated November 18, 2013 between the Company and Certain Holders</u>	Incorporated by reference to Exhibit 10.4 to the registrant's current report on Form 8-K filed on November 22, 2013
5.1	Opinion of Dechert LLP	To be filed by amendment
10.1	<u>Employment Agreement, dated as of September 6, 2016, by and between David G. Kalergis and Diffusion Pharmaceuticals Inc.**</u>	Incorporated by reference to Exhibit 10.1 to the registrant's current report on Form 8-K as filed on September 8, 2016
10.2	<u>Employment Agreement, dated as of October 12, 2016, by and between Ben L. Shealy and Diffusion Pharmaceuticals Inc.**</u>	Incorporated by reference to Exhibit 10.1 to the registrant's current report on Form 8-K as filed on October 13, 2016
10.3	<u>Employment Agreement, dated as of October 18, 2016, by and between John L. Gainer, Ph.D. and Diffusion Pharmaceuticals Inc.**</u>	Incorporated by reference to Exhibit 10.18 to the registrant's annual report on Form 10-K for the year ended December 31, 2016

10.4	<u>Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan**</u>	Incorporated by reference to Exhibit 10.2 to the registrant's current report on Form 8-K as filed on June 18, 2015
10.5	<u>Amendment No. 1 to Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan**</u>	Incorporated by reference to Appendix B to the registrant's definitive proxy statement on Schedule 14A filed on June 10, 2016
10.6	<u>Form of Diffusion Pharmaceuticals Inc. Stock Option Award Agreement**</u>	Incorporated by reference to Exhibit 10.5 to the registrant's annual report on Form 10-K for the year ended December 31, 2016
10.7	<u>Form of Diffusion Pharmaceuticals LLC Stock Option Award Agreement**</u>	Incorporated by reference to Exhibit 10.24 to the registrant's annual report on Form 10-K for the year ended December 31, 2015
10.8	<u>Form of 2015 Incentive Stock Option Agreement under the Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan**</u>	Incorporated by reference to Exhibit 10.3 to the registrant's current report on Form 8-K filed on June 18, 2015
10.9	<u>Form of 2015 Non-Statutory Stock Option Agreement under the Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan**</u>	Incorporated by reference to Exhibit 10.4 to the registrant's current report on Form 8-K filed on June 18, 2015
10.10	<u>Form of Stock Option Agreement between the Company and certain former Executive Officers**</u>	Incorporated by reference to Exhibit 10.12 to the registrant's annual report on Form 10-K for the fiscal year ended December 31, 2014
10.11	<u>Form of Stock Option Agreement between the Company and certain former Directors**</u>	Incorporated by reference to Exhibit 10.13 to the registrant's annual report on Form 10-K for the fiscal year ended December 31, 2014
10.12	<u>Form of Indemnification Agreement between Diffusion Pharmaceuticals Inc. and each of its Directors and Officers**</u>	Incorporated by reference to Exhibit 10.3 to the registrant's annual report on Form 10-K for the year ended December 31, 2015
10.13	<u>Placement Agency Agreement, dated January 27, 2017, by and between Diffusion Pharmaceuticals Inc. and Maxim Merchant Capital, a division of Maxim Group LLC</u>	Incorporated by reference to Exhibit 10.1 to the registrant's current report on Form 8-K filed on March 15, 2017

10.14	<u>Amendment to the Placement Agency Agreement, dated March 14, 2017, by and between Diffusion Pharmaceuticals Inc. and Maxim Merchant Capital, advisor of Maxim Group LLC</u>	Incorporated by reference to Exhibit 10.17 to the registrant's annual report on Form 10-K for the year ended December 31, 2016
10.15	<u>Form of 2017 Private Placement Subscription Agreement</u>	Incorporated by reference to Exhibit 10.2 to the registrant's current report on Form 8-K filed on March 15, 2017
10.16	<u>Settlement Agreement, dated September 27, 2016, by and among Diffusion Pharmaceuticals Inc., Diffusion Pharmaceuticals LLC, David Schmidt and the other parties thereto</u>	Incorporated by reference to Exhibit 10.1 to the registrant's current report on Form 8-K filed on October 3, 2016
10.17	<u>Contingent Value Rights Agreement, dated as of January 8, 2016, by and between Diffusion Pharmaceuticals Inc. and Computershare, Inc., as Rights Agent</u>	Incorporated by reference to Exhibit 10.2 to the registrant's current report on Form 8-K filed on January 8, 2016
10.18	<u>Lease Agreement, dated March 31, 2017, by and between Diffusion Pharmaceuticals Inc. and One Carlton LLC</u>	Incorporated by reference to Exhibit 10.4 to the registrant's current report on Form 10-Q for the fiscal quarter ended March 31, 2017
21.1	<u>Subsidiaries of Diffusion Pharmaceuticals Inc.</u>	Incorporated by reference to Exhibit 21.1 to the registrant's annual report on Form 10-K for the year ended December 31, 2016
23.1	<u>Consent of KPMG LLP, independent registered public accounting firm</u>	Filed herewith
23.2	Consent of Dechert LLP	Included in Exhibit 5.1 hereto
24.1	<u>Powers of Attorney</u>	Included on the signature pages hereto

