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

FORM 10-K

(Mark one)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2022
OR
☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission file number: 000-24477

Diffusion Pharmaceuticals Inc.

(Exact Name of Registrant as specified in its Charter)

Delaware	**30-0645032**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No)
300 East Main Street, Suite 201 **Charlottesville,** VA	**22902**
(Address of Principal Executive Offices)	(Zip Code)

(434) 220-0718
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Trading Symbol**	**Name of Each Exchange on Which Registered**
Common Stock, par value $0.001 per share	DFFN	The Nasdaq Capital Market

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

Large accelerated filer ☐ Accelerated filer ☐
Non-accelerated filer ☒ Smaller reporting company ☒
Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicated by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of the registrant's common stock beneficially owned by non-affiliates of the registrant, calculated based upon the closing sale price of the common stock as quoted by the Nasdaq Capital Market on June 30, 2022 (the last business day of the registrant's second fiscal quarter), was approximately $13.6 million.

As of March 15, 2023, 2,039,878 shares of common stock of the registrant were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

None.

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INTRODUCTORY NOTE

Note Regarding Company References and Other Defined Terms

Unless the context otherwise requires, in this Annual Report, (i) references to "Diffusion," "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 and all share and per share amounts related to our common stock give effect to our 1-for-50 reverse stock split effected April 18, 2022. We have also used several other defined terms in this Annual Report, many of which are explained or defined below:

Term	Definition
2015 Equity Plan	Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan, as amended
2021 Annual Report	our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on March 18, 2022
2022 Sales Agreement	our At-The-Market Sales Agreement, dated July 22, 2022, with BTIG, as agent
401(k) Plan	Diffusion Pharmaceuticals Inc. 401(k) Defined Contribution Plan
ACA	collectively, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, each as amended
Altitude Trial	our Phase 1b clinical trial evaluating TSC in normal healthy volunteers subjected to incremental levels of physical exertion while exposed to hypoxic and hypobaric conditions, or "simulated altitude," completed in April 2022
Annual Report	this Annual Report on Form 10-K
ASC	Accounting Standard Codification of the FASB
ASUs	Accounting Standards Updates of the FASB
Black-Scholes Model	Black-Scholes-Merton derivative investment instrument pricing model
Board	our board of directors
BTIG	BTIG LLC
Bylaws	the Company's bylaws, as amended
Canaccord	Canaccord Genuity, our financial advisor
COVID-19	Corona Virus Disease 2019, the novel coronavirus disease known as COVID-19, caused by severe acute respiratory syndrome coronavirus 2 viral infection
COVID Trial	our Phase 1b clinical trial evaluating TSC in hospitalized COVID-19 patients, completed in February 2021
cGMP	current good manufacturing practices
CMO	contract manufacturing organization
CRO	contract research organization
CTA	clinical trial application
December 2019 Offering	our registered direct public offering and sale of common stock and concurrent private placement of warrants to purchase shares of common stock completed in December 2019
Diffusion LLC	Diffusion Pharmaceuticals LLC, a Virginia limited liability company and our wholly owned subsidiary
DLCO	diffusion capacity of lung for carbon monoxide
Dodd-Frank Act	Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010

E.U.	European Union
Exchange Act	Securities Exchange Act of 1934, as amended
FASB	Financial Accounting Standards Board
FDA	U.S. Food and Drug Administration
FDC Act	Federal Food, Drug, and Cosmetic Act
February 2021 Offering	our public offering and sale of shares of common stock completed in February 2021
G&A	general and administrative
GAAP	U.S. generally accepted accounting principles
GBM	glioblastoma multiforme brain cancer
GBM Trial	our Phase 3 clinical trial evaluating TSC in a newly diagnosed inoperable GBM patient population, initiated in December 2017
GCP	good clinical practice
GLP	good laboratory practice
HIPAA	Health Insurance Portability and Accountability Act of 1996
HITECH	Health Information Technology for Economic and Clinical Health Act of 2009
ILD	interstitial lung disease
ILD-DLCO Trial	our Phase 2a clinical trial evaluating TSC in patients with previously diagnosed ILD who have a baseline DLCO test result that is abnormal using DLCO as a surrogate measure of oxygen transfer efficiency, initiated in December 2021
IMM	irreversible morbidity and mortality
IND	investigational new drug application
IPR&D	in-process research and development
IRB	institutional review board
May 2019 Offering	our registered direct public offering and sale of shares of common stock and concurrent private placement of warrants to purchase common stock completed in May 2019
May 2020 Investor Warrant Exercise	the exercise of a previously outstanding warrant to purchase shares of common stock in May 2020 pursuant to a warrant exercise agreement
May 2020 Offering	our registered direct public offering and sale of shares of common stock completed in May 2020
Nasdaq	Nasdaq Stock Market, LLC
NDA	new drug application
NOL	net operating loss
November 2019 Offering	our public offering and sale of shares of common stock, pre-funded warrants to purchase shares of common stock, and warrants to purchase shares of common stock completed in November 2019
Oxygenation Trials	collectively, the TCOM Trial, the Altitude Trial, and the ILD-DLCO Trial
R&D	research and development
Regulation S-K	Regulation S-K promulgated under the Securities Act
REMS	risk evaluation and mitigation strategy
Reverse Stock Split	the reclassification and combination of all shares of our common stock outstanding at a ratio of one-for-50 approved by our stockholders at the Special Meeting and effective April 18, 2022
SEC	U.S. Securities and Exchange Commission
Securities Act	Securities Act of 1933, as amended
SOX	Sarbanes-Oxley Act of 2002, as amended
Special Meeting	the special meeting of our stockholders held on April 18, 2022

Stroke Trial	our Phase 2 clinical trial evaluating TSC in the treatment of acute ischemic or hemorrhagic stroke, initiated in October 2019
Tax Code	U.S. Internal Revenue Code of 1986, as amended
TCOM	transcutaneous oxygen measurement
TCOM Trial	our Phase 1b clinical trial evaluating the effects of TSC on peripheral tissue oxygenation in healthy normal volunteers using a TCOM device, completed in March 2021
TSC	trans sodium crocetinate, our most advanced product candidate
U.S.	United States
USPTO	U.S. Patent and Trademark Office

Note Regarding Forward-Looking Statements

This Annual Report (including, for purposes of this Note Regarding Forward-Looking Statements, any information or documents incorporated herein by reference) includes 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 Annual Report, 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 Annual Report. In addition, even if our results of operations, financial condition, liquidity, and prospects are consistent with the forward-looking statements contained in this Annual Report, 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 Annual Report. 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:

- the outcome and timing of our ongoing strategic review process, including any transaction we may undertake in connection therewith, which could significantly impact our future operations and financial position;
- the terms, timing, structure, benefits, and costs of any strategic transaction or restructuring and whether either will be consummated at all;
- the impact of any strategic transaction or restructuring on the Company and its stockholders;
- our ability to obtain additional financing in the future and continue as a going concern;
- the success and timing of our clinical and preclinical studies, including our ability to enroll subjects in our future clinical studies at anticipated rates and our ability to manufacture an adequate amount of drug supply for our studies;
- obtaining and maintaining intellectual property protection for our current or future product candidates and our proprietary technology;
- the performance of third parties, including contract research organizations, manufacturers, suppliers, and outside consultants, to whom we outsource certain operational, staff and other functions;
- our ability to obtain and maintain regulatory approval of our current or future 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 current or future product candidates and the outcomes of our research and development activities;
- our estimates regarding expenses, future revenues, capital requirements, and needs for additional financing;
- 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 current or future product candidates, the rate and degree of market acceptance of any of our current or future 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 current or future product candidates;
- our ability to operate our business without infringing the intellectual property rights of others and the potential for others to infringe upon our intellectual property rights;
- any significant breakdown, infiltration, or interruption of our information technology systems and infrastructure;
- recently enacted and future legislation related to 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 Affordable Care Act;

- other regulatory developments in the U.S., E.U., and other foreign jurisdictions;
- 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;
- uncertainties related to general economic, political, business, industry, and market conditions; and
- other risks and uncertainties, including those discussed under the heading "Risk Factors" in our Annual Report and elsewhere in 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 Annual Report. Accordingly, we cannot assure you that the forward-looking statements contained in this Annual Report 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 Annual Report 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 Annual Report 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 Annual Report contains certain trademarks, trade names, and service marks of ours, including “DIFFUSIO2N.” All other trade names, trademarks, and service marks appearing in this Annual Report 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.

