Filed Pursuant to Rule 424(b)(3)
Registration No. 333- 238818

PROSPECTUS

Diffusio$_2$n Pharmaceuticals Inc.

5,821,429 Shares of Common Stock
Issuable upon Exercise of Outstanding Warrants

This prospectus relates to the resale, from time to time, by the selling stockholders identified in this prospectus under the caption "Selling Stockholders," of up to 5,821,429 shares of our common stock, par value $0.001 per share, issuable upon exercise of certain outstanding common stock purchase warrants. We are not selling any shares of common stock under this prospectus and will not receive any proceeds from the sale of shares of common stock by the selling stockholders. We will receive proceeds from cash exercise of the warrants which, if exercised in cash with respect to all of the 5,821,429 shares of common stock, would result in gross proceeds of approximately $3.5 million to us. The selling stockholders will bear all commissions and discounts, if any, attributable to the sale of the shares.

The selling stockholders may sell the shares of our common stock offered by this prospectus from time to time on terms to be determined at the time of sale through ordinary brokerage transactions or through any other means described in this prospectus under the caption "Plan of Distribution." The shares of common stock may be sold at fixed prices, at market prices prevailing at the time of sale, at prices related to prevailing market price or at negotiated prices.

Our common stock is listed on the Nasdaq Capital Market under the symbol "DFFN." On June 2, 2020, the last reported sale price of our common stock was $1.13.

Investing in our common stock involves a high degree of risk. Before making an investment decision, please read "Risk Factors" on page 8 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is June 5, 2020.

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ABOUT THIS PROSPECTUS

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This prospectus is part of a registration statement on Form S-1 that we filed with the Securities and Exchange Commission (SEC). It omits some of the information contained in the registration statement and reference is made to the registration statement for further information with regard to us and the securities being offered by the selling stockholders. Any statement contained in the prospectus concerning the provisions of any document filed as an exhibit to the registration statement or otherwise filed with the SEC is not necessarily complete, and in each instance, reference is made to the copy of the document filed.

You should read this prospectus, any documents that we incorporate by reference in this prospectus and the additional information described below under “Where You Can Find Additional Information” and “Incorporation of Certain Information By Reference” before making an investment decision. You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with additional, different or inconsistent information, you should not rely on it. We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus were made solely for the benefit of the parties to such agreement, including in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

You should not assume that the information in this prospectus or any documents we incorporate by reference herein is accurate as of any date other than the date on the front of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

Unless the context indicates otherwise, as used in this prospectus, the terms “Diffusion,” “the Company,” “we,” “us” and “our” refer to Diffusion Pharmaceuticals Inc., a Delaware corporation. We have registered trademarks for Diffusion and RestorGenex. All other trade names, trademarks and service marks appearing in this prospectus are the property of their respective owners. Use or display by us of other parties’ trademarks, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owner.

FORWARD-LOOKING STATEMENTS

This prospectus, any accompanying prospectus supplement 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 any accompanying prospectus supplement and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, our intellectual property position, the degree of clinical utility of our products, particularly in specific patient populations, expectations regarding clinical trial data, our ability to commercialize our product candidates, our results of operations, cash needs, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics and industry change, and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in or incorporated by reference into this prospectus and any accompanying prospectus supplement, 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 any accompanying prospectus supplement. In addition, even if our results of operations, financial condition and/or 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 or any accompanying prospectus supplement, they may not be predictive of results or developments in future periods.

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

- our ability to obtain additional financing;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- the success and timing of our preclinical studies and clinical trials;
- the difficulties in obtaining and maintaining regulatory approval of our products and product candidates, and the labeling under any approval we may obtain;
- our plans and ability to develop and commercialize our product candidates;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the accuracy of our estimates of the size and characteristics of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;
- the rate and degree of market acceptance of any of our product candidates;
- obtaining and maintaining intellectual property protection for our product candidates and our proprietary technology;

- our ability to operate our business without infringing the intellectual property rights of others;
- recently enacted and future legislation regarding the healthcare system;
- our ability to satisfy the continued listing requirements of the Nasdaq Capital Market or any other exchange that our securities may trade on in the future;
- our ability to continue as a going concern;
- risks associated with the COVID-19 pandemic, which may adversely impact our business, preclinical studies and clinical trials;
- the uncertainty as to whether our Investigational New Drug Application ("IND") submission for our clinical program using TSC in COVID-19 patients displaying acute respiratory distress syndrome ("ARDS") symptoms will be approved by the Food and Drug Administration (the "FDA") for commencement of trials in the U.S. or that the FDA will not require significant changes that might take significant time to implement, if at all, or that any such required changes will be financially feasible;
- even if the IND submission protocol is approved by the FDA, there can be no assurance as to when the program might be able to commence, if at all;
- the uncertainty that as of yet the FDA has not approved a trial evaluating TSC for the treatment of ARDS, or if approved, such a trial possibly entailing significant additional time, effort and expense, particularly in light of the difficulty of doing business during the COVID-19 pandemic;
- the uncertainty as to whether our protocol for the clinical trial program with the Romanian Institute of Infectious Disease will be ultimately acceptable to the Romanian healthcare regulatory authorities or that such regulators will not require significant changes that might take significant time to implement, if at all, or that any such required changes will be financially feasible;
- if our protocol for the Romanian trial or a revised protocol is acceptable to the Romanian healthcare regulatory authorities, there can be no assurance as to when they might provide such guidance or when the program might be able to commence, if at all;
- the uncertainty that as of yet the Romanian healthcare regulatory authorities have not approved a trial evaluating TSC for the treatment of ARDS, or if approved, such a trial could entail significant additional time, effort and expense, particularly in light of the difficulty of doing business during the COVID-19 pandemic;
- the success of competing products that are or may become available; and
- the performance of third parties, including contract research organizations and manufacturers.

