

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

SUBJECT TO COMPLETION, DATED FEBRUARY 11, 2021

PROSPECTUS SUPPLEMENT
(To Prospectus dated October 2, 2020)

Diffusio₂n

Pharmaceuticals Inc.

Shares of Common Stock Underwriter Warrants to Purchase Shares of Common Stock

We are offering _____ shares of our common stock, par value \$0.001 per share, pursuant to this prospectus supplement and the accompanying prospectus. The public offering price for each share of common stock is \$ _____. In addition, in connection with the offering, we are issuing common stock purchase warrants to the offering's underwriter. These warrants and the shares of common stock issuable upon exercise of the warrants will also be registered pursuant to the registration statement on Form S-3 of which this prospectus supplement and the accompanying prospectus form a part.

Our common stock is listed on the Nasdaq Capital Market under the symbol "DDFN." The last reported sale price of our common stock on the Nasdaq Capital Market on February 10, 2021 was \$1.40 per share.

The offering is being underwritten on a firm commitment basis. The underwriter may offer the shares of common stock from time to time to purchasers directly or through agents, through brokers in brokerage transactions on The Nasdaq Capital Market, to dealers in negotiated transactions or in a combination of such methods of sale, or otherwise, at fixed price or prices, which may be changed, or at market prices prevailing at the time of sale, at prices related to such prevailing market prices.

Investing in our securities involves significant risks. You should review carefully the "Risk Factors" beginning on page S-4 of this prospectus supplement, page 6 of the accompanying prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus supplement before investing 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 supplement. 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	\$ _____	\$ _____

(1) We have agreed to pay a management fee to the underwriter equal to 1.0% of the aggregate gross proceeds raised in this offering, to reimburse certain expenses of the underwriter in connection with this offering, and to issue to the underwriter (or its designees) warrants to purchase shares of common stock equal to 5.0% of the aggregate number of shares of common stock issued in this offering, including shares of common stock issued upon exercise of the underwriter option to purchase additional shares of common stock. See the section of this prospectus supplement entitled "Underwriting" for additional disclosure regarding underwriting compensation.

We have granted the underwriter an option for a period of up to 30 days from the date of this prospectus supplement to purchase up to _____ additional shares of our common stock at the public offering price, less underwriting discounts and commissions. If the underwriter exercises the option in full, the total underwriting discounts and commissions payable by us will be \$ _____ and the total proceeds to us, before expenses, will be \$ _____.

Delivery of the shares of common stock being offered pursuant to this prospectus supplement and the accompanying prospectus is expected to be made on or about _____, 2021, subject to the satisfaction of certain closing conditions.

H.C. Wainwright & Co.

The date of this prospectus supplement is _____, 2021

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is the prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under “Where You Can Find More Information” on page S-19 and “Incorporation of Certain Information by Reference” on page S-20 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update, or change information contained in the accompanying prospectus. To the extent that any statement that we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we authorize for use in connection with this offering. Neither we nor the underwriter have authorized any other person to provide you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, the securities offered hereby only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the securities offered hereby in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the securities offered hereby and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

The information appearing in this prospectus supplement, the accompanying prospectus or any related free writing prospectus that we authorize for use in connection with this offering is accurate only as of the date on the front of the document and any information we have incorporated by reference is accurate only as of the date of such document incorporated by reference, regardless of the time of delivery of this prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein contain summaries of certain provisions contained in some of the documents described herein and therein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus supplement and the accompanying prospectus are a part, and you may obtain copies of those documents as described below under the heading “Where You Can Find More Information.”

Unless the context otherwise requires, (i) references to the “Company,” “we,” “our,” or “us” refer to Diffusion Pharmaceuticals Inc. and its subsidiaries and (ii) references to “common stock” refer to the common stock, par value \$0.001 per share, of the Company.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the other information and documents incorporated herein or therein by reference include express and implied forward-looking statements. 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 this prospectus supplement, the accompanying prospectus and the other information and documents incorporated herein or therein by reference, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition, liquidity and prospects may differ materially from the forward-looking statements contained in this prospectus supplement, the accompanying prospectus and the other information and documents incorporated herein or therein by reference. In addition, even if our results of operations, financial condition, liquidity, and prospects are consistent with the forward-looking statements contained in this prospectus supplement, the accompanying prospectus and the other information and documents incorporated herein or therein by reference, they may not be predictive of actual results or reflect unanticipated developments in future periods.

Forward-looking statements appear in a number of places throughout this prospectus supplement, the accompanying prospectus and the other information and documents incorporated herein or therein by reference. 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 also include statements regarding our intentions, beliefs, projections, outlook, analyses, or expectations, including our intentions, beliefs, projections, outlook, analyses, or expectations concerning, among other things:

- our ability to obtain additional financing;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the success and timing of our clinical and preclinical studies, including our ability to enroll subjects in our ongoing clinical studies at anticipated rates;
- our ability to obtain and maintain regulatory approval of our product candidates and, if approved, our products, including the labeling under any approval we may obtain;
- our plans and ability to develop and commercialize our product candidates and the outcomes of our research and development activities;
- the accuracy of our estimates of the size and characteristics of the potential markets for our product candidates, the rate and degree of market acceptance of any of our product candidates that may be approved in the future, and our ability to serve those markets;
- the success of products that are or may become available which also target the potential markets for our product candidates;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the performance of third parties, including contract research organizations, manufacturers, and outside consultants to whom we outsource certain operational and staff functions;
- 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;
- regulatory developments in the U.S., European Union, and other foreign jurisdictions;
- recently enacted and future legislation regarding the healthcare system, including trends towards managed care and healthcare cost containment, the impact of any significant spending reductions or cost controls affecting publicly funded or subsidized healthcare programs, or any replacement, repeal, modification, or invalidation of some or all of the provisions of the U.S. Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act;
- any significant breakdown, infiltration or interruption of our information technology systems and infrastructure;
- our ability to satisfy the continued listing requirements of the NASDAQ Capital Market or any other exchange on which our securities may trade in the future;

- our ability to continue as a going concern;
- uncertainties related to general economic, political, business, industry, and market conditions, including the recent U.S. presidential election;
- the ongoing COVID-19 pandemic; and
- other risks and uncertainties, including those discussed elsewhere in our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and our other public filings.

As a result of these and other factors, known and unknown, actual results could differ materially from our intentions, beliefs, projections, outlook, analyses, or expectations expressed in any forward-looking statements in this prospectus supplement, the accompanying prospectus and the other information and documents incorporated herein or therein by reference. Accordingly, we cannot assure you that the forward-looking statements contained in this prospectus supplement, the accompanying prospectus and the other information and documents incorporated herein or therein by reference will prove to be accurate or that any such inaccuracy will not be material. You should also understand that it is not possible to predict or identify all such factors, and you should not consider any such list to be a complete set of all potential risk or uncertainties. In light of the foregoing and 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. 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.

Any forward-looking statement that we make in this prospectus supplement, the accompanying prospectus and the other information and documents incorporated herein or therein by reference speaks only as of the date of such statement, and, except as required by applicable law or by the rules and regulations of the SEC, we undertake no obligation to update such statements to reflect events or circumstances after the date of this prospectus supplement or to reflect the occurrence of unanticipated events. Comparisons of current and any prior period results are not intended to express any ongoing or future trends or indications of future performance, unless explicitly expressed as such, and should only be viewed as historical data.

Note Regarding Trademarks, Trade Names and Service Marks

This prospectus supplement, the accompanying prospectus and the other information and documents incorporated herein or therein by reference may contain the following trademarks, trade names and service marks of ours: “DIFFUSIO2N.” All other trade names, trademarks and service marks appearing in this prospectus supplement, the accompanying prospectus and the other information and documents incorporated herein or therein by reference are, to the knowledge of Diffusion, the property of their respective owners. To the extent any such terms appear without the trade name, trademark or service mark notice, such presentation is for convenience only and should not be construed as being used in a descriptive or generic sense.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about us, this offering and the information appearing elsewhere in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus supplement, the accompanying prospectus and any related free writing prospectus that we authorize for use in connection with this offering, including the risks of investing in our securities discussed under the heading “Risk Factors” beginning on page S-4 of this prospectus supplement and under similar headings in the accompanying prospectus or the documents incorporated by reference herein or therein, including our Annual Report on Form 10-K for the year ended December 31, 2019. You should also carefully read the information incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements and related notes, and the exhibits to the registration statement of which this prospectus supplement and the accompanying prospectus are a part, before making your investment decision.

Overview

We are an innovative, clinical stage biopharmaceutical company developing novel therapies that enhance the body’s ability to deliver oxygen to the areas where it is needed most. Our lead product candidate, trans sodium crocetinate (“TSC”), is being developed to enhance the diffusion of oxygen to tissues with low oxygen levels, also known as hypoxia, a serious complication of many of medicine’s most intractable and difficult-to-treat conditions.

TSC was designed to enhance the level of organization among water molecules by increasing the amount of hydrogen bonding. This creates a less dense matrix of water molecules, which facilitates the diffusion of oxygen molecules from areas of high to low oxygen concentrations, such as from oxygenated red blood cells into tissues where the oxygen is used to power the cells. In animal models, this diffusion-enhancing mechanism of action has been observed to affect hypoxic tissue preferentially while avoiding excessive oxygen-related tissue toxicity, also known as hyperoxia.

TSC previously has been demonstrated safe and tolerable in certain dosages in over 180 subjects included in our clinical programs across a variety of medical conditions often complicated by hypoxia, including our clinical studies conducted in patients afflicted with glioblastoma multiforme brain cancer (“GBM”), peripheral artery disease with intermittent claudication, and stroke, as well as our Phase 1b clinical trial evaluating TSC in hospitalized COVID-19 patients, designated as Protocol 100-303, initiated in September 2020 (the “100-303 COVID Trial”). In each of these conditions and many others, hypoxia is a significant contributor to morbidity and mortality, and a considerable treatment obstacle for medical providers.