PART I

ITEM 1. BUSINESS

Overview

Diffusion is a biopharmaceutical company that has historically focused on developing novel therapies that may enhance the body's ability to deliver oxygen to the areas where it is needed most. Our most advanced product candidate, TSC, has been investigated and 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, including hypoxic solid tumors like GBM.

Ongoing Evaluation of Strategic Opportunities

In early 2022, we identified the pursuit of an opportunistic transaction with the potential to complement and diversify our portfolio of product candidates as one of our key strategic objectives for the year. The intended purpose is to reduce the Company's overall risk profile as an investment and enhance long-term value for our stockholders. In pursuit of this objective, during the fourth quarter of 2021 and first half of 2022, our management team held conversations with several potential counterparties and, in July 2022, we engaged Canaccord Genuity LLC as our financial advisor to support the ongoing evaluation. In October 2022, following further deterioration of the public capital markets throughout 2022, and the corresponding increase in the cost of capital for small biopharmaceutical companies, we publicly announced our Board's authorization of an expanded evaluation and review of potential transactions, including a joint venture, licensing, merger, reverse merger, sale or divestiture of some of the Company's proprietary technologies or a sale of the Company, among others. Since that time, our management team has been increasingly focused on advancing this strategic review process through conversations about potential deal constructs with multiple companies, both including and excluding the Company's lead asset, TSC. However, there is no assurance the Board's review will result in any transaction being consummated. Any further comments or disclosures regarding the strategic review process will be made from time to time as and when we determine an update is appropriate.

Our Most Advanced Historical Development Programs: Trans Sodium Crocetinate

Prior to the initiation of our strategic review process, our core focus was the development and commercialization of novel therapies that enhance the body's ability to deliver oxygen to areas where it is needed most and improve treatment outcomes for patients suffering from conditions complicated by hypoxia. The Company's development efforts have been primarily focused on advancing our most advanced product candidate, TSC, and we continue to believe TSC has potential benefits for patients, particularly as an adjuvant treatment to standard of care therapy for GBM and other hypoxic solid tumors. In connection with our strategic review process and pending its conclusion, we have paused significant portions of our TSC development activities, including initiation of our previously announced Phase 2 study of TSC in newly diagnosed GBM patients.

Trans Sodium Crocetinate: Enhancing Oxygen, Fueling Life

We believe TSC is the first therapeutic candidate specifically designed to enhance the efficiency of the oxygen diffusion process. By supporting normal, physiologic levels of oxygen diffusion at the uptake and delivery points of the circulatory system, we believe TSC may have the ability to improve the current standard-of-care treatment for conditions complicated by hypoxia. Furthermore, in animal models, TSC's diffusion-enhancing mechanism of action has been observed to affect hypoxic tissue preferentially while avoiding excessive oxygen-related tissue toxicity.

TSC's Demonstrated Clinical Safety Profile

TSC has been observed to be safe and well-tolerated at a variety of doses in over 220 subjects included in clinical studies conducted to date, including those studies that evaluated the effects of TSC in patients with medical conditions often complicated by hypoxia, such as GBM, peripheral artery disease with intermittent claudication, stroke, COVID-19, and interstitial lung disease. We have also obtained valuable new data from our COVID Trial and Oxygenation Trials demonstrating TSC's safety and effects on oxygenation at higher doses and increased dosing frequencies compared to those previously evaluated.

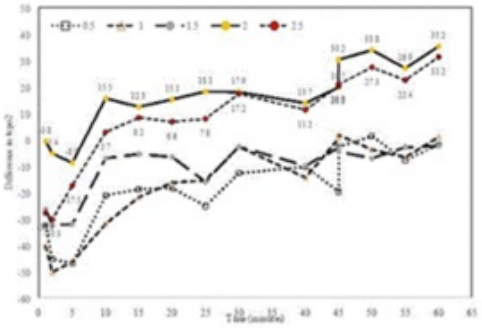
The TSC Oxygenation Trials: Evaluating the Clinical Effects of TSC

Our Oxygenation Trials, conducted during 2021 and 2022, were a series of three, short-term clinical studies using experimental models to evaluate the clinical effects of TSC on oxygenation. Each of these three studies was designed to look at the effects of TSC on a different component of the oxygenation pathway and fill information gaps related to the effects of TSC on tissue oxygen levels and other direct clinical parameters related to oxygen levels. We believe the results of the Oxygenation Trials provide proof of concept of TSC's effects on tissue oxygenation, in addition to supplementing our knowledge with new information related to TSC's pharmacokinetics and pharmacodynamics.

TCOM Trial: TSC's Effects on Peripheral Tissue Oxygenation

In June 2021, we reported a positive trend among patients who received TSC, when compared to placebo, in peripheral tissue oxygenation measured with the use of a transcutaneous oxygen monitoring (TCOM) device. These results can be seen in the figure below which was created during a supplemental analysis of the TCOM Trial results by subtracting the median response observed in the TCOM Trial's placebo group from the median response observed in each TSC dosage group at each of the measurement times during the one-hour period following dosing.

These data highlight the persistent increase in peripheral tissue oxygenation relative to that observed in the placebo group through the duration of the one-hour measurement period following TSC administration, particularly at the two highest TSC doses tested (2.0 mg/kg and 2.5 mg/kg administered intravenously).



Effects of TSC on transcutaneous oxygen pressure.

Altitude Trial: TSC's Effects Under Induced Hypoxic Conditions

In June 2022, we reported that, following exercise under hypoxic (i.e., simulated high altitude) conditions, participants in our Altitude Trial treated with the highest dose of TSC (2.5 mg/kg) demonstrated an effect on physiologic indicators of enhanced oxygenation when compared to placebo, including an increase in plasma pH and a decrease in plasma lactate, both at the end of the exercise period and at 10 minutes post-exercise. We believe these data suggest the 2.5 mg/kg dose of TSC decreased blood acidity (i.e., lactic acid accumulation) and enhanced metabolic recovery at 10 minutes after completion of exercise under the stressful conditions of exercise at simulated high altitude.