You should also read carefully the factors described in the "Risk Factors" section contained in this prospectus and incorporated by reference herein from our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, 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.

PROSPECTUS SUMMARY

The following summary highlights information contained elsewhere or incorporated by reference in this prospectus. This summary does not contain all of the information you should consider before investing in the securities. Before making an investment decision, you should read the entire prospectus carefully, including the matters discussed under the heading "Risk Factors" in this prospectus.

Diffusion Pharmaceuticals Inc.

Business Overview

We are a clinical stage biotechnology company developing new treatments for life threatening conditions by improving the body's ability to bring oxygen to the areas where it is needed most. We are developing our lead product candidate, transcrocetinate sodium, also known as trans sodium crocetinate ("TSC"), for use in those life-threatening conditions in which cellular oxygen deprivation ("hypoxia") is the basis for significant unmet medical needs. TSC is designed to safely and selectively target and re-oxygenate the micro-environment of hypoxic cells, and can potentially be used in many indications, including stroke, oncology, multiple organ failure and cardiovascular disease. In stroke, TSC helps promote the diffusion of oxygen into those brain cells in which oxygen-deprivation causes neuronal death resulting in patient mortality or morbidity. In cancer, TSC re-oxygenates treatment-resistant cancerous tissue, making the cancer cells up to three times more susceptible to the therapeutic effects of standard-of-care radiation therapy and chemotherapy. In multiple organ failure, we have begun a cooperative research effort with University of Virginia Health (UVA) and the Integrated Translational Research Institute of Virginia (iTHRIV), to evaluate TSC in patients with Acute Respiratory Distress Syndrome (ARDS) associated with COVID-19 infection. iTHRIV is a National Institutes of Health (NIH)-funded Clinical and Translational Awards (CTSA) program.

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

We believe that TSC has potential applications in stroke and emergency medicine. In stroke, a Phase 2 trial in cooperation with the University of California Los Angeles (UCLA) and the University of Virginia (UVA) to test TSC in the treatment of acute ischemic or hemorrhagic stroke is currently enrolling patients. Stroke is the 5th leading cause of death in the U.S. and the No. 1 cause of adult disability. Our stroke trial, which features in-ambulance dosing of TSC, is named the "PreHospital Acute Stroke Therapy - TSC" (PHAST - TSC) study, and is expected to enroll 160 patients, with 80 in the treatment arm and 80 in the control arm. We believe in-ambulance dosing of TSC will significantly cut the time in which the stroke-related oxygen deprivation to brain cells goes untreated, potentially leading to a better outcome for stroke victims treated in this manner. Near term enrollment in this trial is expected to be minimal for the duration of the COVID-19 pandemic.

Patients with COVID-19 infections are at risk for developing ARDS, which can lead to death from systemic hypoxemia (general lack of oxygen to body tissue and vital organs). We, along with researchers affiliated with UVA and iTHRIV, believe the oxygen-enhancing mechanism of action of TSC could benefit COVID-19 patients by mitigating the multiple organ failure that often accompanies systemic hypoxemia, and are, together, exploring avenues to advance TSC's development as quickly as possible for this use. Preclinical data indicate TSC increases oxygen availability in animal models of acute lung injury, mitigating the negative effects of systemic hypoxemia. Preclinical publications also indicate TSC's ability to mitigate systemic hypoxemia in other animal models, including hemorrhagic shock. Clinical data from 150 patients receiving TSC for other indications demonstrate that the drug has an acceptable safety profile in both healthy and critically ill patients.

In April 2020, we announced our pre-IND submission to the FDA of a planned clinical program using TSC in COVID-19 patients displaying severe respiratory symptoms and low oxygen levels, which received an accelerated review by the FDA under its Coronavirus Treatment Acceleration Program (CTAP). Clinical trial preparations at multiple potential sites are continuing as we move forward with implementing the FDA's suggestions and prepare our IND submission.