In addition to TSC, the Company’s product candidate DFN-529, a novel, allosteric PI3K/Akt/mTOR pathway inhibitor, is in early-stage development. The Company previously completed two Phase 1 clinical trials evaluating DFN-529 in age-related macular degeneration, and DFN-529 was also previously in preclinical development in oncology, specifically GBM.

100-303 COVID Trial

On September 10, 2020, we announced the dosing of the first two patients in our 100-303 COVID Trial evaluating TSC in hospitalized COVID-19 patients at the NIID in Bucharest, Romania. The primary endpoint of the 100-303 COVID Trial was to evaluate the safety and tolerability of TSC administered every six (6) hours for up to 15 days, a more frequent dosing regimen than has been used in our previous clinical studies. Secondary endpoints included pharmacokinetic measurement of TSC levels after dosing, relative improvements in blood oxygen levels, and certain other clinical parameters related to COVID-19.

On February 9, 2021, we completed dosing of the twenty-fourth and final patient in the 100-303 COVID Trial. No dose-limiting toxicities were observed among any patients who received doses of 0.25 mg/kg, 0.5 mg/kg, or 1.0 mg/kg every 6 hours. Data for the final 1.5 mg/kg dose group of patients are currently being prepared for review by the trial’s external safety monitoring committee. Diffusion anticipates the committee will hold its initial meeting to evaluate the data from the final dose group on Friday, February 12, 2021. We will announce the topline, safety and tolerability data for the final dose group promptly following completion of the committee’s evaluation. Analyses of the secondary endpoint data are anticipated to be completed and announced before the end of the first quarter of 2021.

Anticipated Next Steps in TSC Development Program

Looking beyond the 100-303 COVID Trial, the next step we have planned in the development of TSC is the design and execution of clinical studies using short-term, experimental models to evaluate the clinical effects of TSC on oxygenation. To date, TSC has been administered to more than 180 subjects in clinical studies. Data from these clinical studies have contributed significantly to our understanding of the safety, tolerability, and pharmacokinetics of TSC. In addition, potential indications of efficacy have been observed in two studies, including a small study in patients with peripheral artery disease with claudication and also in a post hoc analysis of patients with unresected GBM tumors. However, neither of these studies was statistically powered to formally evaluate efficacy, so we believe that further, robust clinical development of TSC requires a prospective exploration of the relationship between dose and oxygenation. To this end, we plan to conduct these short-term clinical studies over the coming months.

The first study (the “TCOM Study”), which we expect to initiate in March 2021, will measure the effects of TSC on peripheral tissue oxygenation using a device called a transcutaneous oximeter (“TCOM”). This device directly measures the release of oxygen from the blood vessels through the skin and is commonly used to predict the likelihood of wound healing, the potential for success with hyperbaric therapy, and to map the appropriate location for limb amputation. The TCOM Study is designed as a double-blind, randomized, placebo-controlled study in healthy volunteers breathing 100% oxygen. The TCOM Study will test escalating doses of TSC in an attempt to establish a dose-response relationship on enhanced oxygen delivery and will be statistically powered to evaluate the effect on tissue oxygenation levels versus placebo. We anticipate this study to be completed in the second quarter of 2021, with topline results available within one to two months following study completion.

The second planned study (the “DLCO Study”) will measure the diffusion of carbon monoxide through the lungs (“DLCO”) as a surrogate measure of oxygen transfer efficiency, or uptake, from the alveoli of the lungs, through the plasma, and onto hemoglobin within red blood cells. \ DLCO testing is commonly performed as part of standard pulmonary function testing and aids in the diagnosis or dyspnea (a.k.a. shortness of breath), as well as tracking improvement or progression over time on prescribed treatments. We plan to use the DLCO Study to evaluate the diffusion enhancing effects of TSC in patients with previously diagnosed interstitial lung disease who have a baseline DLCO test result that is abnormal. The DLCO Study will be designed as a double-blind, randomized, placebo-controlled study of escalating doses of TSC in an attempt to establish a dose-response relationship and will be statistically powered to evaluate the effect versus placebo. We anticipate this study to be initiated in the second quarter and be completed in the third quarter of 2021, with topline results available within one to two months of study completion.

Assuming we are successful in these next steps, we believe that the data from these studies will provide definitive proof of effect on enhanced oxygenation from uptake in the lungs to delivery at the tissue level, and also provide important dose-response data that will guide our efforts to optimize our clinical development strategy focusing on the hypoxia continuum (agnostic of the causation or therapeutic space), including the specification of relevant patient populations and indications and our corresponding regulatory strategy.

Corporation 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	Shares
Common stock to be outstanding immediately after this offering	shares (or shares if the underwriter exercises in full its option to purchase additional shares).
Underwriter option to purchase additional shares	We have granted the underwriter an option to purchase up to additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.
Use of Proceeds	We currently intend to use the net proceeds from this offering to fund research and development of our lead product candidate, TSC, including the TCOM Study, the DLCO Study, and other clinical trial activities, and for general corporate purposes. See “Use of Proceeds” on page S-8 of this prospectus supplement.
Risk Factors	Investing in our common stock involves significant risks. You should read the “Risk Factors” section beginning on page S-4 of this prospectus supplement and the accompanying prospectus, as well as all other information included in this prospectus supplement, the accompanying prospectus, and the information incorporated herein and therein by reference 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 “DDFN.”

The number of shares of our common stock to be outstanding after this offering is based on 68,018,555 shares of common stock outstanding as of February 10, 2021, and excludes:

- As of February 10, 2021, 2,240,204 shares of common stock issuable upon the exercise of outstanding stock options and vesting of restricted stock units under the Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan, as amended (the “2015 Equity Plan”), and with respect to such options, at a weighted-average exercise price of \$8.28 per share;
- As of February 10, 2021, 5,100,066 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 \$10.34 per share; and
- As of February 10, 2021, 2,105,744 shares of common stock reserved for future issuance under the 2015 Equity Plan.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below and under the section captioned “Risk Factors” contained in our most recent Annual Report on Form 10-K, as revised and supplemented by our Quarterly Reports on Form 10-Q filed since the filing of our most recent Annual Report on Form 10-K, each of which is incorporated by reference herein, together with the other information contained or incorporated by reference in this prospectus before making a decision to invest in our securities. We cannot assure you that any of the events discussed in the risk factors below will not occur. These risks could have a material and adverse impact on our business, results of operations, financial condition and cash flows, and our future prospects would likely be materially and adversely affected. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment.

Risks Related to the Offering

Our stock price is volatile, and your investment may suffer a decline in value.

The closing market price for our common stock has varied between a high of \$1.60 on July 21, 2020, and a low of \$0.25 on March 17, 2020, in the twelve-month period ended February 10, 2021. As a result of fluctuations in the price of our common stock, you may be unable to sell your shares at or above the price you paid for them. The market price of our common stock is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market, industry and other factors, including the risk factors described under the section captioned “Risk Factors” contained in our Annual Report on Form 10-K for the year ended December 31, 2019 and our subsequent Quarterly Reports on Form 10-Q, all of which are incorporated by reference in this prospectus supplement in their entirety. The market price of our common stock may also be dependent upon the valuations and recommendations of the analysts who cover our business. If the results of our business do not meet these analysts’ forecasts, the expectations of investors or the financial guidance we provide to investors in any period, the market price of our common stock could decline.

In addition, the stock markets in general, and the markets for biotechnology stocks in particular, have experienced significant volatility that has often been unrelated to the financial condition or results of operations of particular companies. These broad market fluctuations may adversely affect the trading price of our common stock and, consequently, adversely affect the price at which you could sell the shares that you purchase in this offering. In the past, following periods of volatility in the market or significant price declines, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management’s attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

If you purchase shares in this offering, you will suffer immediate dilution of your investment.

Because the public offering price per share of our common stock is higher than the net tangible book value per share of our common stock, you will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Investors purchasing shares of common stock in this offering will incur immediate dilution of approximately \$ per share, after giving effect to this offering. In addition, we have stock options and warrants outstanding. To the extent that such outstanding securities are exercised for shares of our common stock, investors purchasing our securities in this offering may experience further dilution.

You may experience significant dilution as a result of future financings and the exercise of outstanding options or warrants.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock, including offerings pursuant to the accompanying base prospectus. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering.

In addition, as described above under the heading , “The Offering,” we have a significant number of securities convertible into, or allowing the purchase of, our common stock. The exercise of outstanding options or warrants having an exercise price per share that is less than the offering price per share in this offering will increase dilution to investors in this offering. Moreover, to the extent that we issue additional options to purchase, or securities convertible into or exchangeable for, shares of our common stock in the future and those options or other securities are exercised, converted, or exchanged, stockholders may experience further dilution.

We will have broad discretion in the use of the net proceeds from this offering and may allocate the net proceeds from this offering in ways that you and other stockholders may not approve.

Our management will have broad discretion in the use of the net proceeds, including for any of the purposes described in the section entitled “Use of Proceeds,” and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, the ultimate use of proceeds may vary substantially from their currently intended use. The failure of our management to use these funds effectively could have a material adverse effect on our business, cause the market price of our common stock to decline and delay the development or commercialization of our product candidates. Pending use, we may invest any net proceeds from this offering in a manner that does not produce income or loses value. Please see the section entitled “Use of Proceeds” on page S-8 of this prospectus supplement for further information.

If we sell additional equity or debt securities to fund our operations, it may impose restrictions on our business.

In order to raise additional funds to support our operations, we may in the future sell additional equity or debt securities, which may impose restrictive covenants that adversely impact our business. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we are unable to expand our operations or otherwise capitalize on our business opportunities due to such restrictions, our business, financial condition, and results of operations could be materially adversely affected.

Future sales of our common stock in the public market or other financings could cause our stock price to fall, and a substantial number of shares of common stock may be sold in the market following this offering, which may depress the market price for our common stock.