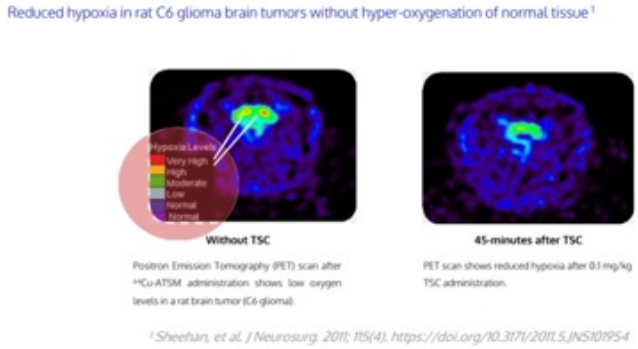
Additional positive results observed in the Altitude Trial included:

- Positive effects on lactate and pH relative to participants' baseline measurements were observed among the TSC 2.5 mg/kg dose cohort at the end of the exercise period;
- A "carry-over" effect was observed in participants who received TSC in the first treatment ("ascent") of the day versus those who received placebo first and TSC for the second ascent; and
- The 2.5 mg/kg dose appeared to have a positive effect on post-exercise recovery based on comparison of the measurements for pH, lactate, oxygen saturation (SpO2) and other markers of oxygenation at 10 minutes post-exercise versus last exercise measurements.

ILD-DLCO Trial: TSC's Effects on Oxygen Transfer Efficiency

In December 2021, we announced dosing of the first patients in our ILD-DLCO Trial, which was designed to evaluate the effects of TSC in certain patients with previously diagnosed ILD using the diffusion of carbon monoxide through the lungs, or DLCO, as a surrogate measure of oxygen transfer efficiency. In August 2022, in order to dedicate more of our human and other resources to our strategic review process and ongoing challenges enrolling patients in clinical trials for respiratory indications due to the COVID-19 pandemic, we made the decision to terminate recruitment and enrollment in the ILD-DLCO Trial and wind the trial down.

TSC's Potential as Supplement to Standard of Care Therapy for Hypoxic Solid Tumors



Positron emission tomography scans showing reduction in hypoxia in a rat C6 glioma brain tumor model 45 min after TSC administration.

As seen in the positron emission tomography scans above, we have previously obtained and published evidence supporting TSC's ability to enhance oxygenation of C6 glioma tumors in animals. We also have obtained clinical evidence of TSC's effects in unresectable GBM tumors from our previously completed Phase 2 clinical trial evaluating 59 patients with newly diagnosed GBM. Although not prospectively defined, a post hoc 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 these data, we made the decision to pursue the development of TSC as a treatment for hypoxic solid tumors when administered with standard-of-care radiation therapy and chemotherapy.

Our Phase 2 GBM Trial

GBM is an aggressive, deadly, and treatment-resistant type of malignant brain tumor, affecting approximately 13,000 newly diagnosed patients each year in the United States. Few treatment options are available for patients with GBM, and none have extended life expectancy beyond a few months. In fact, according to the National Brain Tumor Society, the five-year survival rate for GBM is only 6.8 percent with an average survival time of eight months. Despite recent advances in treatment modalities, we believe an effective treatment for GBM remains a significant unmet medical need.

Based upon data from the inoperable patient subgroup in our Phase 2 GBM trial and guidance from the FDA received at our End-of-Phase-2 meeting, we initiated a Phase 2b/3 GBM Trial in patients with newly diagnosed inoperable GBM in December 2017. The trial was designed to enroll 236 patients, split evenly between the TSC treatment arm and the control arm, with TSC to be administered in combination with standard of care radiotherapy and temozolomide, an anti-cancer chemotherapy drug, during the adjuvant treatment chemotherapy period. The trial began with a 19 patient, FDA-mandated, open-label, dose-escalation safety run-in phase for which enrollment was completed in 2019. At a meeting in the third quarter of 2019, the data safety monitoring board for the trial concluded that no adverse safety signal was present and unanimously recommended the GBM Trial continue as planned. However, due to a lack of financial resources at the time, the Company did not initiate the randomized portion of the study.

Our Hypoxic Solid Tumor Program

In July 2022, we announced alignment with the FDA on the design of an open-label, dose-escalation, Phase 2 safety and efficacy study of TSC administered with standard of care to newly diagnosed GBM patients, designated "Study 200-208." The design of this trial has been reviewed and cleared to proceed by the FDA's Office of Oncologic Diseases. Key elements of the Study 200-208 trial design include the following:

- Innovative incorporation of PET scans and hypoxia-specific radiotracers to evaluate the oxygenating enhancing effects of TSC on tumor hypoxia;

- PET scan data readouts from the first phase of the trial are expected to be available within one year of the first patient being dosed, multiple years earlier than the survival data readout in most clinical trials involving hypoxic solid tumor patients; and

- Building upon the knowledge obtained in our COVID and Oxygenation Trials, patients in Study 200-208 would receive TSC at a significantly increased dose (up to 2.5 mg/kg v. 0.25 mg/kg) and frequency (five days/week v. 3 days/week) as compared to our prior GBM trials, representing an increase in weekly TSC exposure of nearly 1,700% at the highest potential dose.

As of the date of this Annual Report, the design of Study 200-208 is complete, but in connection with our ongoing strategic review process and pending its conclusion, we have paused significant portions of our TSC development activities including initiation of Study 200-208.

Studies of TSC in Other Conditions Complicated by Hypoxia and Beyond

Beyond cancer, hypoxia is a complicating factor in many other intractable and difficult-to-treat conditions, including cardiovascular diseases, cerebrovascular diseases, respiratory diseases, skin and soft tissue diseases, and neurodegenerative diseases. In addition to our oncology programs, we have previously conducted a variety of preclinical and clinical studies evaluating the effects of TSC in several of these other potential indication areas and conditions complicated by hypoxia, including COVID-19, stroke, peripheral artery disease with intermittent claudication, and we believe TSC's oxygen-enhancing mechanism of action could potentially provide benefits to patients and individuals suffering from one or more of these or other related indications or conditions.

TSC has also been evaluated in a variety of preclinical models intended to mimic relevant human conditions known to be complicated by hypoxia. In these studies, a variety of positive effects have been observed in connection with TSC administration, including:

- Reducing hypoxia in rat brain tumors without hyper-oxygenation of normal tissue;
- Improving survival in highly lethal adult and pediatric brain tumor models when added to standard of care therapy, including radiotherapy administered either alone or in combination with chemotherapy;
- Improving tissue oxygenation without hyper-oxygenation of normal tissue and reducing infarct size in a rat ischemic stroke model;
- Demonstrating a functional benefit in a rabbit ischemic stroke model, with or without tissue plasminogen activator at one-hour post-clot infection and with tissue plasminogen activator at three hours post-clot infection; and
- Improving levels of arterial partial pressure of blood oxygen in a rat model of acute respiratory distress syndrome.

Product Development

Research and Development

In recent years, the majority of our research and development expenditures have been directed to the development of TSC. For example, during the year ended December 31, 2022, we incurred approximately $7.2 million in costs related to research and development of our products, a decrease of approximately $1.3 million compared to the year ended December 31, 2021. The majority of these costs were related to the development of TSC and related personnel, including costs associated with the Oxygenation Trials.

Intellectual Property

We believe that a strong intellectual property portfolio is critical to our success. We are committed to obtaining and maintaining appropriate patent and other protections for our products candidates and other technologies, preserving and protecting our trade secrets and other confidential and proprietary information, and fiercely defending our intellectual property portfolio against any potential infringement by third parties. We attempt to protect our intellectual property through among other things, the filing of applications for patent, trademark, and other appropriate intellectual property protections, the use of confidentiality agreements with consultants, contractors and other third parties, our employee policies regarding confidentiality, invention disclosure, and the assignment of inventions, as well as regular meetings of members of our internal development and legal teams, which contains key members of our management team. We are also committed to operating our business without infringing on the intellectual property of others.