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

The trial began with an FDA-mandated open label 8 patient safety run-in for which enrollment has completed and is now closed. With the FDA's permission, a total of 19 patients were enrolled to ensure that at least 8 complete data sets meeting the FDA's specified 4-month exposure period would be available for review. The INTACT Trial Data Safety Monitoring Board (DSMB) met in the third quarter of 2019 and, based on their analysis, recommended that the study be continued. The DSMB concluded that no adverse safety signal had been observed, and unanimously recommended continuing the study as planned using the highest tested dose of TSC - 1.5 mg/kg - during the adjuvant treatment chemotherapy period with temozolomide. We believe that a preliminary efficacy signal was also received. A total of 10 patients were enrolled into the higher dose cohorts and 9 in the lower dose cohorts. In the higher dose patients, where the best results were expected, 3 discontinued treatment before meeting the FDA exposure period criteria. Of the 7 patients who met the criteria, 5 remain alive as of March 12, 2020. Commencement of enrollment in the randomization portion of the INTACT Phase 3 Trial is contingent upon our entering into a strategic partnership providing the necessary resources to undertake the full trial.

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

Recent Developments

In May 2020, we entered into a warrant exercise agreement with an accredited investor who held existing warrants to purchase common stock to exercise certain outstanding warrants (the "Exercise") to purchase up to an aggregate of 5,000,000 shares of our common stock having an exercise price of $0.35 per share. In consideration for the immediate exercise of the warrants for cash and an additional $0.125 per each share being exercised, the exercising investor received new unregistered warrants to purchase up to an aggregate of 5,000,000 shares of our common stock (the "Investor Warrants") in a private placement pursuant to Section 4(a)(2) of the Securities Act of 1933 (the "Securities Act"). The Investor Warrants are exercisable immediately upon issuance at an exercise price of $0.5263 per share and are exercisable until November 8, 2025. In connection with the Exercise, we issued to the placement agent (or its designees) warrants to purchase up to an aggregate of 250,000 shares of our common stock (the "Placement Agent Exercise Warrants," and together with the Investor Warrants, the "Exercise Warrants"). The Placement Agent Exercise Warrants have an exercise price of $0.5938 per share and otherwise have identical terms to the Investor Warrants (other than the exercise price noted above).

In addition, in May 2020, we sold 11,428,572 shares of our common stock in a registered direct offering for a purchase price of $1.05 per share for gross proceeds of approximately $12.0 million before the deduction of the placement agent fees and offering expenses (the "Offering"). In connection with the Offering, we issued warrants to purchase up to 571,429 shares of our common stock to the placement agent or its designees (the "Placement Agent Offering Warrants," and collectively with the Exercise Warrants, the "Warrants") in a private placement pursuant to Section 4(a)(2) of the Securities Act. The Placement Agent Offering Warrants are immediately exercisable upon issuance at an exercise price of $1.3125 per share and are exercisable through May 18, 2025.

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

In the event of a fundamental transaction, as described in the Warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the holders of the Warrants will be entitled to receive upon exercise of the Warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the Warrants immediately prior to such fundamental transaction. In addition, upon a fundamental transaction, the holder shall have the right to receive a payment in cash, or under certain circumstances in other consideration, from us at the Black Scholes value as described in the Warrants.

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

Shares of common stock offered by the selling stockholders:	5,821,429 shares of common stock issuable upon exercise of the Warrants.
Shares of common stock outstanding after completion of this offering, assuming full exercise of the Warrants for cash:	65,452,308
Terms of the Offering:	The selling stockholders, including their transferees, donees, pledgees, assignees and successors-in-interest, may sell, transfer or otherwise dispose of any or all of the shares of common stock offered by this prospectus from time to time on the Nasdaq Capital Market or any other stock exchange, market or trading facility on which the shares are traded or in private transactions. The shares of common stock may be sold at fixed prices, at market prices prevailing at the time of sale, at prices related to prevailing market price or at negotiated prices. See the section titled "Plan of Distribution" in this prospectus.
Use of Proceeds:	All proceeds from the sale of shares of common stock issuable upon exercise of the Warrants will be for the account of the selling stockholders. We will not receive any proceeds from the sale of common stock offered pursuant to this prospectus. However, we will receive proceeds upon any cash exercise of the Warrants. See the section titled "Use of Proceeds" in this prospectus.
NASDAQ Capital Market symbol:	DFFN
Trading:	Our shares of common stock currently trade on the Nasdaq Capital Market. There is no established trading market for the common stock purchase warrants and we do not intend to list the common stock purchase warrants on any exchange or other trading system.
Risk Factors:	Investing in our securities involves a high degree of risk and purchasers of our securities may lose their entire investment. See "Risk Factors" below and the other information included elsewhere in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our securities.

The number of shares of our common stock to be outstanding after this offering is based on 48,202,307 shares of common stock outstanding as of May 19, 2020, after giving effect to the 11,428,752 shares of common stock issued in the Offering (for a total of 59,630,879 shares of common stock outstanding prior to the issuance of shares sold pursuant to this prospectus), and excludes:

- As of March 31, 2020, 560,524 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 $30.60 per share;
- As of May 19, 2020, 13,473,082 shares of common stock issuable upon the exercise of outstanding warrants (including shares of common stock issuable upon exercise of the Warrants), at a weighted-average exercise price of $4.22 per share; and
- As of March 31, 2020, 485,602 shares of common stock reserved for future issuance under the 2015 Equity Plan.