Sales of a substantial number of shares of our common stock in the public market, the perception that these sales might occur, or other financings could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. A substantial portion of the outstanding shares of our common stock are, and all of the shares sold in this offering upon issuance will be freely tradable without restriction or further registration under the Securities Act unless these shares are owned or purchased by “affiliates” as that term is defined in Rule 144 (“Rule 144”) promulgated under the Securities Act of 1933, as amended. In addition, shares of common stock issuable upon exercise of outstanding warrants and options, as well as shares reserved for future issuance under our incentive stock plan, will be eligible for sale in the public market to the extent permitted by applicable vesting requirements, if any, and, in some cases, subject to compliance with the requirements of Rule 144. As a result, these shares will be eligible to be freely sold in the public market upon issuance, subject to restrictions under the securities laws.

Sales of a substantial number of shares of our common stock in the public market following this offering could cause the market price of our common stock to decline. A substantial majority of the outstanding shares of our common stock are, and the shares of our common stock offered hereby will be, freely tradable without restriction or further registration under the Securities Act.

Because we do not currently intend to declare cash dividends on our shares of common stock in the foreseeable future, stockholders must rely on appreciation of the value of our common stock for any return on their investment.

We have never declared or paid cash dividends on our common stock and do not currently anticipate declaring or paying any cash dividends in the foreseeable future. In addition, the terms of any existing or future debt agreements may preclude us from paying dividends. As a result, we expect that only appreciation of the price of our common stock, if any, will provide a return to investors in this offering for the foreseeable future.

Other Risks Related to Our Business

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 COVID-19 pandemic has resulted in significant financial market volatility, and its impact on the global economy and our operations remains uncertain. While we have business continuity plans in place to help mitigate the impact of COVID-19, 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 the pandemic continues, and if conditions worsen, we may experience adverse effects on our operational activities and our financial condition. It is unclear which adverse effects may be material, and it remains uncertain the degree to which these adverse effects would impact our future operational activities and financial condition. With the recent relaxation of restrictions on business operations and in-person gatherings there has been a resurgence in COVID-19 infections in numerous jurisdictions, resulting in the reinstatement of stricter restrictions and shutdowns. It is expected that there will be an ebb and flow to the pandemic with different jurisdictions having higher levels of infections than others over the course of the pandemic. In addition to existing travel restrictions, jurisdictions may continue or reinstate border closures, impose, or reimpose prolonged quarantines and further restrict travel and business activity.

As a result of the ongoing COVID-19 pandemic, we have experienced and may continue to experience disruptions that could severely impact our business and clinical trials. Any negative impact that the COVID-19 pandemic has had or will continue to have 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 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.

Our product candidates, if approved, will face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration.

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition, and a strong emphasis on developing proprietary therapeutics. Numerous companies are engaged in the development, patenting, manufacturing, and marketing of health care products competitive with those that we are developing. For example, in January 2021, the Company became aware of a third party affiliated with a former outside consultant of the Company which claims to be in early-stage development of a product candidate that purportedly may operate through a similar mechanism of action to TSC. While it is unclear if this particular product candidate would, if developed and approved, actually be competitive with TSC or any of our other product candidates, we face competition from a number of sources, such as pharmaceutical companies, generic drug companies, biotechnology companies and academic and research institutions, many of which have greater financial resources, marketing capabilities, sales forces, manufacturing capabilities, research and development capabilities, clinical trial expertise, intellectual property portfolios, experience in obtaining patents and regulatory approvals for product candidates and other resources than us.

Many pharmaceutical companies currently offer products, and continue to develop additional alternative product candidates and technologies, for indications similar to those targeted by our product candidates. We anticipate that, if we obtain regulatory approval of any of our product candidates, we will face significant competition from other approved therapies including therapies manufactured, sold, and distributed by companies with a broad range of other product offerings, large direct sales forces and long-term customer relationships with our expected target physicians, which could inhibit our market penetration efforts. If approved, our product candidates may also compete with unregulated, unapproved, and off-label treatments. Certain of our product candidates, if approved, will present novel therapeutic approaches for the approved indications and will have to compete with existing therapies, some of which are widely known and accepted by physicians and patients. To compete successfully in this market, we will have to demonstrate that the relative cost, safety, and efficacy of our products, when and if approved, provide an attractive alternative to existing and other new therapies. Such competition could lead to reduced market share for our product candidates and contribute to downward pressure on the pricing of our product candidates, which could harm our business, financial condition, operating results, and prospects.

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, as amended (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.

USE OF PROCEEDS

We estimate that the net proceeds from the offering will be approximately \$ million (or approximately \$ million if the underwriter exercises in full its option to purchase up to additional shares), after deducting 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 the TCOM Study, the DLCO Study, and other clinical trial activities, and for general corporate purposes.

The amounts and timing of our use of the net proceeds from this offering will depend on a number of factors, such as the timing and progress of our research and development efforts for TSC, the timing and progress of any clinical trial activities, partnering, or future commercialization efforts, technological advances, and the competitive environment for TSC, among other things. Accordingly, our management will have broad discretion in the timing and application of these proceeds. 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.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock in the past and do not currently intend to pay cash dividends on our common stock in the foreseeable future. Any future determination to pay cash dividends will be at the discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements and other factors our board of directors deems relevant.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the offering price per share of our common stock and the as adjusted net tangible book value per share of our common stock immediately after this offering.

As of September 30, 2020, we had a historical net tangible book value of \$20.1 million, or \$0.31 per share of common stock. Our historical net tangible book deficit per share represents the amount of our total tangible assets less total liabilities, divided by the total number of shares of common stock outstanding at September 30, 2020.

After giving effect to this offering of _____ shares common stock at a public offering price of \$ _____ per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value per share of our common stock as of September 30, 2020 would have been approximately \$ _____ million, or \$ _____ per share of common stock. This represents an immediate increase in net tangible book value of approximately \$ _____ per share to our existing stockholders and an immediate dilution of approximately \$ _____ per share to purchasers of our common stock in this offering, as illustrated by the following table:

The following table illustrates this hypothetical dilution on a per share basis:

Public offering price per share		\$
Historical net tangible book value per share at September 30, 2020	\$	0.31
Increase in net tangible book value per share attributable to new investors participating in this offering	_____	
As adjusted net tangible book value per share after giving effect to this offering		\$
Dilution per share to new investors participating in this offering		_____

If the underwriter exercises its option to purchase additional shares in full, our as adjusted net tangible book value per share at September 30, 2020 after giving effect to this offering would have been \$ _____ per share, and the dilution in as adjusted net tangible book value per share to investors in this offering would have been \$ _____ per share.

The number of shares of our common stock to be outstanding after this offering is based on 64,015,441 shares of common stock outstanding as of September 30, 2020, and excludes:

- As of September 30, 2020, 2,040,204 shares of common stock issuable upon the exercise of outstanding stock options and vesting of restricted stock units under the Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan, as amended (the "2015 Equity Plan"), and with respect to such options, at a weighted-average exercise price of \$9.01 per share; and
- As of September 30, 2020, 9,100,112 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 \$6.04 per share.

Additionally, the foregoing calculations assume no exercise by the underwriter of its option to purchase additional shares of our common stock and do not reflect any of the following transactions or events that occurred after September 30, 2020:

- the issuance, exercise, expiration or forfeiture of any additional equity awards under our equity incentive plans or our outstanding warrants; and;
- the automatic increase, effective January 1, 2021 in the number of shares available for future grant pursuant to our equity incentive plans pursuant to the evergreen provisions of such plans.

To the extent that additional options or other convertible securities are issued, or outstanding options or warrants are exercised, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

The discussion of dilution, and the table quantifying it, assume no exercise or settlement of any outstanding equity awards, exercise of warrants, including the underwriter warrants issued as compensation to the underwriter for this offering, or other potentially dilutive securities. The exercise of potentially dilutive securities having an exercise price less than the offering price would increase the dilutive effect to new investors.

DESCRIPTION OF SECURITIES OFFERED

Common Stock

The descriptions of our common stock included in the accompanying prospectus under the headings “Description of Capital Stock – Company Capitalization” and “Description of Capital Stock – Common Stock” are incorporated herein by reference.

Underwriter’s Warrants

We have agreed to grant the underwriter (or its designees) warrants to purchase _____ shares of our common stock, which represents 5.0% of the aggregate number of shares sold this offering, including any shares of common stock issued upon exercise of option to purchase additional shares (and warrants to purchase up to an additional _____ shares if the underwriter exercises its option to purchase additional shares in full), with an exercise price of \$ _____ per share. The underwriter warrants will be exercisable immediately and for five years from the commencement of the sales of this offering. The warrants issued to the underwriter and the shares of common stock issuable upon exercise of the warrants issued to the underwriter are registered on the registration statement of which this prospectus forms a part.

The following summary of certain terms and provisions of the underwriter warrants is not complete and is subject to, and qualified in its entirety by, the provisions of the underwriter warrants, the form of which will be filed with the SEC as an exhibit to a Current Report on Form 8-K in connection with this offering and incorporated by reference into the registration statement of which this prospectus supplement forms a part.

Duration and Exercise Price

The exercise price and number of shares issuable upon exercise is subject to appropriate adjustment in the event of share dividends, share splits, reorganizations or similar events affecting our shares and the exercise price.

Exercisability

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

Cashless Exercise

If, at the time a holder exercises its underwriter warrants, a registration statement registering the issuance of the shares underlying the underwriter warrants under the Securities Act is not then effective or available for the issuance of such shares, 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 and subject to the nominal value of the shares being paid up as described below, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares determined according to a formula set forth in the underwriter warrants.

Fractional Shares

No underwriter warrant for fractional shares will be issued, rather underwriter warrants will be issued only for whole shares. No fractional share will be issued upon the exercise of the underwriter warrants. Rather, the number of shares to be issued will be rounded down to the nearest whole number.

Transferability

Subject to applicable laws, an underwriter warrant may be transferred at the option of the holder upon surrender of the underwriter warrant to us together with the appropriate instruments of transfer.