In general, patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in various countries where patent protection is obtained, with term adjustments or extensions possible in certain cases based on patent office delays or pursuant to certain administrative and legislative exceptions. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country.

We have invested significant time, effort, and resources into the development and maintenance of our patent portfolio. As of December 31, 2022, we owned 19 issued U.S. patents and 34 issued non-U.S. patents, and had numerous patent applications pending worldwide including issued patents and applications in major markets such as the U.S., E.U., China, Japan, and India. The normal life (i.e. with no adjustments or extensions) of our key issued patents related to the current liquid formulation of TSC extends to 2026, with potential patent term extensions to 2031, and the normal life of our patents related to an oral formulation of TSC extends to 2031, with potential patent term extensions to 2036. The normal life of our key issued patents related to methods of use of TSC extends to 2037, with potential patent term extensions to 2042. For additional information regarding patent term extensions, see "*Business — Government Regulation— The Hatch-Waxman Amendments — Patent Term Restoration and Marketing Exclusivity*. In addition, TSC has been granted Orphan Drug designation by the FDA for the treatment of both GBM and metastatic brain cancer, which may provide us with a right of exclusivity under certain FDA regulations. For additional information regarding orphan and ultra-orphan designations, see "*Business — Government Regulation — Certain Other FDA Regulations — The Orphan Drug Act of 1983*."

Chemistry, Manufacturing, and Controls

We do not currently own or operate any manufacturing facilities. We have used third-party CMOs to manufacture API, other starting materials, and finished drug product for our preclinical studies, although we do not have any formal agreements at this time with any CMO to cover commercial production of any of our product candidates.

Commercial Outlook

Competition

Our future commercial and competitive outlook is highly dependent on the outcome of our ongoing strategic review process and therefore currently subject to a high degree of uncertainty.

With respect to our most advanced current product candidate, TSC, current medical options to improve oxygenation without risk of hyper-oxygenation are limited. However, there are several companies currently developing or marketing oxygen enhancing products, therapeutics, or devices that may nevertheless be competitive with TSC, if approved, including Hemoglobin Oxygen Therapeutics LLC, Hemotek Medical Inc., NuvOx Pharma LLC, Omniox, Inc., and VirTech Bio Inc.

More generally, our industry is highly competitive and subject to rapid and significant change. Potential competitors in the United States are numerous and include major pharmaceutical and specialty pharmaceutical companies, smaller biopharmaceutical companies, research universities, and others. The biopharmaceutical and pharmaceutical industries are 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. Many of our competitors have longer operating histories, greater name recognition, substantially greater financial resources, and larger research and development staffs than we do, as well as substantially greater experience than us in developing products, obtaining regulatory approvals, and manufacturing and marketing pharmaceutical products. In addition, a significant amount of research is carried out at academic and government institutions. These institutions are aware of the commercial value of their findings and are aggressive in pursuing patent protection and negotiating licensing arrangements to collect royalties for use of technology that they have developed. One or more of these companies or other entities may have one or more products under development that would be competitive with our current or future product candidates.

Sales and Marketing

We currently have no marketed products and, accordingly, currently have no sales or marketing personnel.

Government Regulation

Pharmaceutical product candidates are highly regulated by governmental authorities in the U.S. and other countries at the federal, state, and local levels. These regulations are numerous and extensive in their scope, relating to, among other things, the research and development, manufacture, storage, quality control and testing, approval, labeling and packaging, promotion, marketing, and advertising, distribution, post-approval monitoring and reporting, export and import, and record keeping of pharmaceutical products.

The FDA Drug Approval Process

Generally, before a new pharmaceutical product can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each applicable regulatory authority, submitted for review, and approved by the competent regulatory authority. In the United States, the competent regulatory authority is the FDA, which, pursuant to the FDC Act, is responsible for the review and approval of all data required to support a license to commercially market pharmaceutical products.

The process of obtaining regulatory approvals and the subsequent compliance with FDA regulations requires the expenditure of substantial time and financial resources and failure to comply with the applicable requirements at any time during the product development process, approval process, or, if approved, following approval may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, license revocation, a clinical hold, untitled or warning letters, voluntary or mandatory product recalls, market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties, any of which could have a material adverse effect on our business, financial position, or results of operations.

Process Overview

The FDA drug approval process generally involves the following steps:

- completion of extensive preclinical laboratory studies, including studies conducted in accordance with GLP requirements;
- submission to the FDA of an IND application, which must become effective before clinical trials involving human subjects or patients may begin;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, GCP requirements, and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication, including approval by an IRB or independent ethics committee before each trial may be initiated;
- submission to the FDA of an NDA;
- a determination by the FDA within 60 days of its receipt of an NDA as to whether it will accept the filing for review;
- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the drug will be produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- a potential FDA audit of the clinical trial sites that generated the data in support of the NDA;
- payment of user fees for FDA review of the NDA; and
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the biologic or drug in the United States.

The preclinical and clinical testing and approval process requires substantial time, effort, and financial resources and satisfaction of FDA pre-market approval requirements typically takes many years, though the actual time required may vary substantially based upon the type, complexity, and novelty of the applicable product or indication to be treated. We cannot be certain that any approvals for any product candidates we attempt to develop in the future will be granted on a timely basis or at all.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the drug. The results of preclinical testing are submitted to the FDA as part of an IND along with other information related to the drug, including information regarding its chemical make-up, manufacturing process, and quality controls, as well as a proposed clinical trial protocol. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

Clinical Trials

Following completion of preclinical studies and the submission on an IND to the FDA, a 30-day waiting period is required. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin.

Clinical trials involve the administration of an investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. These trials must be conducted in compliance with federal regulations as well as GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors. Each trial is conducted under a protocol detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap, especially in certain indications such as cancer.

- Phase 1 - In Phase 1 trials, an investigational new drug is introduced into healthy human subjects and is evaluated to assess pharmacological actions, side effects associated with increasing doses and, in certain cases, early evidence on efficacy.
- Phase 2 - In Phase 2 trials, the drug is introduced to a limited patient population in a particular indication to determine metabolism, pharmacokinetics, the effectiveness of the drug for the indication, dosage tolerance and optimum dosage, and to identify potential adverse effects and safety risks.
- Phase 3 - In Phase 3 trials, if a drug has demonstrated evidence of effectiveness and an acceptable safety profile in prior Phase 2 trials, the drug is introduced to a larger patient population in the relevant indication to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug, and to provide adequate information for the labeling of the drug, if approved.

Not all drug development programs are required to follow the order and content of all three phases. For example, in August 2018, the FDA released a draft guidance entitled “Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics,” which outlines how drug developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology drug development, i.e., the first-in-human clinical trial, to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts is included in IND applications and assessed by FDA. Expansion cohort trials can potentially bring efficiency to drug development and reduce developmental costs and time.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a clinical setting. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators 15 calendar days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor’s initial receipt of the information.

Phase 1, Phase 2, Phase 3, and other types of clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk.