* All exhibits and schedules to this agreement have been omitted pursuant to Item 601(b)(2) of Regulation S-K. The registrant will furnish the omitted exhibits and schedules to the SEC upon request by the SEC.

** A management contract or compensatory plan or arrangement.

SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Charlottesville, Virginia, on the 20th day of December, 2017.

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

POWER OF ATTORNEY

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

Pursuant to the requirements of the Securities Act, 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 of the Board <i>(Principal Executive Officer)</i>	December 20, 2017
<u>/s/ Ben L. Shealy</u> Ben L. Shealy	Senior Vice President, Finance, Treasurer and Secretary <i>(Principal Financial & Accounting Officer)</i>	December 20, 2017
<u>/s/ Isaac Blech</u> Isaac Blech	Vice Chairman of the Board of Directors	December 20, 2017
<u>/s/ Robert Adams</u> Robert Adams	Director	December 20, 2017
<u>/s/ John L. Gainer</u> John L. Gainer, Ph.D.	Director	December 20, 2017
<u>/s/ Mark T. Giles</u> Mark T. Giles	Director	December 20, 2017
<u>/s/ Alan Levin</u> Alan Levin	Director	December 20, 2017
<u>/s/ Robert R. Ruffolo</u> Robert R. Ruffolo	Director	December 20, 2017

**CERTIFICATE OF DESIGNATION OF PREFERENCES,
RIGHTS AND LIMITATIONS
OF THE
SERIES A CONVERTIBLE PREFERRED STOCK
OF
DIFFUSION PHARMACEUTICALS INC.**

**Pursuant to Section 151 of the
General Corporation Law of the State of Delaware**

WHEREAS, the undersigned does hereby certify that the following resolution was duly adopted by the Board of Directors (the “**Board**”) of Diffusion Pharmaceuticals Inc., a Delaware corporation (the “**Corporation**”), with the voting powers, designations, preferences and relative, participating, optional or other special rights, qualifications, limitations or restrictions set forth therein having been fixed by the Board pursuant to authority granted to it under Article IV of the Corporation’s Certificate of Incorporation, as amended (the “**Certificate of Incorporation**”) and in accordance with the provisions of Section 151 of the General Corporation Law of the State of Delaware:

RESOLVED, that, pursuant to authority conferred upon the Board by the Certificate of Incorporation, the Board hereby authorizes 13,750,000 shares of Series A Convertible Preferred Stock, par value \$0.001 per share, of the Corporation and hereby fixes the voting powers, designations, preferences and relative, participating, optional or other special rights, qualifications, limitations or restrictions, of such shares in accordance with this Certificate of Designation of Preferences, Rights and Limitations (the “**Certificate of Designation**”), in addition to those set forth in the Certificate of Incorporation, as follows:

Capitalized terms used but not separately defined herein shall have the meanings given to them in the Certificate of Incorporation.

1. Designation, Amount and Par Value: Series A Convertible Preferred Stock, \$0.001 par value (“**Series A Preferred Stock**”).

(a) *Stated Value*. The stated value of the Series A Preferred Stock shall be \$2.02 per share (the “**Stated Value**”), subject to adjustment for stock splits, dividends, combinations and related transactions as set forth herein.