Trading Market

There is no trading market available for the underwriter warrants on any securities exchange or nationally recognized trading system, and we do not expect a trading market to develop. We do not intend to list the underwriter warrants on any securities exchange or nationally recognized trading market. Without a trading market, the liquidity of the underwriter warrants will be extremely limited. The shares issuable upon exercise of the underwriter warrants are currently traded on the Nasdaq Capital Market.

Right as a Shareholder

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

Fundamental Transaction

In the event of a fundamental transaction, as described in the underwriter warrants and generally including any reorganization, recapitalization or reclassification of our shares, 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 shares, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding shares, the holders of the underwriter warrants will be entitled to receive upon exercise of the underwriter warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the underwriter warrants immediately prior to such fundamental transaction.

UNDERWRITING

Pursuant to the underwriting agreement with H.C. Wainwright & Co., LLC, or the underwriter and the sole book-running manager of this offering, we have agreed to issue and sell, and the underwriter has agreed to purchase, the number of shares of common stock listed opposite its name below, less the underwriting discounts and commissions, on the closing date, subject to the terms and conditions contained in the underwriting agreement. The underwriting agreement provides that the obligations of the underwriter are subject to certain customary conditions precedent, representations and warranties contained therein.

Underwriter	Number of Shares
H.C. Wainwright & Co., LLC	

Pursuant to the underwriting agreement, the underwriter has agreed to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. The underwriter has advised us that it does not intend to confirm sales to any account over which it exercises discretionary authority.

Discounts, Commissions, and Expenses

The underwriter may offer the shares of common stock from time to time to purchasers directly or through agents, or through brokers in brokerage transactions on The Nasdaq Capital Market, or to dealers in negotiated transactions or in a combination of such methods of sale, or otherwise, at a fixed price or prices, which may be changed, or at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices, subject to receipt and acceptance by it and subject to its right to reject any order in whole or in part. The difference between the price at which the underwriter purchases shares from us and the price at which the underwriter resells such shares may be deemed underwriting compensation. If the underwriter effects such transactions by selling shares of common stock to or through dealers, such dealers may receive compensation in the form of discounts, concessions, or commissions from the underwriter and/or purchasers of shares of common stock for whom they may act as agents or to whom they may sell as principal.

The underwriter is offering the shares, subject to prior sale, when, as and if issued to and accepted by it, subject to approval of legal matters and other conditions specified in the underwriting agreement. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

We have granted to the underwriter an option to purchase up to _____ additional shares of common stock at the public offering price, less the underwriting discount. The option is exercisable for 30 days from the date of this prospectus supplement.

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.

Per Share	Total Without Option	Total With Option
Public offering price	\$	
Underwriting discounts and commissions payable by us	\$	
Proceeds, before expenses, to us	\$	

We have agreed to pay the legal fees and expenses of the underwriter, in the sum of up to \$100,000 in connection with this offering, \$50,000 for nonaccountable expenses and clearing fees of \$15,950. We have also agreed to pay the underwriter a management fee equal to 1.0% of the aggregate gross proceeds in this offering. We estimate that the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$_____ and are payable by us.

Additionally, we agreed to grant the underwriter (or its designees) warrants to purchase _____ shares of our common stock, which represents 5.0% of the aggregate number of shares sold this offering, including any shares of common stock issued upon exercise of option to purchase additional shares (and warrants to purchase up to an additional _____ shares if the underwriter exercises its option to purchase additional shares in full), with an exercise price of \$_____ per share (representing 125% of the public offering price per share).. The underwriter warrants will be exercisable immediately and for five years from the commencement of the sales of this offering. The warrants issued to the underwriter and the shares of common stock issuable upon exercise of the warrants issued to the underwriter are registered on the registration statement of which this prospectus forms a part.

Right of First Refusal

We have granted the underwriter a 12-month right of first refusal to act as sole book-running manager, sole underwriter, or sole placement agent if we or any of our subsidiaries raise funds by means of a public offering or a private placement or any other capital-raising financing of equity, equity-linked or debt securities using an underwriter or placement agent other than with respect to certain excluded transactions. If the underwriter or an affiliate of the underwriter accepts any such engagement, the agreement governing such engagement will contain, among other things, provisions for customary fees and terms for transactions of similar size and nature, including indemnification, which are appropriate to such a transaction.

Tail

In the event that any investors that were contacted about this offering or were introduced to us in connection with this offering by the underwriter provide any capital to us in a public or private offering or capital-raising transaction within six months following the date of our engagement of the underwriter, we shall pay the underwriter the cash and warrant compensation provided above on the gross proceeds from such investors.

Indemnification

We have agreed to indemnify the underwriter against certain liabilities, including civil liabilities under the Securities Act, or to contribute to payments that the underwriter may be required to make in respect of those liabilities.

Lock-Up Agreements

We and our officers and directors have agreed to not sell any shares of our common stock or any securities convertible into or exercisable or exchangeable into share of common stock, subject to certain exceptions, for a period of 90 days after the date of closing of the offering pursuant to this prospectus supplement unless we or our officers and directors obtain prior written consent of the underwriter. This consent may be given at any time without public notice, and the underwriter may consent in its sole discretion. The exceptions to the restriction include, among other things, the issuance of any shares of our capital stock or securities convertible into shares of our capital stock that are issued (i) pursuant to a stock or option plan, (ii) pursuant to the exercise or exchange of or conversion of any securities exercisable or exchangeable for or convertible into shares of common stock issued and outstanding on the date of this prospectus supplement, provided that such securities are not amended after the date of this prospectus supplement, (iii) as consideration in an acquisition, merger or similar strategic transaction approved by a majority of the disinterested directors, provided that such securities are issued as “restricted securities” as defined in Rule 144 and carry no registration rights that require or permit the filing of any registration statement in connection therewith within 90 days after the date of this prospectus supplement, and provided that any such issuance shall only be to a person providing us business synergies and additional benefits in addition to the investment of funds, but shall not include a transaction in which we are issuing securities primarily for the purpose of raising capital or to an entity whose primary business is investing in securities. In addition, subject to an exception for an “at the market” offering, after 90 days following the date of closing of this offering, we have agreed to not issue any securities that are subject to a price reset based on the trading prices of our common stock or upon a specified or contingent event in the future, or enter into any agreement to issue securities at a future determined price, for one year following the date of closing of this offering, which prohibition may be waived at any time without public notice by the underwriter.

Price Stabilization, Short Positions, and Penalty Bids

In connection with this offering, the underwriter may engage in stabilizing transactions, over-allotment transactions, syndicate covering transactions and penalty bids in connection with our common stock.

Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum.

Over-allotment transactions involve sales by the underwriter of common shares in excess of the number of shares the underwriter is obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriter is not greater than the number of shares that it may purchase in the over-allotment option. In a naked short position, the number of shares involved is greater than the number of shares in the over-allotment option. The underwriter may close out any short position by exercising its over-allotment option and/or purchasing shares in the open market.

Syndicate covering transactions involve purchases of common stock 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 securities 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 securities in the open market after pricing that could adversely affect investors who purchase in the offering.

Penalty bids permit the underwriter to reclaim a selling concession from a syndicate member when the securities originally sold by the syndicate member are purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriter makes 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 otherwise 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.

Electronic Distribution

A prospectus in electronic format may be made available on the websites maintained by the underwriter, if any, participating in this offering and the underwriter may distribute prospectuses electronically. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or the underwriter, and should not be relied upon by investors.

Other Relationships

From time to time, the underwriter and its affiliates have provided, and may provide in the future, various advisory, investment and commercial banking and other services to us in the ordinary course of business, for which it has received and may continue to receive customary fees and commissions. In particular, the underwriter served as our exclusive underwriter in connection with our public offering in January 2018, as the exclusive placement agent in connection with our registered direct offering that we consummated in May 2019, as the placement agent in connection with our public offering that we consummated in November 2019, as the exclusive placement agent for the registered direct offering that we consummated in December 2019, as the exclusive placement agent for the warrant exercise and related issuance that we consummated in May 2020, and as the exclusive placement agent for the public offering that we consummated in May 2020, for which it received compensation.

Transfer Agent

The transfer agent and registrar for our common stock is Computershare, Inc. The transfer agent's address is 150 Royall Street, Canton, Massachusetts 02021.

Listing on the Nasdaq Capital Market Listing

Our stock is currently traded on the Nasdaq Capital Market under the symbol "DFFN." On February 10, 2021, the last reported sale price of our common stock was \$1.40 per share.

NOTICE TO INVESTORS

European Economic Area and the United Kingdom

This prospectus has been prepared on the basis that any offer of shares of common stock in any member state of the European Economic Area or the United Kingdom (each a “Relevant State”) will be made pursuant to an exemption under the Prospectus Regulation from the requirement to publish a prospectus for offers of shares of common stock. Accordingly, any person making or intending to make an offer in that Relevant State of shares of common stock which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the company or the underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation, in each case in relation to such offer. Neither the company nor the underwriter have authorized, nor do they authorize, the making of any offer of shares of common stock in circumstances in which an obligation arises for the company or the underwriter to publish or supplement a prospectus for such offer. Neither the company nor the underwriter have authorized, nor do they authorize, the making of any offer of shares of common stock through any financial intermediary, other than offers made by the underwriter, which constitute the final placement of the shares of common stock contemplated in this prospectus.

The expression “Prospectus Regulation” means Regulation (EU) 2017/1129 (as amended or superseded). In relation to each Relevant State, no shares of common stock have been offered or will be offered to the public in that Relevant State, except that offers of shares of common stock may be made to the public in that Relevant State:

- to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares of common stock shall require the company or the underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

Each person in a Relevant State who receives any communication in respect of, or who acquires any shares of common stock under, the offers to the public contemplated in this prospectus, or to whom the shares of common stock are otherwise made available, will be deemed to have represented, acknowledged and agreed to and with the company and the underwriter that it and any person on whose behalf it acquires shares of common stock is a (a) qualified investor within the meaning of Article 2(e) of the Prospectus Regulation; and (b) in the case of any shares of common stock acquired by it as a financial intermediary as that term is used in Article 5(1) of the Prospectus Regulation, (i) the shares of common stock acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant State other than qualified investors, as that term is defined in the Prospectus Regulation, or in circumstances in which the prior consent of the underwriter has been obtained to each such proposed offer or resale, or (ii) where shares of common stock have been acquired by it on behalf of persons in any Relevant State other than qualified investors, the offer of those shares of common stock to it is not treated under the Prospectus Regulation as having been made to such persons.