New Drug Application and FDA Review Process

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA containing data intended to provide substantial evidence that the drug is safe and effective in the relevant indication, and FDA approval of the NDA is required before commercial marketing of the product may begin in the United States. The NDA must include the results of all preclinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacturing, and controls. The cost of preparing and submitting an NDA is substantial, and the submission of most NDAs is also subject to substantial initial and ongoing fees.

The FDA has 60 days from its receipt of an NDA to determine whether the NDA will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review subject to certain performance goals agreed upon by the FDA. Priority review can be applied in certain instances, including with respect to drugs that the FDA determines offer major advances in treatment or provide a treatment where no adequate therapy exists. The review process, whether standard or priority, may be extended by the FDA for three additional months to consider certain late-submitted information or information intended to clarify information already provided in the submission.

Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or facilities at which the drug is manufactured to confirm compliance with cGMP. The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an advisory committee. This advisory committee is typically a panel that includes clinicians and other experts in the relevant indication or subject matter who review and evaluate the NDA and provide a recommendation to the FDA as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

After the FDA evaluates the NDA, the clinical sites, the manufacturing facilities, and, as needed, receives a recommendation from the advisory committee, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. The FDA has committed to reviewing such resubmissions in two to six months depending on the type of new information included.

FDA Approval Letter

An FDA approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy including, in certain cases, REMS as described in more detail under the heading "*—Certain Other FDA Regulations – Risk Evaluation and Mitigation Strategies*." Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Further, changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses similar procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

The Hatch-Waxman Amendments

The Drug Price Competition and Patent Term Restoration Act, commonly referred to as the Hatch-Waxman Amendments, is a 1984 U.S. federal law which established the modern system of generic drug regulation in the U.S. The Hatch-Waxman Amendments were enacted to encourage the manufacture of generic drugs by outlining the process for generic pharmaceutical manufacturers to file an abbreviated new drug application and to provide certain related protections to drug development innovators, namely a new kind of market exclusivity period and the ability to potentially extend patent life by a portion of the time a drug is under regulatory review by the FDA.

Orange Book Listing and Abbreviated New Drug Applications

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an ANDA.

An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug.

An ANDA applicant is required to make certain certifications to the FDA concerning any such patents listed in the Orange Book for the approved reference drug intended to confirm that the proposed generic equivalent will not infringe on any intellectual property related to the reference drug, commonly referred to as a Paragraph IV certification. The ANDA process gives the owner of the reference drug an opportunity to assert a patent infringement claim if it believes its intellectual property rights are being infringed upon following the submission of a Paragraph IV certification.

An ANDA will not be approved until all patents and non-patent exclusivity periods listed in the Orange Book for the reference drug have expired.

Patent Term Restoration and Marketing Exclusivity

Certain of our current and future product candidates may be eligible for patent term restoration and marketing exclusivity under the Hatch-Waxman Amendment.

The Hatch-Waxman Amendments permit restoration of the patent term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. Patent term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally 50% of the amount of time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for such an extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Marketing exclusivity provisions under the FDC Act can also delay the submission or the approval of certain marketing applications. The FDC Act provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example investigations related to new indications, dosages, or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. The FDC Act also provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity, meaning the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance.

During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. Three-year and five-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy.

Certain Other FDA Regulations

The Orphan Drug Act of 1983

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. For example, we previously announced that our product candidate TSC was granted orphan drug designation by the FDA for the treatment of GBM and metastatic brain cancer in July 2011 and in December 2012, respectively. However, orphan drug designation on its own does not convey any advantage in or shorten the duration of the regulatory review and approval process but may result in certain financial and marketing incentives if approved.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety, or providing a major contribution to patient care, or in instances of drug supply issues. Competitors, however, may receive approval of either a different product for the same indication or the same product for a different indication. In the latter case, because health care professionals are free to prescribe products for off-label uses, the competitor's product could be used for the orphan indication despite our orphan exclusivity. Orphan drug exclusivity could also block the approval of one of our products for seven years if a competitor obtains approval before we do for the same drug and same indication, as defined by the FDA, for which we are seeking approval, or if our product is determined to be contained within the scope of the competitor's product for the same indication or disease. If we pursue marketing approval for an indication broader than the orphan drug designation we have received, we may not be entitled to orphan drug exclusivity. Orphan drug status in the E.U. has similar, but not identical, requirements and benefits.

Expedited Development and Review Programs

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for fast track status any time before receiving NDA approval, but ideally no later than the pre-NDA meeting. Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review.

A product may also be eligible for accelerated approval, if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than IMM that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it will require such post-marketing restrictions, as it deems necessary to assure safe use of the product. If the FDA determines that the conditions of approval are not being met, the FDA can withdraw its accelerated approval for such drug.

Additionally, a drug may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast track designation, plus intensive guidance from the FDA to ensure an efficient drug development program.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, fast track designation, priority review, accelerated approval, and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process.

Rare Pediatric Disease Priority Review Voucher Program

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a “rare pediatric disease” may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U.S. within one year following the date of approval.

For purposes of this program, a “rare pediatric disease” is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare diseases or conditions within the meaning of the Orphan Drug Act. On December 27, 2020, the Rare Pediatric Disease Priority Review Voucher Program was extended. Under the current statutory sunset provisions, after September 30, 2024, FDA may only award a voucher for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the drug, and that designation was granted by September 30, 2024. After September 30, 2026, FDA may not award any Rare Pediatric Disease Priority Review Voucher.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products are required to register and disclose to the public certain clinical trial information, including information related to the product, patient population, phase of investigation, study sites, investigators, and other aspects of the trial design. Sponsors are also obligated to discuss the results of their clinical trials after completion. However, disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved as competitors may otherwise use this or other publicly-available information to gain knowledge regarding the progress of development programs and gain a competitive advantage.

Risk Evaluation and Mitigation Strategies and Other Post-Approval Requirements

As a condition of NDA approval, the FDA may require a REMS to help ensure that the benefits of the drug's continued approval outweigh the potential risks. In determining whether a REMS is necessary, the FDA must consider the size of the population likely to use the drug, the seriousness of the disease or condition to be treated, the expected benefit of the drug, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug is a new molecular entity. If the FDA determines a REMS is necessary, the drug sponsor must agree to the REMS plan at the time of approval. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use. Elements to assure safe use can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring requirements, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of a drug product.

Even if the FDA does not require a REMS, once an NDA is approved, a product will be subject to certain post-approval regulations. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the internet. Adverse event reporting and the submission of periodic reports are also required following FDA approval of an NDA.

Drug Approval Process and Other Regulations Outside of the U.S.

In addition to regulations in the U.S., we are and will be subject to the regulations of other countries in which we conduct any of our clinical trials or engage in commercial sales or other distribution of our products, if approved. Whether or not we obtain FDA approval for conduct of a clinical trial or distribution of a product, we must obtain approval from the competent regulatory authority of any country or economic area in which we would seek to commence a clinical trial or market products. For example, conduct of the COVID Trial in Bucharest, Romania, required certain approvals from regulatory authorities in Romania and the E.U. Certain countries outside of the United States have a process similar to the FDA's IND process which requires the submission of a CTA prior to the commencement of human clinical trials. In the E.U., for example, a CTA must be submitted to each country's national health authority and an independent ethics committee, which operates similar to an IRB under U.S. regulations. Once the CTA is approved in accordance with a country's requirements, the clinical trial may proceed in the applicable country. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

In particular, in the E.U. a company may submit marketing authorization applications (comparable to an NDA submission in the US to the FDA) under either a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicines produced by biotechnology or those medicines intended to treat AIDS, cancer, neurodegenerative disorders, or diabetes and is optional for medicines which are highly innovative, provides for the grant of a single marketing authorization that is valid for all E.U. member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this decentralized procedure, the holder of a national marketing authorization in any E.U. member state may submit an application to the remaining member states. Within ninety days of receiving the applications and assessments report, each member state must decide whether to recognize approval. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states. The E.U. also has procedures similar to those of the FDA pursuant to which a company may obtain marketing exclusivity for a product for up to 11 years and/or orphan drug designation and related exclusivity for up to ten years, as well as other expedited approval pathways available to certain drugs.