(b) *Number and Designation*. 13,750,000 shares of Preferred Stock shall be designated as Series A Preferred Stock, which shall not be subject to increase without the vote or written consent of the holders (each, a “**Holder**” and collectively, the “**Holders**”) of a majority of the voting power of the then outstanding Series A Preferred Stock (a “**Majority Vote**”), unless otherwise specified herein

(c) *Rank*. The Series A Preferred Stock shall rank, with respect to rights upon liquidation, dissolution and winding up, (i) senior to the Common Stock and each other class of capital stock of the Corporation or series of Preferred Stock of the Corporation established hereafter by the Board, the terms of which do not expressly provide that such class or series ranks senior to, or on a parity with, the Series A Preferred Stock as to rights upon liquidation, dissolution and winding up (collectively, “**Junior Securities**”); (ii) equally with each other class or series of capital stock of the Corporation established hereafter by the Board the terms of which expressly provide that such class or series will rank on equally with the Series A Preferred Stock as to rights upon liquidation, dissolution and winding up (collectively, “**Parity Securities**”); and (iii) junior to each other class or series of capital stock of the Corporation established hereafter by the Board the terms of which expressly provide that such class or series will rank senior to the Series A Preferred Stock as to rights upon liquidation, dissolution and winding up (collectively, “**Senior Securities**”). The definitions of Junior Securities, Parity Securities and Senior Securities shall each also include any rights or options exercisable for or convertible into Junior Securities, Parity Securities and Senior Securities, respectively. The Series A Preferred Stock shall also rank junior to the Corporation’s existing and future indebtedness.

2. Dividends.

(a) The Corporation shall pay a cumulative preferential dividend (the “**Regular Dividend**”) on each share of Series A Preferred Stock from the issue date of such share of Series A Preferred Stock, accruing at a rate of 8.0% of the Stated Value per annum (computed on the basis of a 360-day year of twelve 30-day months, accruing daily), payable semiannually in arrears on April 1 and October 1 of each year commencing on October 1, 2017, or if any such date is not a business day, on the next succeeding business day (each such date, a “**Dividend Payment Date**”), to the Holders of record on the preceding March 15 and September 15 of each year, respectively, in cash or shares of Common Stock in the Corporation’s sole discretion. For purposes of determining the number of shares of Common Stock issuable to a Holder in connection with any such dividend, the value of a share of Common Stock shall be deemed to be the closing price of the Common Stock on the NASDAQ Capital Market (or such other national securities exchange as the Common Stock may be principally traded on at such time) on the business day immediately preceding the Dividend Payment Date. The Regular Dividend shall begin to accrue and be cumulative on the first day of each applicable Regular Dividend period and shall remain accumulated dividends with respect to such Series A Preferred Stock until paid; *provided*, that the first Regular Dividend payable with respect to any share of Preferred Stock shall not begin to accrue until the date of original issuance of such share of Preferred Stock. Regular Dividends shall accrue whether or not there are profits, surplus or other funds of the Corporation legally available for the payment of dividends but shall not be payable until legally permissible, as applicable.