We, the underwriter, and affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements, and agreements.

For the purposes of this provision, the expression an “offer to the public” in relation to any shares of common stock in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of common stock to be offered so as to enable an investor to decide to purchase or subscribe for any shares of common stock, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

Any distributor subject to Directive 2014/65/EU (as amended, “MiFID II”) subsequently offering, selling, or recommending the shares of common stock is responsible for undertaking its own target market assessment in respect of the shares of common stock and determining the appropriate distribution channels for the purposes of the MiFID II product governance rules under Commission Delegated Directive (EU) 2017/593 (“Delegated Directive”). Neither the company nor the underwriter makes any representations or warranties as to a Distributor’s compliance with the Delegated Directive.

References to Regulations or Directives include, in relation to the United Kingdom, those Regulations or Directives as they form part of United Kingdom domestic law by virtue of the European Union (Withdrawal) Act 2018 or have been implemented in United Kingdom domestic law, as appropriate. The above selling restriction is in addition to any other selling restrictions set out below.

In connection with the offering, the underwriter is not acting for anyone other than the issuer and will not be responsible to anyone other than the issuer for providing the protections afforded to their clients nor for providing advice in relation to the offering.

United Kingdom

This document is for distribution only to persons who (i) have professional experience in matters relating to investments and who qualify as investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended, the “Financial Promotion Order”), (ii) are persons falling within Article 49(2)(a) to (d) (“high net worth companies, unincorporated associations etc.”) of the Financial Promotion Order, (iii) are outside the United Kingdom, or (iv) are persons to whom an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, as amended (“FSMA”)) in connection with the issue or sale of any securities may otherwise lawfully be communicated or caused to be communicated (all such persons together being referred to as “relevant persons”). This document is directed only at relevant persons and must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.

Switzerland

This document is not intended to constitute an offer to, or solicitation of, investors in Switzerland to purchase or invest in shares of common stock. The shares of common stock may not be publicly offered, directly or indirectly, in Switzerland within the meaning of FinSA (unless in circumstances falling within article 36 of the FinSA). This document does not constitute a prospectus pursuant to the FinSA and has been prepared without regard to the disclosure standards for issuance prospectuses under the FinSA, art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares of common stock or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the company, or the shares of common stock have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document has not been and will not be reviewed or approved by a Swiss reviewing body (“Prüfstelle”) pursuant to article 51 of the FinSA and does not comply with the disclosure requirements applicable to a prospectus within the meaning of article 35 of the FinSA. Further, this document will not be filed with, and the offer of shares of common stock will not be supervised by, the Swiss Financial Market Supervisory Authority (“FINMA”), and the offer of shares of common stock has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (“CISA”). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares of common stock.

Canada

The shares of common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares of common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In the State of Israel, this document is being distributed only to, and is directed only at, and any offer of the shares of common stock is directed only at, investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and "qualified individuals", each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors will be required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

LEGAL MATTERS

The validity of the shares of common stock offered hereby is being passed upon by Dechert LLP, Ellenoff Grossman & Schole LLP, New York, New York is acting as counsel to the underwriter in connection with this offering.

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 MORE INFORMATION

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 we filed with the Commission under the Securities Act and do not contain all the information set forth or incorporated by reference in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus as to the contents of any contract or any other document referred to herein 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. Our SEC filings are also available to you, free of charge, through our Internet web site at www.diffusionpharma.com.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information into this prospectus supplement. This means we can disclose information to you by referring you to another document we filed with the SEC. We will make those documents available to you without charge upon your oral or written request. Requests for those documents should be directed to Investor Relations Department, Diffusion Pharmaceuticals Inc., 1317 Carlton Avenue, Suite 200, Charlottesville, Virginia 22902, Attention: General Counsel & Secretary, telephone: (434) 220-0718. This prospectus supplement 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 supplement:

- 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 Reports on Form 10-Q for the fiscal quarters ended March 31, 2020, filed with the SEC on [May 11, 2020](#), June 30, 2020, filed with the SEC on [August 7, 2020](#), and September 30, 2020, filed with the SEC on [November 12, 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 26, 2020](#), [June 1, 2020](#), [June 12, 2020](#), [June 17, 2020](#), [July 7, 2020](#), [July 29, 2020](#), [September 4, 2020](#), [September 9, 2020](#), [September 10, 2020](#), [September 25, 2020](#), [October 9, 2020](#), [October 20, 2020](#), and [January 26, 2021](#); and
- our Definitive Proxy Statement on [Schedule 14A](#) filed with the SEC on April 29, 2020.

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 supplement (other than current reports or portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K).

You may request a free copy of any or all of the documents incorporated by reference in this prospectus supplement 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.

This prospectus supplement is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus supplement or those documents.

PROSPECTUS

\$75,000,000

Diffusio₂n
Pharmaceuticals Inc.

DIFFUSION PHARMACEUTICALS INC.

Common Stock
Preferred Stock
Debt Securities
Warrants
Units

Rights to Purchase Common Stock, Preferred Stock, Debt Securities or Units

We may offer and sell from time to time shares of our common stock; shares of our preferred stock; debt securities, which may be issued in one or more series and which may be senior debt securities or subordinated debt securities; warrants to purchase shares of our common stock, shares of our preferred stock or our debt securities; units that include any of the foregoing securities; and rights to purchase shares of our common stock, shares of our preferred stock, our debt securities or units. We may sell any combination of these securities in one or more offerings with an aggregate initial offering price of up to \$75,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we offer securities pursuant to this prospectus, we will provide a prospectus supplement containing specific terms of the particular offering together with this base prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this base prospectus. You should carefully read this base prospectus, the accompanying prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference herein or therein before you invest in any of our securities. **This prospectus may not be used to consummate a sale of securities unless accompanied by the accompanying prospectus supplement.**

Our common stock is listed on the NASDAQ Capital Market under the symbol "DFFN." On October 1, 2020, the last reported sale price of our common stock was \$0.82.

Investing in our securities involves a number of significant risks. We strongly recommend that you read carefully the risks we describe in this base prospectus and in any accompanying prospectus supplement, as well as the risk factors that are incorporated by reference into this prospectus from our filings made with the Securities and Exchange Commission. See "Risk Factors" on page 6 of this base prospectus.

We may offer and sell securities to or through underwriting syndicates or dealers, through agents or directly to purchasers. The names of any underwriters, dealers or agents that participate in a sale or offer of securities pursuant to this prospectus, any applicable commissions or discounts, the price to the public of the securities offered or sold, and the net proceeds we expect to receive from such sale will, in each case, be stated in an accompanying prospectus supplement. In addition, the underwriters, if any, may over-allot a portion of the 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.

The date of this prospectus is October 2, 2020

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process. Under this shelf registration process, we may sell from time to time any combination of the securities described in this prospectus in one or more offerings up to a total dollar amount of \$75,000,000. This prospectus only provides you with a general description of the securities we may offer. Each time we sell securities under this shelf registration, we will provide a prospectus supplement that will contain specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered. We may also provide or authorize to be provided one or more free writing prospectuses that may contain material information relating to an offering. The prospectus supplement and any related free writing prospectus that we may provide or authorize to be provided may also add, update or change information contained in this base prospectus or in any documents that we have incorporated by reference into this prospectus. You should read this base prospectus, any accompanying prospectus supplement and any related free writing prospectus prepared by or on behalf of us, together with the additional information described under the heading, “Where You Can Find More Information” and “Information Incorporated by Reference.”

This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement.

You should rely only on the information that we have provided or incorporated by reference in this base prospectus, any accompanying prospectus supplement and any related free writing prospectus that we may provide or authorize to be provided to you. We have not authorized anyone to provide any information or to make any representation other than those contained or incorporated by reference in this base prospectus, any accompanying prospectus supplement, or any related free writing prospectus. You must not rely upon any information or representation not contained or incorporated by reference in this base prospectus, the accompanying prospectus supplement or related free writing prospectus. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you.

This base prospectus, any accompanying prospectus supplement and any related free writing prospectus, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this base prospectus, any accompanying prospectus supplement or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

The information in this base prospectus is accurate as of the date on the front cover. You should not assume that the information contained in this base prospectus, any accompanying prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front cover or that any information we have incorporated by reference herein is correct on any date subsequent to the date of the document incorporated by reference, even though this base prospectus, any accompanying prospectus supplement or any related free writing prospectus is delivered, or the applicable securities are sold, on a later date.

We may sell our securities to or through underwriters, initial purchasers, dealers, or agents, directly to purchasers or through a combination of any of these methods of sale, as designated from time to time. We and our agents, if any, reserve the sole right to accept or reject in whole or in part any proposed purchase of our securities. An accompanying prospectus supplement, which we will provide each time we offer the securities, will set forth the names of any underwriters, initial purchasers, dealers or agents involved in the sale of our securities, and any related fee, commission or discount arrangements. See “Plan of Distribution.”

When used in this prospectus, the terms “Diffusion,” “Diffusion Pharmaceuticals,” the “Company,” “we,” “our” and “us” refer to Diffusion Pharmaceuticals, Inc., unless otherwise specified or the context otherwise requires.

“Diffusion Pharmaceuticals,” the Diffusion logo and other trademarks, trade names or service marks of Diffusion appearing in this prospectus are the property of Diffusion Pharmaceuticals, Inc. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references or the omission thereof should not be construed as any indicator that their respective owners will or will not assert their rights thereto.