All share information contained in this prospectus reflects the completion on December 13, 2018, of a 1-to-15 reverse stock split (the "Reverse Stock Split") of our common stock. No fractional shares were issued in connection with the Reverse Stock Split. Stockholders who otherwise would have been entitled to receive fractional shares of common stock had their holdings rounded up to the next whole share. Proportional adjustments were made to the Company's outstanding warrants, stock options and other equity securities and to the 2015 Equity Incentive Plan, as amended, to reflect the Reverse Stock Split, in each case, in accordance with the terms thereof.

RISK FACTORS

Investing in our securities involves a high degree of risk. Prior to making a decision about investing in our securities, you should consider carefully all of the information included and incorporated by reference or deemed to be incorporated by reference in this prospectus or the applicable prospectus supplement, including the risk factors incorporated by reference herein from our Annual Report on Form 10-K for the year ended December 31, 2019, as updated by annual, quarterly and other reports and documents we file with the SEC after the date of this prospectus and that are incorporated by reference herein, or in the applicable prospectus supplement. Each of these risk factors could have a material and adverse effect on our business, results of operations, financial position or cash flows, which may result in the loss of all or part of your investment. Please also read carefully the section above entitled "Forward-Looking Statements."

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.

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 maintain compliance with 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 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 and warrants 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 warrants, 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.

Events outside of our control, including public health crises such as the COVID-19 pandemic, could negatively affect our business and our operating results.

The novel coronavirus ("COVID-19") pandemic has resulted in significant financial market volatility, and its impact on the global economy and our operations remains uncertain. A continuation or worsening of the pandemic could have a material adverse impact on our business, results of operations and financial condition and on the market price of our common stock.

On March 12, 2020, the World Health Organization declared COVID-19 to be a pandemic. In an effort to contain and mitigate the spread of COVID-19, many countries worldwide have imposed quarantines, business closures and unprecedented restrictions on travel. The outbreak and government measures taken in response, have had a significant impact, both direct and indirect, on economic activity, as worker shortages have occurred, supply chains have been disrupted, facilities and production have been suspended and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services has fallen.

As a result of the COVID-19 pandemic, we may experience disruptions that could severely impact our business and clinical trials, including:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical trial site activities, including difficulties in recruiting clinical trial staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (i.e., those that are deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies for productions of our product candidates from our third party suppliers due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- interruptions in preclinical studies due to restricted or limited operations at laboratory facilities; and
- interruption or delays to our clinical activities.

Any negative impact that the COVID-19 pandemic has on recruiting or retaining patients in our clinical trials, the ability of our suppliers to provide materials for our product candidates, or the regulatory review process could cause additional delays with respect to product development activities, which could materially and adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, affect our ability to raise additional capital, and have a material adverse effect on our financial results. In addition, our clinical trial patients who contract COVID-19 may have adverse health outcomes that could impact the results of our clinical trials.

The COVID-19 pandemic has resulted in significant financial market volatility and uncertainty in recent weeks and continues to rapidly evolve. The extent to which the outbreak impacts our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the outbreak, new information that may emerge concerning the severity of COVID-19 and the actions to contain COVID-19 or treat its impact, among others. A continuation or worsening of the levels of market disruption and volatility seen in the recent past could have an adverse effect on our ability to access capital, on our business, results of operations and financial condition, and on the market price of our common stock.

We face risks related to the planned clinical program to test TSC as a treatment for COVID-19, which has not been approved by the FDA or any other regulatory authority.

In response to the recent global outbreak of COVID-19, on April 24, 2020, we submitted a Pre-IND to the FDA related to a planned clinical program using TSC in COVID-19 patients displaying severe respiratory symptoms and low oxygen levels, which received an accelerated review by the FDA under its Coronavirus Treatment Acceleration Program. Clinical trial start-up preparations are continuing as we move forward with with implementing the FDA's suggestions in the preparation of our IND submission. The estimated timing of regulatory approval is based on factors beyond our control, including but not limited to, unforeseen scheduling difficulties and unfavorable results at various stages in the pre-market application process. This FDA approval or clearance process may be time-consuming and costly. Moreover, there is no guarantee that the IND submission will ultimately be acceptable to the FDA. Even if the IND is approved by the FDA, there can be no assurance as to when the FDA might provide such approved or when the program might be able to commence, if at all. We intend to work closely with the FDA to determine the best path forward to obtain approval, but we cannot guarantee that these efforts will be successful. Even if FDA approval for trials evaluating TSC for the treatment of ARDS is ultimately granted and we are able to move forward with clinical trials, such trials may entail significant additional time, effort and expense, particularly in light of the difficulty of doing business during the COVID-19 pandemic. In addition, there is no assurance of favorable results from any clinical trials, or that one or more of such trials will be completed in the currently anticipated timelines or at all. Further, we may make a strategic decision to discontinue clinical testing of TSC in COVID-19 patients, including in the event that other parties are successful in developing a more effective treatment for COVID-19.