3. Liquidation Preference.

(a) In the event of a Liquidation Event (as defined below), before any payment or distribution of the assets of the Corporation (whether capital or surplus) shall be made to or set apart for the holders of Junior Securities, and after and subject to the payment in full of all amounts required to be distributed to the Corporation’s creditors or the holders of Senior Securities, each Holder shall be entitled to receive, *pari passu* with the holders of Parity Securities, out of the assets of the Corporation or proceeds thereof (whether capital, surplus or earnings) legally available therefor, an amount in cash equal to 100% of the Stated Value (the “**Liquidation Preference**”) with respect to each share of Series A Preferred Stock held by the Holder; *provided*, that the Corporation shall provide the Holders with notice of any Liquidation Event at least ten (10) calendar days prior to the record date with respect to such Liquidation Event (or, with respect to any Liquidation Event for which no record date is set, the effective date thereof) and, for the avoidance of doubt, following receipt of such notice, any Holder may exercise such Holder’s voluntary conversion rights in accordance with Section 4(a). If, upon the occurrence of any Liquidation Event, the assets of the Corporation, or proceeds thereof, distributable after payment in full of the Corporation’s creditors and Senior Securities shall be insufficient to pay in full the aggregate Liquidation Preference to all Holders and any Parity Securities, the assets of the Corporation, or the proceeds thereof, shall be distributed among the Holders and any such Parity Securities ratably. For purposes of this Certificate of Designation, the term “**Liquidation Event**” shall mean, at any time while a share of Series A Preferred Stock is outstanding, (i) any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or (ii) the Company, directly or indirectly, in one or more related transactions, (A) effects any merger or consolidation of the Company with or into another person, (B) effects any sale, lease, license, assignment, transfer, conveyance or other disposition of all or substantially all of its assets, (C) is the subject of any purchase offer, tender offer or exchange offer (whether by the Company or another person) and is completed pursuant to which holders of Common Stock are permitted to sell, tender or exchange their shares for other securities, cash or property and such offer has been accepted by the holders of 50% or more of the outstanding Common Stock, (D) effects any reclassification, reorganization or recapitalization of the Common Stock or any compulsory share exchange pursuant to which the Common Stock is effectively converted into or exchanged for other securities, cash or property, (E) consummates a stock or share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off or scheme of arrangement) with another person or “group” (as such term is defined in Section 13(d) of the Exchange Act) whereby such other person or group acquires more than 50% of the outstanding shares of Common Stock (not including any shares of Common Stock held by the other person or other persons making or party to, or associated or affiliated with the other persons making or party to, such stock or share purchase agreement or other business combination), in each case other than any such transaction (1) that does not result in a reclassification, conversion, exchange or cancellation of outstanding Common Stock; (2) which is effected solely to change the Corporation’s jurisdiction of incorporation and results in a reclassification, conversion or exchange of outstanding shares of the Common Stock solely into shares of common stock of the surviving entity; (3) where the voting capital stock of the Corporation outstanding immediately prior to such transaction is converted into or exchanged for voting capital stock of the surviving entity constituting a majority of the outstanding shares of such voting capital stock of such surviving entity immediately after giving effect to such issuance; or (4) that the Holders deem not to be a Liquidation Event by a Majority Vote.

(b) For the avoidance of doubt, the Series A Preferred Stock shall not be convertible into Common Stock after the payment of the Liquidation Preference pursuant to Section 3(a), and the Holders shall not participate in any distribution made to the holders of Common Stock pursuant to the Certificate of Incorporation in connection with such Liquidation Event.

(c) In the event of a Liquidation Event, subject to the rights of the holders of any Senior Securities or Parity Securities, after payment shall have been made in full to the Holders as provided in Section 3(a), any other series or class of Junior Securities shall, subject to the respective terms and provisions (if any) applying thereto, be entitled to receive any and all assets remaining to be paid or distributed to holders of capital stock of the Corporation, and the Holders shall not be entitled to share therein.

4. Conversion Rights.

(a) *Voluntary Right to Convert.* At the Holder's sole option, each share of Series A Preferred Stock may be converted, at any time and from time to time, from and after the date of the Final Closing (as defined in the Subscription Agreements by and between the Company and the Holders (the "**Subscription Agreements**") related to Holders' subscription for the Series A Preferred Stock) (the "**Final Closing Date**") into a number of whole shares of Common Stock determined by dividing the Stated Value by the Conversion Price (as defined below).

(b) *Mandatory Conversion.* Each outstanding share of Series A Preferred Stock may be converted into a number of whole shares of Common Stock, determined by dividing the Stated Value by the Conversion Price, (i) on any date more than 30 trading days after the Original Issuance Date that the thirty-day moving average of the closing price of the Common Stock on the NASDAQ Capital Market (or any other market or exchange where the same is traded) exceeds \$8.00 per share (subject to adjustment in the manner described herein with respect to the Conversion Price), (ii) upon the Corporation's receipt of aggregate gross proceeds of at least \$10 million in any financing completed after the Original Issue Date or (iii) upon a Majority Vote to convert (any of (i), (ii) or (iii), a "**Mandatory Conversion Trigger**").

(c) *Conversion Price; Conversion Shares.* The “**Conversion Price**” of the Series A Preferred Stock shall be \$2.02, subject to adjustment as described herein. Any shares of Common Stock issuable upon a conversion of Series A Preferred Stock pursuant to Section 4(a) or 4(b) are referred to herein as the “**Conversion Shares**.”