In addition, in some non-U.S. jurisdictions, the proposed pricing for a product candidate must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the E.U. provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, product candidates launched in the E.U. do not follow price structures of the U.S. and generally tend to be significantly lower.

Certain Other Legislation and Regulations

Current Healthcare Laws and Regulations

Healthcare providers, physicians, and third party payors, including governmental payors such as Medicare and Medicaid, will play a significant role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with third party payors, healthcare providers, and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute any drugs for which we obtain marketing approval.

These laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, and other federal, state, and local regulations and legislation impacting the pharmaceutical and biopharmaceutical industries, including but not limited to those described below.

- Health Insurance Portability and Accountability Act - HIPAA imposes criminal and civil liability for, among other things, knowingly and willfully executing a scheme, or attempting to execute a scheme, to defraud any healthcare benefit program, including private payors, or falsifying, concealing, or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. HIPAA, as amended by HITECH and their respective implementing regulations, imposes, among other things, specified requirements on covered entities and their business associates relating to the privacy and security of individually identifiable health information, including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state Attorneys General new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.

- Affordable Care Act - The ACA was enacted in March 2010 and included measures intended to significantly change the way healthcare is financed in the U.S. by both governmental and private insurers which have and may continue to impact the pharmaceutical and biopharmaceutical industries, including expanded Medicare and Medicaid benefits, expansion of healthcare fraud and abuse laws, establishment of the Centers for Medicare & Medicaid Services, annual reporting requirements for manufacturers and distributors. Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. In addition, subsequent legislation, including the Budget Control Act of 2011, American Taxpayer Relief Act of 2012, and Coronavirus Aid, Relief, and Economic Security Act of 2020, has limited and supplemented various provisions of the ACA. While we cannot predict what effect further changes to the ACA would have on our business, the ACA is likely to continue to impact the regulatory regime to which we are subject for the foreseeable future, and we cannot predict the ultimate content, timing, or effect of any healthcare reform legislation or the impact of potential legislation on us.

- 21st Century Cures Act - The 21st Century Cures Act, signed into law in December 2016, provided for a wide range of reforms to our industry, such as broadening the types of data required to support drug approval, extending protections from genetic competition, accelerating approval of breakthrough therapies, expanding the orphan drug product and compassionate use programs, and clarifying how manufacturers communicate about their products.

- Anti-Kickback Laws - The federal Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer, or pay any remuneration, directly or indirectly, in cash or in kind, that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug or any other good or service, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties, and exclusion from participation in federal healthcare programs. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it.

- False Claims Laws - The federal False Claims Act imposes civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities (including manufacturers) for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing, or concealing an obligation to pay money to the federal government. The government may deem manufacturers to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label.

- Medicare Prescription Drug, Improvement, and Modernization Act - The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 imposes requirements on the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans, but plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any reduction in payment that results from the these or similar regulations may result in a similar reduction in payments from non-governmental payors.

- The Physician Payments Sunshine Act - The Physician Payments Sunshine Act, enacted as part of the ACA, imposed new annual reporting requirements for certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, for certain payments and "transfers of value" provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

- American Rescue Plan Act of 2021 and Inflation Reduction Act of 2022 - Other legislative changes have been proposed and adopted in the U.S. since the ACA was enacted. On March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, or AMP, beginning January 1, 2024. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated.

- State, Local, and Non-U.S. Legislation and Regulations - In addition, to the legislation summarized above, we may also be subject now or in the future to analogous state, local, and non-U.S. laws and regulations, such as state anti-kickback and false claims laws, which may be broader in scope and apply regardless of payor. Such laws are enforced by various state agencies and through private actions. For example, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant federal government compliance guidance, require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, and restrict marketing practices or require disclosure of marketing expenditures. Certain state and foreign laws also govern the privacy and security of health information in some circumstances and these data privacy and security laws may differ from both HIPAA and each other in significant ways, which would potentially increase our compliance burden.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions, and settlements in the healthcare industry. If our operations are found to be in violation of any of these laws or any other related governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight, and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations.

Future Healthcare Laws and Regulations

In the United States and foreign jurisdictions, there have been a number of proposed changes regarding the healthcare system and its regulation that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. We expect that further implementation of current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any strategic collaborators, may receive for any approved products. Further, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries, presidential executive orders and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products.

For example, in July 2021, the Biden administration released an executive order with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report within 90 days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries.

U.S. Environmental, Health, and Safety Laws

We are subject to numerous environmental, health, and safety laws and regulations. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

In addition, we may incur substantial costs in order to comply with current or future environmental, health, and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Public Company Status

As a public company, we incur significant legal, accounting and other expenses to comply with the reporting requirements of the Exchange Act and applicable requirements of SOX and the Dodd-Frank Act, as well as rules and regulations subsequently implemented by the SEC and Nasdaq, including the establishment and maintenance of effective disclosure and financial controls, changes in corporate governance practices and required filing of annual, quarterly and current reports with respect to our business and operating results. These requirements increase our legal and financial compliance costs and make some activities more time-consuming and costly. In addition, our management and other personnel devote significant time and attention to these public company requirements.

Our People and Human Capital Resources

As of December 31, 2022, we had 13 full-time employees, down from 16 employees as of December 31, 2021. On February 16, 2023, in connection with our ongoing strategic review process and efforts to utilize and preserve assets in a manner that maximizes value for its stockholders, Diffusion we committed to a reduction in force that impacted six of our employees and, as of the date of this Annual Report, we have seven full-time employees.

Diversity and Inclusion

We believe that an inclusive culture is required to understand and develop products that benefit all patients. By embracing differences, we aim to foster an environment of respect and trust in an effort to facilitate creativity, spark passion, and help us achieve better outcomes for all those who work at and with Diffusion. We are committed to creating and maintaining a workplace free from discrimination or harassment, including on the basis of any class protected by applicable law, and our recruitment, hiring, development, training, compensation, and advancement practices are based on qualifications, performance, skills, and experience without regard to gender, race, or ethnicity. Our management team and employees are expected to exhibit and promote honest, ethical, and respectful conduct in the workplace, including adhering to the standards for appropriate behavior set forth in our code of conduct.

Compensation and Benefits

We operate in a highly competitive environment for human capital, particularly as we seek to attract and retain talent with relevant experience in the biotechnology and pharmaceutical sectors. Therefore, we strive to provide a total rewards package to our employees that is competitive with our peer companies, currently including competitive pay, a comprehensive healthcare benefits package (including an 80% employer contribution to family medical coverage), 25 days of paid leave, a company-sponsored 401(k) savings plan, short-term and long-term disability, and other benefits, as well as remote working and flexible work schedules. We also offer every full-time employee the benefit of equity ownership in Diffusion through stock option grants. We believe these grants both help promote alignment between our employees and our stockholders and provide retention benefits, as the awards generally vest over a three-year period.