We have committed significant capital and resources to begin funding and supplying the clinical trials for the COVID-19 program. If we are unable to obtain regulatory approvals, or if clinical trials fail to demonstrate the clinical safety profile or the efficacy of TSC for the treatment of ARDS in COVID-19 patients, or if we make a strategic decision to discontinue testing TSC as a treatment for COVID-19 patients, we will be unable to recoup our significant expenses incurred to date and in the future related to the clinical program and the FDA approval process.

The Bylaws of the Company include a forum selection clause, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents.

Our Bylaws (the "Bylaws") require that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim for breach of a fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our Certificate of Incorporation or our Bylaws or (iv) any action asserting a claim governed by the internal affairs doctrine, in each case subject to said Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein.

This exclusive forum provision will not apply to claims under the Exchange Act, but will apply to other state and federal law claims including actions arising under the Securities Act (although our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder). Section 22 of the Securities Act, however, creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Accordingly, there is uncertainty as to whether a court would enforce such a forum selection provision as written in connection with claims arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the foregoing provisions. This forum selection provision in our Bylaws may limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents, which may discourage lawsuits against us and such persons. It is also possible that, notwithstanding the forum selection clause included in our Bylaws, a court could rule that such a provision is inapplicable or unenforceable.

SECURITY OWNERSHIP OF BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth certain information with respect to the beneficial ownership of our common stock as of May 19, 2020, for:

(1) each person or group of affiliated persons known by us to be the beneficial owner of more than 5% of our common stock, if any;

(2) each of our named executive officers;

(3) each of our directors; and

(4) all current executive officers and directors as a group.

Applicable percentage ownership is based on 59,630,879 shares of common stock outstanding as of May 19, 2020, after giving effect to the shares of common stock issued in the Offering. We have determined beneficial ownership in accordance with SEC rules. The information does not necessarily indicate beneficial ownership for any other purpose. Under these rules, the number of shares of common stock deemed outstanding includes shares issuable upon exercise of options or warrants, or the conversion of convertible notes, held by the respective person or group that may be exercised or converted within 60 days after May 19, 2020. For purposes of calculating each person's or group's percentage ownership, stock options and warrants exercisable, and notes convertible, within 60 days after May 19, 2020 are included for that person or group, but not the stock options of any other person or group. As of May 19, 2020, no beneficial owner owned 5% or more of the shares of common stock then outstanding.

Unless otherwise indicated and subject to applicable community property laws, to our knowledge, each stockholder named in the following table possesses sole voting and investment power over the shares listed. The address for each beneficial owner, unless otherwise noted, is c/o Diffusion Pharmaceuticals Inc. 1317 Carlton Avenue, Suite 200, Charlottesville, VA 22902.

Name of Beneficial Owner	Amount and Nature of Beneficial Ownership[1]	Percent of Class(%)[1]
Named Executive Officers and Directors		
David Kalergis[2]	78,793	*
Robert Adams[3]	36,772	*
Robert J. Cobuzzi, Ph.D.[4]	39,533	*
John L. Gainer[5]	289,890	*
Mark T. Giles[6]	86,398	*
Alan Levin[7]	33,611	*
William K. Hornung[8]	21,938	*
Thomas Byrne[9]	26,458	*
All current officers and directors as a group (eight persons)[10]	613,393	*

Less than 1%

(1) Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to securities. Shares of common stock subject to options and warrants currently exercisable, or exercisable within 60 days after May 19, 2020, are deemed outstanding for computing the percentage of the person holding such options or warrants but are not deemed outstanding for computing the percentage of any other person.

(2) Consists of (a) 4,578 shares held directly by Mr. Kalergis directly, (b) 493 shares held by Mr. Kalergis' wife, (c) 2,551 shares held jointly with Mr. Kalergis' wife and (d) 71,171 shares of common stock issuable upon the exercise of options exercisable within 60 days of May 19, 2020.

(3) Consists of (a) 1,706 shares held directly by Mr. Adams directly, (b) 631 shares held jointly with Mr. Adams' wife, (c) 1,260 shares held for the benefit of Mr. Adams in his 401(k) retirement account and (d) 33,175 shares of common stock issuable upon the exercise of options exercisable within 60 days of May 19, 2020.

(4) Consists of shares of common stock issuable upon the exercise of options exercisable within 60 days of May 19, 2020.

(5) Consists of (a) 4,389 shares held by the John L. Gainer Declaration of Trust dated February 19, 2008 and (b) 258,501 shares of common stock issuable upon the exercise of options exercisable within 60 days of May 19, 2020. Dr. Gainer is a trustee of the revocable trust, and, as such, may be deemed to share beneficial ownership of such shares. Dr. Gainer expressly disclaims beneficial ownership of any such shares except to the extent of his pecuniary interest therein.