(d) *Mechanics of Conversion.*

(i) *Voluntary Conversion Mechanics.* The Holder will give notice of its decision to exercise its right to convert the Series A Preferred Stock pursuant to Section 4(a) by delivering an executed and completed Notice of Conversion in the form attached as Annex A to this Certificate of Designation to the Corporation in accordance with Section 6(a). The Holder’s election shall be deemed effective upon receipt of a properly completed Notice of Conversion by the Corporation; provided, that if the Notice of Conversion is received by the Corporation after 3:00 p.m. Eastern Time on any day or at any time on a non-business day, it shall be deemed to be received on the following business day (the “**Conversion Date**”). The Corporation will, or will cause the Corporation’s transfer agent to, transmit the Common Stock certificates (or similar electronic notification) representing such Conversion Shares to the Holder within five (5) business days after receipt by the Corporation of the properly completed Notice of Conversion and the certificate(s) representing the converted shares of Series A Preferred Stock (the “**Delivery Date**”). A new Series A Preferred Stock certificate representing any shares of Series A Preferred Stock not converted will also be provided by the Corporation promptly following the Conversion Date. To the extent a Holder elects not to surrender its Series A Preferred Stock for reissuance upon partial payment or conversion, the Holder hereby indemnifies the Corporation against any and all loss or damage attributable to a third-party claim in an amount in excess of the actual amount of the Series A Stated Value then owned by the Holder. Shares of Series A Preferred Stock converted into Common Stock or redeemed in accordance with the terms hereof shall be canceled and shall not be reissued.

(ii) *Mandatory Conversion Mechanics.* The Corporation shall effect a mandatory conversion pursuant to Section 4(b) by providing the Holders with written notice as provided in Section 6(a) and (i) stating that the Mandatory Conversion Trigger has been satisfied, (ii) specifying the then applicable Conversion Price, the aggregate number of shares of Series A Preferred Stock outstanding, and the aggregate number of Conversion Shares to be issued in connection with such conversion, and (iii) the date on which such conversion will be effective (the “**Mandatory Conversion Date**”). The calculations and entries set forth in the Corporation’s notice shall control in the absence of manifest or mathematical error. From and after the date of such notice, the shares of Series A Preferred Stock shall be null and void and only represent the right to receive the applicable number of Conversion Shares. The Corporation shall issue the Conversion Shares promptly following surrender by a Holder of the certificate(s) representing the converted shares of Series A Preferred Stock to the Corporation.

(iii) *Date of Conversion.* In the case of the exercise of the conversion rights set forth in Section 4(a) or 4(b), the record date for such conversion shall be the Conversion Date or the Mandatory Conversion Date, respectively, and the record Holder as of such date shall be entitled to receive the corresponding Conversion Shares.

(v) *Adjustments.* Upon the conversion of any shares of Series A Preferred Stock, no adjustment or payment shall be made with respect to the corresponding Conversion Shares on account of any cash dividend paid to the holders of Common Stock after the Original Issuance Date.

(vi) *Fractional Shares.* The Corporation shall not be required, in connection with any conversion of Series A Preferred Stock, to issue any fractional shares of Series A Preferred Stock or any fractional Conversion Shares and may, in each case, at the Company's discretion, pay the Holder such amount in cash or deliver an additional whole share in lieu thereof.

(e) *Limitations of Conversion.* Notwithstanding anything to the contrary contained herein, the number of Conversion Shares that may be acquired by the Holder upon conversion of the Series A Preferred Stock (or otherwise in respect hereof) 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 Securities and Exchange Act of 1934, as amended (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). For such purposes, beneficial ownership shall be determined in accordance with Section 13(d) of the Exchange Act and the rules and regulations promulgated thereunder. The Holder, upon not less than 61 days' prior notice to the Corporation, may increase or decrease the beneficial ownership limitations provision of this Section, provided that the beneficial ownership limitation in no event exceeds 9.99% of the number of shares of the Common Stock outstanding immediately after giving effect to the issuance of shares of Common Stock upon conversion of the Series A Preferred Stock held by the Holder and the provisions of this Section shall continue to apply. Any such increase or decrease will not be effective until the 61st day after such notice is delivered to the Corporation. The provisions of this paragraph shall be construed and implemented in a manner otherwise than in strict conformity with the terms of this Section to correct this paragraph (or any portion hereof) which may be defective or inconsistent with the intended beneficial ownership limitation herein contained or to make changes or supplements necessary or desirable to properly give effect to such limitation. The limitations contained in this paragraph shall apply to a successor Holder.