MARKET AND INDUSTRY DATA

Certain market and industry data included in this prospectus were obtained from independent third-party surveys, market research, publicly available information, reports of governmental agencies and industry publications and surveys. All of the market and industry data used in this prospectus involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Although we are responsible for all of the disclosure contained in this prospectus and we believe the information from the industry publications and other third-party sources included in this prospectus is reliable, such information is inherently imprecise. The industry in which we operate is subject to a high degree of uncertainty, volatility, and risk due to a variety of factors, including those described in the section titled “Risk Factors.” These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

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 and it is qualified in its entirety by, and should be read in conjunction with, the accompanying prospectus supplement, any related free writing prospectus, and the more detailed information appearing elsewhere or incorporated by reference into this prospectus. You should read the entire base prospectus, any accompanying prospectus supplement, the registration statement of which this prospectus is a part, and the information incorporated by reference herein in their entirety, including the information contained under the heading “Risk Factors” and our financial statements and the related notes contained in and incorporated by reference into this prospectus, before purchasing our securities.

Diffusion Pharmaceuticals Inc.

Business Overview

Diffusion Pharmaceuticals Inc. is an innovative biopharmaceutical company developing novel therapies to improve the body’s ability to deliver oxygen to the areas where it is needed most, offering new hope for the treatment of life-threatening medical conditions.

Our lead drug candidate, trans sodium crocetinate (“TSC”), was originally developed in conjunction with the United States (“U.S.”) Office of Naval Research to treat multiple organ failure and its resulting mortality caused by low oxygen levels due to blood loss on the battlefield. Evolutions in research have led the Company to focus on addressing some of medicine’s most intractable and difficult-to-treat conditions involving cellular oxygen deficiency, or hypoxia, such as COVID-19, stroke, glioblastoma multiforme (“GBM”) brain cancer, and other conditions and diseases in which hypoxia is a critical factor which presents a significant obstacle for medical providers and is the target for TSC’s novel mechanism.

Using principles of physical chemistry, TSC was developed to increase the amount of hydrogen bonding among water molecules. The increased level of hydrogen bonding may increase the level of organization among the water molecules, creating a less dense matrix through which oxygen molecules can move more efficiently from areas of high to low oxygen concentrations. We believe this novel mechanism of action results in an enhancement of the rate of oxygen diffusion from the lungs onto red blood cells and then from red blood cells into body tissue where the oxygen is used to power the cells. This novel diffusion-enhancing mechanism has been observed to affect hypoxic tissue selectively, thus avoiding problems of tissue over-oxygenation and related oxygen toxicity.

COVID-19

We believe TSC’s oxygen-enhancing mechanism could potentially provide an important new treatment option for low oxygen levels and the associated risk of acute respiratory distress syndrome (“ARDS”) and multiple organ failure that can occur in COVID-19 patients.

An open-label Phase 1b lead-in trial of TSC in hospitalized COVID-19 patients was initiated in September 2020 at the Romanian National Institute of Infectious Diseases (“NIID”) to evaluate the safety and tolerability of TSC administered intravenously four-times daily in this patient population. In addition to evaluating safety and tolerability, we will collect preliminary data on TSC’s effects on blood oxygenation, which are sometimes referred to as pharmacodynamic effects, and on certain clinical endpoints related to COVID-19 disease status. Although the study is not powered to detect statistical differences in effect, we believe positive changes from baseline in pharmacodynamic and/or clinical efficacy data will support proof of concept for use of TSC in patients with COVID-19 who suffer from low oxygen level. The safety and tolerability of TSC will be evaluated in this trial at pre-set intervals by a Safety Monitoring Committee (“SMC”).

On September 10, 2020, we announced the first two patients were randomized and began dosing in the Phase 1b lead-in trial. With enrollment now in progress, we currently expect topline data to be available in the fourth quarter of 2020. If a safe, well-tolerated dose of TSC is identified at which there is evidence of elevated oxygen levels and/or clinical effect, we will use these data to determine the appropriate dosing regimen to begin our planned, randomized, controlled Phase 2/3 clinical trial testing TSC in hospitalized COVID-19 patients to evaluate TSC’s effects on certain clinical endpoints. We intend to incorporate feedback on the program and protocol design from regulatory authorities, including the U.S. Food and Drug Administration (“FDA”). Pending this feedback, we are planning to conduct the study in multiple sites in the U.S., the European Union (“E.U.”) and other non-E.U. Eastern European countries.

In July 2020, we filed an Investigational New Drug (“IND”) application with FDA in connection with the COVID-19 program, which incorporated pre-IND regulatory guidance from the FDA and certain European regulatory agencies. Based on subsequent communications with the FDA, the IND was withdrawn for administrative reasons. We do not anticipate that withdrawal of the IND will have a significant effect on our overall timeline for the program, and we intend to re-submit the IND after data from the Phase 1b study are available.

Cancer

Hypoxia is a critical factor in multiple conditions and the resistance of those conditions to treatment, including glioblastoma multiforme (“GBM”), stroke, infections, and other conditions with a significant unmet medical need. In addition to our ongoing COVID-19 program, we have evaluated TSC in preclinical and clinical studies of GBM, acute stroke, acute lung injury and peripheral artery disease (“PAD”).

In GBM, we believe TSC can be used to re-oxygenate treatment-resistant cancerous tissue, making the cells more susceptible to the therapeutic effects of standard-of-care radiation therapy and chemotherapy. A Phase 2 clinical study was completed in the second quarter of 2015 that evaluated 59 patients with newly diagnosed GBM, a particularly deadly form of brain cancer for which TSC has received an Orphan Drug Designation from the FDA. Each year GBM affects approximately 12,000 patients in the U.S. and approximately 35,000 patients worldwide. This open-label, historically controlled study demonstrated a favorable safety profile for TSC when combined with standard of care treatment for GBM. Although not prospectively defined, a subgroup analysis of inoperable patients suggested a higher proportion of TSC-treated patients survived at two years compared to those in the historical control group.

Based upon data from the inoperable patient subgroup in the Phase 2 study, we initiated the INvestigation of TSC Against Cancerous Tumors (“INTACT”) Phase 3 trial in the newly diagnosed inoperable GBM patient population in December 2017. The trial was 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 dose-escalation, safety run-in for which enrollment was completed and is now closed. A total of 19 patients were enrolled to ensure that at least 8 completed the FDA-specified 42-month exposure period. At a meeting in the third quarter of 2019, the INTACT Trial Data Safety Monitoring Board (“DSMB”) concluded, based on their analysis, that no adverse safety signal was present and unanimously recommended the study continue as planned using the highest tested dose of TSC (1.5 mg/kg) during the adjuvant treatment chemotherapy period with temozolomide. Commencement of enrollment in the randomization portion of the INTACT Phase 3 Trial has been suspended, as the Company reprioritizes its resources to the shorter duration COVID-19 studies designed to demonstrate TSC’s effectiveness. Restart and completion of the INTACT GBM study is contingent upon the availability of significant additional capital, which would need to be obtained through a financing event, strategic partnership or otherwise.

Stroke

Based upon preclinical safety and efficacy data, as well as certain clinical safety data, we believe TSC also has potential applications in both ischemic and hemorrhagic stroke. Stroke is the fifth leading cause of death in the U.S. and the leading cause of adult disability. TSC may enhance the diffusion of oxygen into brain cells in which stroke-induced oxygen-deprivation causes neuronal death. The hypoxic conditions in the brain of stroke patients may be a significant factor contributing to morbidity and mortality. On October 17, 2019, we began enrolling patients in a randomized Phase 2 trial to test TSC in the treatment of acute ischemic or hemorrhagic stroke. This trial was planned to enroll 160 patients, with 80 in the TSC treatment arm and 80 in the control arm. Patients were to receive treatment while in the ambulance to ensure all eligible patients received treatment as soon as possible after the onset of clinical symptoms. However, the COVID-19 pandemic created logistical problems for the study, including with respect to in-ambulance treatment, and currently enrollment in this trial is suspended as the Company reprioritizes its resources to the shorter duration COVID-19 studies designed to demonstrate TSC’s effectiveness.

DFN-529 (formerly RES-529)

In addition to TSC, our product candidate DFN-529 is a novel PI3K/Akt/mTOR pathway inhibitor which has completed two Phase 1 clinical trials for age-related macular degeneration and was previously in preclinical development in oncology, specifically for 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. We are currently exploring alternatives to best capitalize upon the value of DFN-529 and our related intellectual property, which may include out-licensing or other options.

Corporation 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.

Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities, warrants and rights to purchase shares of common stock or preferred stock, debt securities or units, as well as units to purchase any of such securities, from time to time under this prospectus, together with any applicable prospectus supplement and related free writing prospectus, at prices and on terms to be determined by market conditions at the time of offering. This base prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;
- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking, if any;
- restrictive covenants, if any;
- voting or other rights, if any; and
- important United States federal income tax considerations.

A prospectus supplement and any related free writing prospectus that we may provide or authorize to be provided to you may also add, update, or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part

We may sell the securities directly to or through underwriters, dealers or agents. We, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options or refreshable options, if any; and
- the net proceeds to us.

Common Stock

We may offer shares of our common stock, par value \$0.001 per share, either alone or underlying other registered securities convertible into or exercisable for our common stock. Holders of our common stock are entitled to dividends as our board of directors may declare from time to time out of legally available funds, subject to the preferential rights of the holders of any shares of our preferred stock that we may issue in the future. Currently, we do not pay any dividends and we do not have any issued and outstanding preferred stock. Each holder of our common stock is entitled to one vote per share. In this prospectus, we provide a general description of, among other things, our dividend policy and the rights and restrictions that apply to holders of our common stock. Our common stock is described in greater detail in this prospectus under “Description of Capital Stock—Common Stock.”

Preferred Stock

We may issue shares of preferred stock in one or more classes or series. Our board of directors or a committee designated by our board of directors will determine the dividend, voting and conversion rights and other provisions at the time of sale. The particular terms of each class or series of preferred stock, including redemption privileges, liquidation preferences, voting rights, dividend rights and/or conversion rights, will be more fully described in the accompanying prospectus supplement relating to the preferred stock offered thereby. Our preferred stock is described in greater detail in this prospectus under “Description of Capital Stock—Preferred Stock.”