(6) Consists of (a) 294 shares held for the benefit of Mr. Giles in his individual retirement account, (b) 53,513 shares held by MTG Investment Holdings, LLC and (c) 32,591 shares of common stock issuable upon the exercise of options exercisable within 60 days of May 19, 2020. Mr. Giles is the sole member of MTG Investment Holdings, LLC and may be deemed to be the beneficial owner of such securities. Mr. Giles disclaims beneficial ownership of such securities except to the extent of his pecuniary interest therein.

(7) Consists of (a) 1,654 shares held by Mr. Levin directly and (b) 31,957 shares of common stock issuable upon the exercise of options exercisable within 60 days of May 19, 2020.

(8) Consists of shares of common stock issuable upon the exercise of options exercisable within 60 days of May 19, 2020.

(9) Consists of (a) 9,280 shares held by Mr. Byrne directly and (b) 17,178 shares of common stock issuable upon the exercise of options exercisable within 60 days of May 19, 2020.

(10) Consists of 506,044 shares of common stock issuable upon the exercise of options exercisable within 60 days of May 19, 2020.

USE OF PROCEEDS

All shares of our common stock offered by this prospectus are being registered for the account of the selling stockholders. We will not receive any of the proceeds from the sale of these shares. We will receive proceeds from the cash exercise of the Warrants which, if exercised in cash with respect to all of the 5,821,429 shares of common stock underlying the Warrants, would result in gross proceeds of approximately $3.5 million to us. We will use any proceeds received by us from the cash exercise of the Warrants to fund research and development of our lead product candidate, TSC, including clinical trial activities, and for general corporate purposes. We cannot predict when or if the Warrants will be exercised, and it is possible that the Warrants may expire and never be exercised.

DESCRIPTION OF CAPITAL STOCK

Company Capitalization

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

Common Stock

Authorized. We are authorized to issue 1,000,000,000 shares of common stock, of which 59,630,879 shares were issued and outstanding as of May 19, 2020 (including shares of common stock issued in the Offering). 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." As of May 19, 2020, there were 473 record holders of our common stock.

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

Warrants

The material terms and provisions of the Warrants that are exercisable for the common stock registered in this Form S-1 are summarized below. The following description is subject to, and qualified in its entirety by, the forms of warrant which are incorporated by reference. You should review the forms of warrant for a complete description of the terms and conditions applicable to the warrants. See "Information Incorporated by Reference and Available Information" below.

General. Each selling stockholder received a warrant to purchase a certain number of shares of our common stock in accordance with the terms and conditions set forth in the applicable warrant.

Exercisability. The Investor Warrants may be exercised at any time on or after their date of issuance, have an exercise price of $0.5263 per share and are exercisable until November 8, 2025. The Placement Agent Exercise Warrants may be exercised at any time on or after their date of issuance, have an exercise price of $0.5938 per share and are exercisable until November 8, 2025. The Placement Agent Offering Warrants may be exercised at any time on or after their date of issuance, have an exercise price of $1.3125 per share and are exercisable until May 18, 2025. All Warrants are exercisable, at the option of each holder, in whole or in part by delivering a duly executed exercise notice accompanied by payment in full for the number of shares of our common stock purchased upon such exercise. The exercise price of the Warrant is subject to adjustment in the event of stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock.

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

Transferability. Subject to applicable laws, the Warrants are separately tradeable immediately after issuance at the option of the holders and may be transferred at the option of the holders.

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

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

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

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

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

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

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

Preferred Stock

As of March 31, 2020, no shares of preferred stock of the Company were issued or outstanding. Our Certificate of Incorporation authorizes our board of directors to provide for the issuance of up to 30,000,000 shares of preferred stock in one or more series. Our board is authorized to classify or reclassify any unissued portion of our authorized shares of preferred stock to provide for the issuance of shares of other classes or series, including preferred stock in one or more series. We may issue preferred stock from time to time in one or more classes or series, with the exact terms of each class or series established by our board. Without seeking stockholder approval, our board may issue preferred stock with voting and other rights that could adversely affect the voting power of the holders of our common stock. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of the common stock.

The rights, preferences, privileges and restrictions of the preferred stock of each series will be fixed by the certificate of designation relating to each series. The certificate of designations relating to each series will specify the terms of the preferred stock, including, but not limited to:

- the distinctive designation and the maximum number of shares in the series;
- the terms on which dividends, if any, will be paid;
- the voting rights, if any, on the shares of the series;
- the terms and conditions, if any, on which the shares of the series shall be convertible into, or exchangeable for, shares of any other class or classes of capital stock;
- the terms on which the shares may be redeemed, if at all;
- the liquidation preference, if any; and
- any or all other preferences, rights, restrictions, including restrictions on transferability, and qualifications of shares of the series.

The issuance of preferred stock may delay, deter or prevent a change in control, impair the dividend rights of common stockholders, dilute the voting rights of common stockholders and impair the liquidation rights of common stockholders.