(f) *Stock Dividends and Splits.* If the Corporation, at any time after the first date of issue of the Series A Preferred Stock (the "**Original Issuance Date**") and while at least one share of Series A Preferred Stock is outstanding: (i) pays 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 Corporation upon conversion of the Series A Preferred Stock or any debt securities), (ii) subdivides outstanding shares of Common Stock into a larger number of shares, (iii) combines (including by way of reverse stock split) outstanding shares of Common Stock into a smaller number of shares or (iv) issues by reclassification of shares of Common Stock any shares of capital stock of the Corporation, 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 (i) through (iv) above.

(g) *Subsequent Equity Sales.* Other than in connection with Exempt Issuances (as defined below), if at any time prior to the three year anniversary of the Original Issuance Date, the Corporation shall issue in any offering at least \$10 million of Common Stock or securities convertible into or exercisable for shares of Common Stock to any person or entity at a price per share or conversion or exercise price per share (the “*Dilutive Issuance Price*”) which is less than the purchase price for the Series A Preferred Stock (as set forth in the Subscription Agreement), the Corporation shall substantially concurrently issue to each Holder a number of shares of Common Stock equal to the difference between: (x) the number of shares of Common Stock the Holder’s shares of Series A Preferred Stock would be convertible into if the Conversion Price were equal to 105% of the Dilutive Issuance Price and (y) the number of shares of Common Stock such Holder’s shares of Series A Preferred Stock are convertible into immediately prior to such dilutive issuance, rounded up to the nearest whole share; *provided*, that the foregoing shall only apply with respect to the first such offering by the Corporation after the Original Issue Date. As used herein “*Exempt Issuance*” means the issuance of (i) Common Stock, warrants or options to employees, officers, consultants or directors of the Corporation pursuant to any stock, warrant or option plan or agreement duly adopted for such purpose on or before the Original Issue Date by the Board of Directors of the Corporation or a majority of the members of a committee of directors established for such purpose, (ii) securities upon the exercise or exchange of or conversion of any securities issued hereunder and/or other securities exercisable or exchangeable for or convertible into shares of Common Stock issued and outstanding as of the Original Issue Date, provided that the terms of such securities have not been amended since the Original Issue Date to increase the number of such securities or to decrease the exercise price, exchange price or conversion price of such securities; (iii) shares of Common Stock, or securities convertible or exercisable into shares of Common Stock, that would result in an adjustment to the Conversion Price pursuant to the terms hereof (including the issuance of securities to the Corporation’s shareholders as a dividend or other distribution); (iv) securities as consideration for any acquisition of all or any portion of the equity interest, assets, properties or business of any third party who is not an affiliate of the Corporation (including through a merger, consolidation or other business combination), (v) securities as consideration for the initial capitalization of a joint venture or similar strategic arrangement with any third party who is not an affiliate of the Corporation and (vii) securities to lenders or financial institutions as an “equity kicker” in connection with any borrowings or credit arrangements that are approved by the Board.

(h) *Calculations.* All calculations under this Section 4 shall be made to the nearest cent or the nearest 1/100th of a share, as the case may be.

(i) *Reservation of Shares.* The Corporation covenants and agrees that any Conversion Shares issued upon the conversion of the Series A Preferred Stock will, upon issuance, be validly issued and outstanding, fully paid and non-assessable, and free from all taxes, liens and charges with respect to the issuance thereof. The Corporation further covenants and agrees that the Corporation will at all times have authorized and reserved a sufficient number of shares of its Common Stock to provide for issuance of the Conversion Shares upon the conversion of the Series A Preferred Stock.

(j) *Payment of Taxes.* The Corporation and its paying agent shall be entitled to withhold taxes on all payments on the Series A Preferred Stock and Conversion Shares to the extent required by law. Prior to the date of any such payment, each Holder shall deliver to the Corporation or its paying agent a duly executed, valid, accurate and properly completed Internal Revenue Service Form W-9 or an appropriate Internal Revenue Service Form W-8, as applicable. The Corporation shall pay any and all documentary, stamp and similar issue or transfer tax due on (A) the issue of the Series A Preferred Stock and (B) the issue of Conversion Shares; *provided*, however, in the case of any conversion of Series A Preferred Stock, the Corporation shall not be required to pay any tax or duty that may be payable in respect of any transfer involved in the issue and delivery of Conversion Shares in a name other than that of the Holder of the shares to be converted, and no such issue or delivery shall be made unless and until the person requesting such issue has paid to the Corporation the amount of any such tax or duty, or has established to the satisfaction of the Corporation that such tax or duty has been paid.