Debt Securities

We may offer debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsubordinated debt that we may have and may be secured or unsecured. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all or some portion of our indebtedness. Any convertible debt securities that we issue will be convertible into or exchangeable for our common stock or other securities of ours. Conversion may be mandatory or at the holder’s option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a trustee for the holders of the debt securities. In this prospectus, we have summarized certain general features of the debt securities under “Description of Debt Securities.” We urge you, however, to read the prospectus supplements and any free writing prospectus that we may provide or authorize to be provided to you related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. A form of an indenture has been filed as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of debt securities being offered will be incorporated by reference into the registration statement of which this prospectus is a part from reports we file with the SEC.

Warrants

We may from time to time offer warrants for the purchase of our common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from those securities.

The warrants will be evidenced by warrant certificates issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. In this prospectus, we have summarized certain general features of the warrants under “Description of Warrants.” We urge you, however, to read the prospectus supplements and any free writing prospectus that we may provide or authorize to be provided to you related to the series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement which includes this prospectus.

Rights

We may from time to time issue rights to purchase shares of our common stock or preferred stock, debt securities or units. The rights may be issued independently or together with other securities and may or may not be transferable by the persons purchasing or receiving the rights. In connection with any rights offering, we may enter into a standby underwriting or other arrangement with one or more underwriters or other persons pursuant to which such underwriters or other persons would purchase any offered securities remaining unsubscribed for after such rights offering. In connection with a rights offering to our stockholders, we would make available a prospectus supplement to our stockholders on or about the record date that we set for receiving rights in such rights offering.

In this prospectus, we have summarized certain general features of the rights under “Description of Rights.” We urge you, however, to read the prospectus supplements and any free writing prospectus that we may provide or authorize to be provided to you related to the series of rights being offered.

Units

We may offer units consisting of common stock, preferred stock, debt securities and/or warrants to purchase any of such securities in one or more series. In this prospectus, we have summarized certain general features of the units under “Description of Units.” We urge you, however, to read the prospectus supplements and any free writing prospectus that we may provide or authorize to be provided to you related to the series of units being offered, as well as the unit agreements that contain the terms of the units. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from a current report on Form 8-K that we file with the SEC, the form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

We will evidence each series of units by unit certificates that we will issue under a separate agreement. We will enter into the unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the accompanying prospectus supplement relating to a particular series of units.

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 base prospectus or the applicable prospectus supplement, including the risk factors below and 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.

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

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

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

- our ability to obtain additional financing;
- our estimates regarding expenses, capital requirements and needs for additional financing;
- the success and timing of our preclinical studies and clinical trials;
- the difficulties in obtaining and maintaining regulatory approval of our products and product candidates, and the labeling under any approval we may obtain;
- our plans and ability to develop and commercialize our product candidates;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the accuracy of our estimates of the size and characteristics of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;
- the rate and degree of market acceptance of any of our product candidates;
- obtaining and maintaining intellectual property protection for our product candidates and our proprietary technology;
- our ability to operate our business without infringing the intellectual property rights of others;
- recently enacted and future legislation regarding the healthcare system;
- our ability to satisfy the continued listing requirements of the Nasdaq Capital Market or any other exchange that our securities may trade on in the future;
- our ability to continue as a going concern;
- the success of competing products that are or may become available; and
- the performance of third parties, including contract research organizations and manufacturers.

You should also read carefully the factors described in the “Risk Factors” section contained in this prospectus, any accompanying prospectus supplement and any related free writing prospectus, and incorporated by reference herein from our Annual Report on Form 10-K for the fiscal 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 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

Unless otherwise indicated in any applicable prospectus supplement and in any free writing prospectuses in connection with a specific offering, we currently intend to use the net proceeds from the sale of securities offered hereby, if any, to fund research and development of our lead product candidate, TSC, including clinical trial activities, and for general corporate purposes. See “Risk Factors” in this prospectus and in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, which is incorporated by reference herein, as updated by annual, quarterly and other reports and documents we file with the SEC after the date of this prospectus and that are incorporated by reference herein, for a discussion of certain risks that may affect our intended use of the net proceeds from the sale of securities offered hereby, including that we will need to raise additional capital in the future to complete the development of TSC and our other product candidates. Pending these uses, we intend to invest the net proceeds of any offering under this prospectus in short-term, investment-grade, interest-bearing securities, or certificates of deposit.

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 63,998,298 shares were issued and outstanding as of August 5, 2020. 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 "DFN." As of March 10, 2020, there were 480 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.

Preferred Stock

As of September 25, 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. A prospectus supplement 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.

We will describe the specific terms of a particular series of preferred stock in the prospectus supplement relating to that series. The description of preferred stock above and the description of the terms of a particular series of preferred stock in the prospectus supplement are not complete. You should refer to the applicable certificate of designation for complete information. The prospectus supplement will contain a description of U.S. federal income tax consequences relating to the preferred stock.

Anti-Takeover Provisions

Delaware Anti-Takeover Law

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

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

Section 203 defines a business combination to include:

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

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

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements or free writing prospectuses, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement or free writing prospectus. The terms of any debt securities we offer under a prospectus supplement may differ from the terms we describe below. As of the date of this prospectus, we have no outstanding registered debt securities. Unless the context requires otherwise, whenever we refer to the “indenture,” we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We may offer senior debt securities or subordinated debt securities under the indenture and any supplemental indentures that we will enter into with the trustee named in the indenture. We have filed a form of the indenture as an exhibit to the registration statement, of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The indenture will be qualified under the Trust Indenture Act of 1939, as amended (the “Trust Indenture Act”).

The following summaries of material provisions of the indenture are subject to, and qualified in their entirety by reference to, all of the provisions of the indenture and any supplemental indentures applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in an officer’s certificate or by a supplemental indenture. Debt securities may be issued in separate series without limitation as to aggregate principal amount. We may specify a maximum aggregate principal amount for the debt securities of any series. We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title;
- the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;
- any limit on the amount that may be issued;
- whether or not we will issue the series of debt securities in global form, and, if so, the terms and who the depository will be;
- the maturity date;
- whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;
- the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- the terms of the subordination of any series of subordinated debt;
- the place where payments will be made;
- restrictions on transfer, sale or other assignment, if any;

- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- provisions for a sinking fund purchase or other analogous fund, if any, including the date, if any, on which, and the price at which we are obligated, pursuant thereto or otherwise, to redeem, or at the holder's option, to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- whether the indenture will restrict our ability or the ability of our subsidiaries to:
 - incur additional indebtedness;
 - issue additional securities;
 - create liens;
 - pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;
 - redeem capital stock;
 - place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;
 - make investments or other restricted payments;
 - sell or otherwise dispose of assets;
 - enter into sale-leaseback transactions;
 - engage in transactions with stockholders or affiliates;
 - issue or sell stock of our subsidiaries; or
 - effect a consolidation or merger;
- whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;
- a discussion of certain material or special United States federal income tax considerations applicable to the debt securities;
- information describing any book-entry features;
- the applicability of the provisions in the indenture on discharge;
- whether the debt securities are to be offered at a price such that they will be deemed to be offered at an "original issue discount" as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms under which a series of debt securities may be convertible into or exchangeable for our common stock, our preferred stock or other securities (including securities of a third party). We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock, our preferred stock or other securities (including securities of a third party) that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indenture or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for our other securities or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended;
- if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable at maturity, upon redemption or repurchase or otherwise, and the time for payment has not been extended;
- if we fail to observe or perform any other covenant contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or we and the trustee receive notice from the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

We will describe in each applicable prospectus supplement any additional events of default relating to the relevant series of debt securities.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default arises due to the occurrence of certain specified bankruptcy, insolvency or reorganization events, the unpaid principal, premium, if any, and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under the indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under the indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity or security satisfactory to it against any loss, liability or expense. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

The indenture provides that if an event of default has occurred and is continuing, the trustee will be required in the exercise of its powers to use the degree of care that a prudent person would use in the conduct of its own affairs. The trustee, however, may refuse to follow any direction that conflicts with law or the indenture, or that the trustee determines is unduly prejudicial to the rights of any other holder of the relevant series of debt securities, or that would involve the trustee in personal liability. Prior to taking any action under the indenture, the trustee will be entitled to indemnification against all costs, expenses and liabilities that would be incurred by taking or not taking such action.

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, a holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made a written request and such holders have offered reasonable indemnity to the trustee or security satisfactory to it against any loss, liability or expense or to be incurred in compliance with instituting the proceeding as trustee; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities, or other defaults that may be specified in the applicable prospectus supplement.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

Subject to the terms of the indenture for any series of debt securities that we may issue, we and the trustee may change the indenture without the consent of any holders with respect to the following specific matters:

- to fix any ambiguity, defect or inconsistency in the indenture;
- to comply with the provisions described above under “Description of Debt Securities—Consolidation, Merger or Sale;”
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;
- to add to, delete from or revise the conditions, limitations and restrictions on the authorized amount, terms or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to provide for the issuance of, and establish the form and terms and conditions of, the debt securities of any series as provided under “Description of Debt Securities—General,” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment hereunder by a successor trustee;
- to provide for uncertificated debt securities and to make all appropriate changes for such purpose;
- to add such new covenants, restrictions, conditions or provisions for the benefit of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred to us in the indenture; or
- to change anything that does not adversely affect the interests of any holder of debt securities of any series in any material respect.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected.

However, subject to the terms of the indenture for any series of debt securities that we may issue or otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may only make the following changes with the consent of each holder of any outstanding debt securities affected:

- extending the stated maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

The indenture may provide that, subject to the terms of the indenture and any limitation otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we may elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, and any premium and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms related to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under the indenture, undertakes to perform only those duties as are specifically set forth in the indenture and is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur. However, upon an event of default under the indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest payment.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Ranking Debt Securities

The subordinated debt securities that we may offer will be unsecured and will be subordinate and junior in priority of payment to certain other indebtedness to the extent described in a prospectus supplement.