We do not have any employees that are represented by a labor union or that have entered into a collective bargaining agreement with the Company.

Safety and Wellness

At Diffusion, we believe that health matters to everyone, and the safety health, and wellness of our employees is one of our top priorities. We are committed to developing and fostering a work environment that is safe, professional, and promotes teamwork, diversity, and trust in order to afford all of our employees the opportunity to contribute to the best of their abilities. In recent years, we have taken certain measures and responded to changes in our operational needs, including actions designed to further promote a safe work environment for our employees, including investing in technology solutions to support increased work-from-home capabilities.

Employee Development and Training

Our employees are encouraged to attend scientific, clinical, technological, and other relevant meetings and conferences and we strive to provide employees access to a broad set of internal resources intended to help them be successful, including a variety of training and educational materials. We have also implemented a comprehensive employee evaluation program tied to the achievement of individual, team, and company goals to help further support, retain, and develop our people and further promote alignment of interests between our employees and our stockholders.

Directors and Executive Officers

The information set forth in "*Part III — Item 10 — Directors, Officers, and Corporate Governance*," of this Annual Report is incorporated herein by reference.

Other Information About Our Company

Corporate Information and History

We were originally incorporated under the laws of the State of Nevada on January 10, 1995 and reincorporated under the laws of the State of Delaware on June 18, 2015 under the name, “RestorGenex Corporation.” On January 8, 2016, we completed the merger of our wholly owned subsidiary with and into Diffusion LLC, which was treated as a "reverse acquisition" under GAAP pursuant to which Diffusion LLC's historical results of operations replaced the Company's for all periods prior to the merger. Immediately following the closing of the merger, we changed our name from "RestorGenex Corporation" to "Diffusion Pharmaceuticals Inc."

Our principal corporate office is located at 300 East Main Street, Suite 201, Charlottesville, Virginia 22902, and our telephone number is (434) 220-0718. Our website, www.diffusionpharma.com, including the Investor Relations section, investors.diffusionpharma.com, and our social media channels – Facebook (www.facebook.com/diffusionpharmaceuticalsinc/), Twitter (www.twitter.com/diffusionpharma) and LinkedIn (https://www.linkedin.com/company/diffusion-pharmaceuticals/) -- contain a significant amount of information about the Company. However, the information included on our website and available through our social media channels is not incorporated by reference into, and should not be considered part of, this Annual Report or any other filings we make with the SEC.

Available Information

We make available on or through our website certain reports that we file with or furnish to the SEC in accordance with Exchange Act. These include our Annual Reports on Form 10-K, our Quarterly Reports on Form 10-Q, and our Current Reports on Form 8-K, as well as any amendments to those reports, filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC. The SEC also maintains a website, www.sec.gov, that contains reports, proxy and information statements, and other information regarding the Company and other issuers that file electronically with the SEC. We also make available, free of charge and through our website, the charters of the committees of the Board, our Corporate Governance Guidelines, and our Code of Business Conduct and Ethics.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. Set forth below are certain material risks and uncertainties known to us that could adversely affect our business, financial condition, or results of operations or could cause our actual results to differ materially from our expectations expressed elsewhere in this Annual Report. The occurrence of the events contemplated by one or more of the factors we describe below could cause the market price of our common stock to decline, resulting in the loss of all or part of any investment in our common stock. Furthermore, other risks that are currently unknown to us or that we currently believe to be immaterial may also, nevertheless, adversely affect our business, financial condition, or results of operations in a way that is material.

Before investing in our common stock, you should carefully consider these risks and uncertainties, together with all other information in this Annual Report, including our consolidated financial statements and related notes, the information included in, *Part II — Item 7 — Management's Discussion and Analysis of Financial Condition and Results of Operations,* and the information incorporated herein by reference.

Risks Related to Our Business, Financial Position, Results of Operation, and Organizational Structure

We are engaged in an ongoing strategic review process that could significantly impact our future operations and financial position.

In November 2022, we announced that we are engaged in an ongoing strategic review process with the goal of enhancing shareholder value and have engaged Canaccord as our exclusive financial advisor to assist in this process. Potential strategic alternatives that may be considered as part of this process include an acquisition, merger, reverse merger, other business combinations, sales of assets, licensing or other strategic transactions. There can be no assurance that the exploration of strategic alternatives will result in any agreements or transactions, or that, if completed, any agreements or transactions will be successful or on attractive terms. No timetable has been established for the completion of this process, and we do not expect to disclose developments unless and until the Board has concluded that disclosure is appropriate or required. If we determine to change our business strategy or to seek to engage in a strategic transaction, our future business, prospects, financial position and operating results could be significantly different than those in historical periods or projected by our management. Due to the significant uncertainty regarding our future plans, we are not able to accurately predict the impact of a potential change in our business strategy and future funding requirements as of the date of this Annual Report. Until the review process is concluded, perceived uncertainties related to our future may result in the loss of potential business opportunities, volatility in the market price of our common stock, and may make it more difficult for us to attract and retain qualified personnel and business partners.

The market price of our common stock may decline as a result of our ongoing strategic review process.

The market price of our common stock may decline as a result of our ongoing strategic review process for a number of reasons, including:

- the uncertainty regarding our future plans and operations inherent to such a process;
- in the event we enter into a definitive agreement for a transaction in connection with the process, investors may react negatively to the prospects of the combined organization's business and prospects from any transaction we announce;
- the effect of any such proposed transaction on the combined organization's business and prospects may not be consistent with the expectations of financial or industry analysts; or
- in the event we consummate a transaction in connection with the process, the combined organization may not achieve the perceived benefits of the transaction as rapidly or to the extent anticipated by financial analysts, industry analysts or the Company.

There is no assurance that the strategic review process will result in a transaction be completed in a timely manner or at all. If we are unable to consummate a strategic transaction, our business could suffer materially and our stock price could decline.

If our ongoing strategic review process does not result in a transaction being consummated, we may be subject to a number of material risks, and our business and stock price could be adversely affected due to a variety of factors, including:

- we have incurred and expects to continue to incur significant expenses related to the process;
- the market price of our common stock may decline to the extent that the current market price reflects a market assumption that the process will result in a strategic transaction being consummated; and
- we may not be forced to pursue a liquidation or wind-up of the Company.

If we consummate a transaction with a third party in connection with our ongoing strategic review process that involves the issuance of our securities as consideration, the consummation may result in our stockholders having a reduced ownership and voting interest in, and exercising less influence over the management of, the combined organization as compared to their current ownership and voting interests. Nevertheless, our stockholders may not realize a benefit from any such transaction commensurate with the resulting ownership dilution they experience.

If we consummate a transaction with a third party in connection with our ongoing strategic review process that involves the issuance of our securities as consideration, following the closing date of the transaction, our current stockholders would own a smaller percentage of the combined organization than their ownership of Diffusion prior to the Merger. If such a transaction is completed and the combined organization is unable to realize the strategic and financial benefits anticipated therefrom, our stockholders will have experienced substantial dilution of their ownership interests without receiving a commensurate benefit.

Stockholder litigation and regulatory inquiries and investigations are expensive and could harm our business, financial condition and operating results and could divert management attention.