(k) *Buy-In*. If, following receipt by the Corporation of a duly executed and properly completed conversion notice from a Holder, the Corporation fails, prior to the applicable Delivery Date, to, at its option, (i) deliver to such Holder the applicable certificate or certificates or (ii) cause its transfer agent to credit the account of such Holder or such Holder's broker with the Depository Trust Company through its Deposit Withdrawal Agent Commission system, and if after such Delivery Date such Holder is required by its brokerage firm to purchase (in an open market transaction or otherwise), or the Holder's brokerage firm is required to purchase, shares of Common Stock to deliver in satisfaction of a sale by such Holder of the Conversion Shares which such Holder was entitled to receive upon the conversion relating to such Delivery Date (a "Buy-In"), then the Corporation shall (A) pay in cash to such Holder the amount by which (x) such Holder's total purchase price (including any brokerage commissions) for the shares of Common Stock so purchased exceeds (y) the product of (1) the aggregate number of shares of Common Stock that such Holder was entitled to receive from the conversion at issue (or, if less, the number of shares actually delivered in satisfaction of such sale) multiplied by (2) the actual sale price at which the sell order giving rise to such purchase obligation was executed (including any brokerage commissions) and (B) at the option of such Holder, either reissue (if surrendered) the shares of Series A Preferred Stock equal to the number of shares of Series A Preferred Stock submitted for conversion or deliver to such Holder the number of shares of Common Stock that would have been issued if the Corporation had timely complied with its delivery requirements. For example, if a Holder purchases shares of Common Stock having a total purchase price of \$11,000 to cover a Buy-In with respect to an attempted conversion of shares of Series A Preferred Stock with respect to which the actual sale price (including any brokerage commissions) giving rise to such purchase obligation was a total of \$10,000 under clause (A) of the immediately preceding sentence, the Corporation shall be required to pay such Holder \$1,000. The Holder shall provide the Corporation written notice indicating the amounts payable to such Holder in respect of the Buy-In and, upon request of the Corporation, evidence of the amount of such loss. Nothing herein shall limit a Holder's right to pursue any other remedies available to it hereunder, at law or in equity including, without limitation, a decree of specific performance and/or injunctive relief with respect to the Corporation's failure to timely deliver certificates representing shares of Common Stock upon conversion of the shares of Series A Preferred Stock as required pursuant to the terms hereof.

5. Voting Rights.

(a) Except as otherwise provided herein or as required by law, Holders shall be entitled to vote with the holders of shares of Common Stock (and any other class or series that may similarly be entitled to vote with the holders of Common Stock) and not as a separate class, at any annual or special meeting of stockholders of the Corporation, 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 shall be entitled to that number of votes equal to the whole number of shares of Conversion Shares into which the aggregate number of shares of Series A Preferred Stock held of record by such Holder would be convertible pursuant to Section 4(a) hereof as of the close of business on the record date fixed for such vote or such written consent; *provided*, that solely for purposes of this Section 5(a), as of any date of determination, the Conversion Price shall be deemed to be the greater of (i) the Conversion Price and (ii) the closing price of the Common Stock as reported by NASDAQ on the date of the applicable Closing (as defined in the Subscription Agreements) with respect to such shares of Series A Preferred Stock. The Holders shall be entitled to notice of any meeting of stockholders in accordance with the bylaws of the Corporation (the "**Bylaws**").

(b) In addition to any other vote or consent required herein or by applicable law, for as long as fifty percent (50%) of the shares of Series A Preferred Stock outstanding as of immediately after the Final Closing, a Majority Vote shall be necessary for effecting or validating the following actions:

(i) amending the Corporation's certificate of incorporation, bylaws or other charter documents so as to materially and adversely affect any rights of the Holders;

(ii) increase or decrease (other than by conversion) the authorized number of the Series A Preferred Stock; provided however that the Company may authorize and issue additional shares of Series A Preferred Stock in the event the Maximum Offering Amount (as defined in the Subscription Agreements) is increased in the manner provided in the Subscription Agreements;

(iii) amend this Certificate of Designation;

(iv) repay, repurchase or offer to repay, repurchase or otherwise acquire more than a de minimis number of shares of its Common Stock, common stock equivalents or Junior Securities; or

(v) enter into any agreement or understanding with respect to any of the foregoing.