The senior debt securities that we may offer will be unsecured and will rank equally in right of payment to all our other senior unsecured debt.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and free writing prospectuses, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and may be issued in one or more series. Warrants may be offered independently or together with common stock, preferred stock or debt securities offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants that we may offer in more detail in the applicable prospectus supplement and any applicable free writing prospectus. The terms of any warrants offered under a prospectus supplement may differ from the terms described below.

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from a current report on Form 8-K that we file with the SEC, the form of warrant agreement, if any, including a form of warrant certificate, if any, that describes the terms of the particular series of warrants we are offering before the issuance of the related series of warrants. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. We urge you to read the applicable prospectus supplement and any applicable free writing prospectus related to the particular series of warrants that we sell under this prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms relating to a series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- United States federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate or agreement representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate or agreement and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent.

Upon receipt of the required payment and the warrant certificate or agreement properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate or agreement are exercised, then we will issue a new warrant certificate or agreement for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Enforceability of Rights by Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

DESCRIPTION OF RIGHTS

The following is a general description of the terms of the rights we may issue from time to time unless we provide otherwise in the applicable prospectus supplement. Particular terms of any rights we offer will be described in the prospectus supplement relating to such rights.

General

We may issue rights to purchase common stock, preferred stock, debt securities or units. Rights may be issued independently or together with other securities and may or may not be transferable by the person purchasing or receiving the rights. In connection with any rights offering to our stockholders, we may enter into a standby underwriting, backstop or other arrangement with one or more underwriters or other persons pursuant to which such underwriters or other persons would purchase any offered securities remaining unsubscribed for after such rights offering. In connection with a rights offering to our stockholders, we would distribute certificates evidencing the rights and a prospectus supplement to our stockholders on or about the record date that we set for receiving rights in such rights offering.

The applicable prospectus supplement will describe the following terms of any rights we may issue, including some or all of the following:

- the title and aggregate number of the rights;
- the subscription price or a formula for the determination of the subscription price for the rights and the currency or currencies in which the subscription price may be payable;
- if applicable, the designation and terms of the securities with which the rights are issued and the number of rights issued with each such security or each principal amount of such security;
- the number or a formula for the determination of the number of the rights issued to each stockholder;
- the extent to which the rights are transferable;
- in the case of rights to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one right;
- in the case of rights to purchase common stock or preferred stock, the type of stock and number of shares of stock purchasable upon exercise of one right;
- the date on which the right to exercise the rights will commence, and the date on which the rights will expire (subject to any extension);
- if applicable, the minimum or maximum amount of the rights that may be exercised at any one time;
- the extent to which such rights include an over-subscription privilege with respect to unsubscribed securities;
- if applicable, the procedures for adjusting the subscription price and number of shares of common stock or preferred stock purchasable upon the exercise of each right upon the occurrence of certain events, including stock splits, reverse stock splits, combinations, subdivisions or reclassifications of common stock or preferred stock;
- the effect on the rights of any merger, consolidation, sale or other disposition of our business;
- the terms of any rights to redeem or call the rights;
- information with respect to book-entry procedures, if any;
- the terms of the securities issuable upon exercise of the rights;
- if applicable, the material terms of any standby underwriting, backstop or other purchase arrangement that we may enter into in connection with the rights offering;

- if applicable, a discussion of certain U.S. Federal income tax considerations; and
- any other terms of the rights, including terms, procedures and limitations relating to the exchange and exercise of the rights.

Exercise of Rights

Each right will entitle the holder to purchase for cash or other consideration such shares of stock or principal amount of securities at the subscription price as shall in each case be set forth in, or be determinable as set forth in, the prospectus supplement relating to the rights offered thereby. Rights may be exercised as set forth in the applicable prospectus supplement beginning on the date specified therein and continuing until the close of business on the expiration date set forth in the prospectus supplement relating to the rights offered thereby. After the close of business on the expiration date, unexercised rights will become void.

Upon receipt of payment and a subscription certificate properly completed and duly executed at the corporate trust office of the subscription agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the securities purchasable upon such exercise. If less than all of the rights represented by such subscription certificate are exercised, a new subscription certificate will be issued for the remaining rights. If we so indicate in the applicable prospectus supplement, holders of the rights may surrender securities as all or part of the exercise price for rights.

We may determine to offer any unsubscribed offered securities directly to stockholders, persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby underwriting, backstop or other arrangements, as set forth in the applicable prospectus supplement.

Prior to exercising their rights, holders of rights will not have any of the rights of holders of the securities purchasable upon subscription, including, in the case of rights to purchase common stock or preferred stock, the right to receive dividends, if any, or payments upon our liquidation, dissolution or winding up or to exercise any voting rights or, in the case of rights to purchase debt securities, the right to receive principal, premium, if any, or interest payments, on the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture.

DESCRIPTION OF UNITS

The following description, together with the additional information we may include in any applicable prospectus supplements and free writing prospectuses, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from a current report on Form 8-K that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we sell under this prospectus, as well as the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units comprised of one or more debt securities, shares of common stock, shares of preferred stock and warrants in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Capital Stock,” “Description of Debt Securities” and “Description of Warrants” will apply to each unit and to any common stock, preferred stock, debt security or warrant included in each unit, respectively.

Issuance in Series

We may issue units in such amounts and in numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

We, the unit agents and any of their agents may treat the registered holder of any unit certificate as an absolute owner of the units evidenced by that certificate for any purpose and as the person entitled to exercise the rights attaching to the units so requested, despite any notice to the contrary.

PLAN OF DISTRIBUTION

We may sell the securities, from time to time, to or through underwriters or dealers, through agents or remarketing firms, or directly to one or more purchasers pursuant to:

- underwritten public offerings;
- negotiated transactions;
- block trades;
- “At the Market Offerings,” within the meaning of Rule 415(a)(4) of the Securities Act, into an existing trading market, at prevailing market prices; or
- through a combination of these methods.

We may sell the securities to or through one or more underwriters or dealers (acting as principal or agent), through agents, or directly to one or more purchasers.

We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of the underwriters, dealers or agents, if any;
- if the securities are to be offered through the selling efforts of brokers or dealers, the plan of distribution and the terms of any agreement, arrangement, or understanding entered into with broker(s) or dealer(s) prior to the effective date of the registration statement, and, if known, the identity of any broker(s) or dealer(s) who will participate in the offering and the amount to be offered through each;
- the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;
- if any of the securities being registered are to be offered otherwise than for cash, the general purposes of the distribution, the basis upon which the securities are to be offered, the amount of compensation and other expenses of distribution, and by whom they are to be borne;
- any delayed delivery arrangements;
- any over-allotment or other options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents’ or underwriters’ compensation;
- any public offering price;
- any discounts, commissions or concessions allowed or reallocated or paid to dealers;
- the identity and relationships of any finders, if applicable; and
- any securities exchange or market on which the securities may be listed.

In compliance with the guidelines of the Financial Industry Regulatory Authority, the maximum compensation to the underwriters or dealers in connection with the sale by the Company of its securities pursuant to this prospectus and the accompanying supplement to this prospectus may not exceed 8% of the aggregate offering price of the securities as set forth on the cover page of any prospectus supplement.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Unless otherwise indicated in the prospectus supplement, subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters, dealers or agents with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, dealer or agent, the nature of any such relationship.

We may use a remarketing firm to offer the securities in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own account or as agents for us. These remarketing firms will offer or sell the securities pursuant to the terms of the securities. A prospectus supplement will identify any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection the securities they remarket.

If we offer and sell securities through a dealer, we or an underwriter will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. The name of the dealer and the terms of the transaction will be set forth in the applicable prospectus supplement.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions payable to the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, the agent will act on a best-efforts basis for the period of its appointment.

Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and compensation received by them on resale of the securities may be deemed to be underwriting discounts. If such dealers or agents were deemed to be underwriters, they may be subject to statutory liabilities under the Securities Act.

We may sell securities directly to one or more purchasers without using underwriters or agents. Underwriters, dealers and agents that participate in the distribution of the securities may be underwriters as defined in the Securities Act, and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the Securities Act.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents, underwriters, and dealers with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents, underwriters, or dealers may make with respect to these liabilities. Agents, underwriters and dealers, or their respective affiliates, may engage in transactions with, or perform services for, us in the ordinary course of business.

The securities we offer may be new issues of securities and may have no established trading market. The securities may or may not be listed on a securities exchange. Underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We can make no assurance as to the liquidity of, or the existence of trading markets for, any of the securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters that are qualified market makers on the Nasdaq Global Select Market may engage in passive market making transactions in the common stock on the Nasdaq Global Select Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain 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.

LEGAL MATTERS

Dechert LLP will pass for us upon the validity of the securities being offered by this prospectus and applicable prospectus supplement, and counsel named in the applicable prospectus supplement will pass upon legal matters for any underwriters, dealers or agents.

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 MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 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 Exchange Act. 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 Exchange Act 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.

INFORMATION INCORPORATED BY REFERENCE

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

- [our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC on March 17, 2020;](#)
- [our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2020](#) and [June 30, 2020](#) filed with the SEC on May 1, 2020 and August 7, 2020, respectively;
- [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, June 1, 2020, June 12, 2020, June 17, 2020, July 7, 2020, July 29, 2020, September 4, 2020, September 9, 2020, September 10, 2020 and September 25, 2020;](#)

- [our Definitive Proxy Statement on Schedule 14A filed with the SEC on April 29, 2020; and](#)
- [the description of our common stock included in our amended registration statement on Form 8-A filed on November 8, 2016 under the Exchange Act, and any amendment or report we may file with the SEC for the purpose of updating such description.](#)

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

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

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

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

\$ 75,000,000

Diffusi₂n
Pharmaceuticals Inc.

Common Stock

Preferred Stock

Debt Securities

Warrants

Units

Rights to Purchase Common Stock, Preferred Stock, Debt Securities or Units

PROSPECTUS

October 2, 2020