Anti-Takeover Provisions

Delaware Anti-Takeover Law

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

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

Section 203 defines a business combination to include:

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

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

Warrants and Stock Options Issued and Outstanding

As of May 19, 2020, the Company had the following warrants outstanding to acquire shares of its common stock (including shares of common stock issuable upon exercise of the Placement Agent Offering Warrants):

	Outstanding	Range of exercise price per share	Expiration dates
Common stock warrants issued in 2017 related to Series A convertible preferred stock offering	903,870	$33.30	March 2022
Common stock warrants issued in 2018 related to the common stock offering	1,181,375	$12.00 - $15.00	January 2023
Common stock warrants issued related to the May 2019 Offering	1,382,913	$5.00 - $6.11875	May and December 2024
Common stock warrants issued related to the November 2019 Offering	1,632,018	$0.35 - $0.4375	May 2024 and December 2024
Common stock warrants issued related to the December 2019 Offering	2,551,477	$0.4335 - $0.6981	December 2024 and June 2025
Common stock warrants issued related to the May 2020 Exercise	5,250,000	$0.125 - $0.5263	November 2025
Common stock warrants issued related to the May 2020 Offering	571,429	$1.1325	May 2025
	13,473,082		

Additionally, as of March 31, 2020, we had 560,524 shares of common stock issuable upon the exercise of outstanding stock options under the 2015 Equity Plan at a weighted-average exercise price of $30.60 per share.

THE SELLING STOCKHOLDERS

This prospectus covers an aggregate of up to 5,821,429 shares of our common stock that may be sold or otherwise disposed of by the selling stockholders. Such shares are issuable to the selling stockholders upon the exercise of the Warrants we issued to the selling stockholders in a private placement transaction.

The following table sets forth certain information with respect to each selling stockholder, including (i) the shares of our common stock beneficially owned by the selling stockholder prior to this offering, (ii) the number of shares that may be offered by the selling stockholder pursuant to this prospectus and (iii) the selling stockholder's beneficial ownership after the completion of this offering, assuming that all of the shares covered hereby (but none of the other shares, if any, held by the selling stockholders) are sold.

The table is based on information supplied to us by the selling stockholders, with beneficial ownership and percentage ownership determined in accordance with the rules and regulations of the SEC and include voting or investment power with respect to shares of stock. This information does not necessarily indicate beneficial ownership for any other purpose. In computing the number of shares beneficially owned by a selling stockholder and the percentage ownership of that selling stockholder, shares of common stock subject to warrants held by that selling stockholder that are exercisable as of May 19, 2020, or exercisable within 60 days after May 19, 2020, are deemed outstanding. Such shares, however, are not deemed outstanding for the purposes of computing the percentage ownership of any other person. The percentage of beneficial ownership calculations below are based on 59,630,879 shares of common stock outstanding as of May 19, 2020, after giving effect to shares of common stock issued in the Offering.

The registration of these shares of common stock does not mean that the selling stockholders will sell or otherwise dispose of all or any of those securities. The selling stockholders may sell or otherwise dispose of all, a portion or none of such shares from time to time. We do not know the number of shares, if any, that will be offered for sale or other disposition by any of the selling stockholders under this prospectus. Furthermore, the selling stockholders may have sold, transferred or disposed of the shares of common stock covered hereby in transactions exempt from the registration requirements of the Securities Act since the date on which we filed this prospectus.

The actual number of shares of common stock included in the registration statement of which this prospectus forms a part includes, in accordance with Rule 416 under the Securities Act, such indeterminate number of additional shares of our common stock as may become issuable in connection with any proportionate adjustment for any stock splits, stock combinations, stock dividends, recapitalizations or similar events with respect to common stock.

To our knowledge and except as noted below, none of the selling stockholders has, or within the past three years has had, any position, office or other material relationship with us or any of our predecessors or affiliates.

Selling Stockholder	Beneficial Ownership Before This Offering		Shares Underlying Warrants Offered Hereby	Beneficial Ownership After This Offering	
	Number of Shares Owned	Percentage of Outstanding Shares		Number of Shares Owned	Percentage of Outstanding Shares
Armistice Capital Master Fund, Ltd. 510 Madison Ave, Floor 7 New York, NY 10022	7,677,158 (1)	4.99%(2)	5,000,000	2,677,158	4.30%
Noam Rubinstein c/o H.C. Wainwright & Co., LLC 430 Park Avenue, 4th Floor New York, New York 10022	573,961 (1)	*	258,750	315,211	*
Craig Schwabe c/o H.C. Wainwright & Co., LLC 430 Park Avenue, 4th Floor New York, New York 10022	27,724 (1)	*	27,724	-	-
Michael Vasinkevich c/o H.C. Wainwright & Co., LLC 430 Park Avenue, 4th Floor New York, New York 10022	1,173,673 (1)	1.93%	526,741	646,932	1.07%
Charles Worthman c/o H.C. Wainwright & Co., LLC 430 Park Avenue, 4th Floor New York, New York 10022	18,219 (1)	*	8,214	10,005	*

This table and the information in the notes below are based upon information supplied by the selling stockholders, including reports and amendments thereto filed with the SEC on Schedule 13G and other information available to us.