(c) For the avoidance of doubt, in addition to any other vote or consent required or permitted hereby, the Holders may waive any rights under this Certificate of Designation pursuant to a Majority Vote.

6. Miscellaneous.

(a) *Notices.* All notices or communications in respect of the Series A Preferred Stock shall be sufficiently given if given in writing and delivered in person or by first class mail, postage prepaid, sent in portable document format (“*pdf*”) via electronic mail, or if given in such other manner as may be permitted in this Certificate of Designation, the Certificate of Incorporation, the Corporation’s Bylaws, as amended, or by applicable law or regulation. Notwithstanding the foregoing, if the Series A Preferred Stock is issued in book-entry form through The Depository Trust Corporation or any similar facility, such notices may be given to the Holders in any manner permitted by such facility.

(b) *Lost or Mutilated Preferred Stock Certificate.* If any certificate or instrument evidencing any shares of Series A Preferred Stock is mutilated, lost, stolen or destroyed, the Corporation shall issue or cause to be issued in exchange and substitution for and upon cancellation thereof, or in lieu of and substitution therefor, a new certificate or instrument, but only upon receipt of evidence reasonably satisfactory to the Corporation of such loss, theft or destruction and customary and reasonable indemnity, if requested. The applicants for a new certificate or instrument under such circumstances shall also pay any reasonable third-party costs associated with the issuance of such replacement securities. If a replacement certificate or instrument evidencing any securities is requested due to a mutilation thereof, the Corporation may require delivery of such mutilated certificate or instrument as a condition precedent to any issuance of a replacement.

(c) *Severability.* If any term of the Series A Preferred Stock (or part thereof) set forth herein is invalid, unlawful or incapable of being enforced by reason of any rule of law or public policy, all other terms (or parts thereof) set forth herein which can be given effect without the invalid, unlawful or unenforceable term will, nevertheless, remain in full force and effect, and no term herein (or parts thereof) set forth will be deemed dependent upon any other such term unless so expressed herein.

(e) *Headings.* The headings of the paragraphs of this Certificate of Designation are for convenience of reference only and shall not define, limit or affect any of the provisions hereof.

[REMAINDER OF PAGE INTENTIONALLY LEFT BLANK]

IN WITNESS WHEREOF, Diffusion Pharmaceuticals Inc. has caused this Certificate of Designation to be duly executed by the undersigned authorized officer on the ___ day of March , 2017.

DIFFUSION PHARMACEUTICALS INC.

By: 

David G. Kalergis, Chief Executive Officer

Diffusion Pharmaceuticals Inc.
2020 Avon Court, Suite 4
Charlottesville, Virginia 22902

[Signature Page to Series A Convertible Preferred Stock Certificate of Designation]

ANNEX A

NOTICE OF CONVERSION

(To Be Executed By the Registered Holder in Order to Convert Shares of Series A Convertible Preferred Stock of Diffusion Pharmaceuticals Inc. into Shares of Common Stock of Diffusion Pharmaceuticals Inc.)

The undersigned hereby irrevocably elects to convert \$_____ of the Stated Value of the above Series A Convertible Preferred Stock into shares of Common Stock of Diffusion Pharmaceuticals Inc. pursuant to the terms and conditions of the Certificate of Designation with respect thereto, as of the date written below.

Date of Conversion:

Applicable Conversion Price per Share:

Number of Common Shares Issuable Upon This Conversion:

Select one:

- A Series A Convertible Preferred Stock certificate is being delivered to Diffusion Pharmaceuticals Inc. herewith. The unconverted portion of such certificate should be reissued and delivered to the undersigned.
- A Series A Convertible Preferred Stock certificate is not being delivered to Diffusion Pharmaceuticals Inc. herewith.

Signature:

Print Name:

Address:

This Notice of Conversion Should Be Delivered to:

Diffusion Pharmaceuticals Inc.
2020 Avon Court, Suite 4
Charlottesville, Virginia 22902

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
December 20, 2017