(1) All shares held are in the form of the Warrants or other warrants to purchase common stock of the Company.

(2) All warrants held by the holders are not currently exercisable by the holders if such exercise would result in the holder owning greater than 4.99% of the Company's common stock. As such, the shares that would be received upon the exercise of the warrants, if such exercise would result in the holder owning greater than 4.99% of the Company's common stock, are not included for purposes of calculating these percentages.

* Less than 1%

PLAN OF DISTRIBUTION

The selling stockholders, including their transferees, donees, pledgees, assignees and successors-in-interest, may sell, transfer or otherwise dispose of any or all of the shares of common stock offered by this prospectus from time to time on the Nasdaq Capital Market or any other stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at market prices prevailing at the time of sale, at prices related to prevailing market price or at negotiated prices. The selling stockholders may use any one or more of the following methods when selling shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- broker-dealers may agree with the selling stockholder to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise; or
- any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser in amounts to be negotiated. The selling stockholders do not expect these commissions and discounts relating to their sales of shares to exceed what is customary in the types of transactions involved.

The selling stockholder may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus, as supplemented or amended to reflect such transaction.

The selling stockholders and any broker-dealers or agents that are involved in selling the shares may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each selling stockholder has informed us that it does not have any agreement or understanding, directly or indirectly, with any person to distribute the common stock.

Because the selling stockholders may be deemed to be “underwriters” within the meaning of the Securities Act, they will be subject to the prospectus delivery requirements of the Securities Act. In addition, any securities covered by this prospectus which qualify for sale pursuant to Rule 144 under the Securities Act may be sold under Rule 144 rather than under this prospectus. The selling stockholders have advised us that there is no underwriter or coordinating broker acting in connection with the proposed sale of the resale securities by the selling stockholders.

The shares will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale shares may not simultaneously engage in market making activities with respect to our common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the selling stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of shares of our common stock by the selling stockholders or any other person. We will make copies of this prospectus available to the selling stockholders and have informed the selling stockholders of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

We are required to pay certain fees and expenses in connection with the registration of the shares of common stock issuable upon exercise of the Warrants. We have agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

We will not receive any proceeds from the sale of the shares by the selling stockholders. However, we will receive proceeds from cash exercise of the Warrants.

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon for us by Dechert LLP.

EXPERTS

The consolidated financial statements of Diffusion Pharmaceuticals Inc. as of and for the years ended December 31, 2019 and 2018, 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, 2019 consolidated financial statements contains an explanatory paragraph that states that the Company has suffered recurring losses from operations, has limited resources available to fund current research and development activities, and will require substantial additional financing to continue to fund its research and development activities that raise substantial doubt about its ability to continue as a going concern. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

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

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

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

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information into this prospectus. This means we can disclose information to you by referring you to another document we filed with the SEC. This prospectus incorporates by reference the following documents (other than any portion of the respective filings furnished, rather than filed, under the applicable SEC rules) that we have filed with the SEC but have not included or delivered with this prospectus:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC on March 17, 2020;
- our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2020, filed with the SEC on May 11, 2020;

- our Current Reports on Form 8-K filed with the SEC on January 13, 2020, February 6, 2020, March, 18, 2020, March 24, 2020, April 1, 2020, April 29, 2020, May 6, 2020, May 8, 2020, May 20, 2020, May 20, 2020, May 26, 2020 and June 1, 2020 (in each case, other than the portions of such reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items);

- our Definitive Proxy Statement on Schedule 14A filed with the SEC on April 29, 2020; and

- the description of our common stock included in Exhibit 4.12 to our Annual Report on Form 10-K for the year ended December 31, 2019, filed on March 17, 2020 under the Exchange Act, and any amendment or report we may file with the SEC for the purpose of updating such description.

Any statement contained in any document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any prospectus modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

We also incorporate by reference any future filings made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, in each case, other than those documents or the portions of those documents deemed to be furnished and not filed in accordance with SEC rules, until the offering of the securities under the registration statement of which this prospectus forms a part is terminated or completed. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and later information filed with the SEC may update and supersede some of the information included or incorporated by reference in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded.

We will provide without charge to each person, including any beneficial owners, to whom this prospectus is delivered, upon his or her written or oral request, a copy of any or all reports or documents referred to above which have been or may be incorporated by reference into this prospectus but not delivered with this prospectus, excluding exhibits to those reports or documents unless they are specifically incorporated by reference into those documents. You may request a copy of these documents 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 addition, copies of any or all of the documents incorporated herein by reference may be accessed at our website at www.diffusionpharma.com. Information contained on our website is not incorporated by reference into this prospectus or any supplement to this prospectus, and you should not consider that information to be part of this prospectus or any such supplement.

5,821,429 Shares of Common Stock
Issuable upon Exercise of Outstanding Warrants

PROSPECTUS

June 5, 2020