In the past, securities class action litigation and/or stockholder derivative litigation and inquiries or investigations by regulatory authorities have often

followed certain significant business transactions, such as the sale of a company or announcement of any other strategic transaction or the announcement of negative events, such as negative results from clinical trials. We are currently and may in the future be the target of this type of litigation as a result of changes in our stock price, past transactions, results of clinical trials or other matters, including any transaction we may pursue or consummate in connection with our ongoing strategic review process. Any stockholder litigation and/or regulatory investigations against us, whether or not resolved in our favor, could result in substantial costs and divert our management's attention from other business concerns, which could adversely affect our business and cash resources and our ability to consummate a potential strategic transaction or the ultimate value our stockholders receive in any such transaction.

We substantially dependent on our remaining employees to facilitate the consummation of a strategic transaction.

On February 16, 2023, we announced our commitment to a reduction in force impacting six of our 13 employees, including the departure of Dr. Christopher D. Galloway, M.D., our former Chief Medical Officer, and Ms. Raven Jaeger, our former Chief Regulatory Officer, in each case, effective March 1, 2023. Our ability to successfully complete a strategic transaction depends in large part on our ability to retain certain of our remaining personnel. Despite our efforts to retain these employees, one or more may terminate their employment with us on short notice. The loss of the services of any of these employees could potentially harm our ability to consummate a strategic transaction, to run our day-to-day operations, or fulfill our reporting obligations as a public company.

We currently generate no revenue from the sale of products, have incurred significant losses since our inception, have a history of net losses and negative cash flow from operations, expect to incur losses for the foreseeable future, and may never become profitable. In addition, our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations. As a result, any investment in our common stock is speculative and risky.

We are a clinical stage biotechnology company and, as a result, we have a limited operating history from which to assess how we will respond to competitive, economic, or other challenges to our business, and our business and prospects must be considered in light of the risks and uncertainties frequently encountered by similarly situated companies.

We have limited cash resources, have generated substantial net losses and negative cash flow from operations since our inception, and we continue to incur significant research, development, and other expenses related to our ongoing operations. To date, we have not yet obtained regulatory approvals for any of our product candidates and, accordingly, have not generated any revenues from the sale of products. We expect to continue to incur losses and negative cash flow for the foreseeable future. Furthermore, our future operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the delays in our product development programs including as a result of regulatory review, increased expenditures related to manufacturing or the enforcement of intellectual property rights, other litigation costs, changes in accounting policies, or other unanticipated events.

Our ability to generate sufficient revenues from any of our product candidates, if approved, will depend on numerous factors described throughout this Annual Report. Even if we are able to successfully develop and receive regulatory approval for any of our product candidates, we do not know if or when any such product will achieve commercial success or generate revenue for us, and we will incur significant costs associated with the commercialization that will need to be offset by revenue before achieving a profit. We may also in the future enter into collaboration agreements and license agreements with other companies that include milestone expenditures and payments, in which case our ability to generate revenue or achieve profitability may be dependent on the achievement of those milestones. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods, and our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity. Furthermore, due to the uncertainty of the drug development process, we are often unable to predict the timing or amount of increased expenses, or when we will be able to achieve or maintain profitability, if at all.

If we decide to in-license or acquire one or more additional product candidates or otherwise enter into a strategic transaction, including through our ongoing strategic process, it could impact our liquidity, increase our expenses, and present significant distractions to our management team.

We may, through our ongoing strategic review process or otherwise in the future, implement a strategy to in-license or acquire one or more additional product candidates to supplement our pipeline. We may also consider a variety of other strategic transactions, including spin-offs, partnerships, joint ventures, restructurings, divestitures, business combinations, and minority investments. Any such transaction would expose us to a number of risks and uncertainties, including the potential incurrence of recurring, non-recurring (including unknown liabilities), or other charges (including amortization expenses, write-downs, or other impairment charges), increase of short- and long-term expenditures, or dilution to our stockholders, as well as posing significant integration, implementation, or retention challenges and diverting our management team's focus on other priorities, including the TSC development program. Any of the foregoing could have a material adverse effect on our business, financial condition, or results of operation. which could adversely affect our operations and financial results. There can be no assurance that we will undertake such a transaction or, if we do, that we will successfully complete the transaction or that the transaction will be additive to our business, financial condition, or results of operations.

In connection with our ongoing strategic review process and pending its conclusion, we have paused significant portions of our TSC development activities. However, if we decide to continue development of TSC or in-license or acquire one or more additional product candidates or otherwise enter into a strategic transaction, including through our ongoing strategic process, we will require additional capital to fund our operations which may not be available on acceptable terms or at all. If we fail to obtain necessary financing, we may be forced to delay or curtail our clinical trials and other development activities or be unable to complete the development and commercialization of our product candidates due to a lack of sufficient resources.

Although we expect that our existing cash resources will enable us to fund our operating expenses and capital expenditure requirements are sufficient to fund its current operations for at least 12 months following the issuance of these financial statements, subject to the outcome of our ongoing strategic review process, we will likely need to obtain additional financing in the future in order to continue our development and operational activities.

We cannot be certain that the additional funding we will require will be available on acceptable terms or at all. Investors may demand significant discounts to market prices or that we agree to restrictive covenants or other limitations on our ability to operate our business, and conditions in the capital markets may make equity and debt financing more difficult to obtain or negatively impact our ability to complete a financing transaction at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back, discontinue the development or commercialization of one or more of our product candidates, or seek alternative financing opportunities such as collaborations or licensing opportunities.

Furthermore, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves the associated risks and uncertainties. Although we have based this estimate on assumptions that we believe to be reasonable, they may prove to be wrong, we could utilize our available capital resources sooner than we currently expect, and actual results could vary greatly from our expectations expressed in this Annual Report as a result. The magnitude and timing of our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the outcome and timing of our ongoing strategic review process;
- the number, development stage, and other characteristics of product candidates that we choose to develop, including any product candidates that we may in-license or otherwise acquire in the future through our strategic review process or otherwise;
- the clinical development plans we establish for these product candidates;
- the magnitude of costs associated with filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the initiation, progress, timing, costs, and results of clinical trials for such product candidates;
- the outcome, timing and cost of regulatory approvals by the FDA and comparable foreign regulatory authorities, including the potential for the FDA or comparable foreign regulatory authorities to require that we perform more studies than those that we currently expect;
- the cost and timing of completion of becoming a commercial organization; and
- the effect of competing technological and market developments.

We may need to further increase the size and complexity of our organization in the future including, if any of our product candidates are approved for commercial sale, establishing sales and marketing capabilities. We may experience difficulties in executing our growth strategy or managing any growth that we do experience if we are unable to recruit and retain talented individuals in key positions.

Our ability to succeed in the highly competitive pharmaceuticals industry depends upon our ability to attract and retain highly qualified personnel. As of the date of this Annual Report, we have seven full-time employees and no part-time employees. Our ability to effectively manage our anticipated growth will depend on the outcome and timing of our ongoing strategic review process and multiple other factors, including our ability to:

- effectively retain current talent and effectively recruit sufficient numbers of new talented employees;
- manage our third-party supply and manufacturing operations effectively and in a cost-effective manner,
- while increasing production capabilities for our current product candidates to commercial levels;
- establish and maintain relationships with development and commercialization partners;
- manage our development and commercialization efforts effectively and in a cost-effective manner; and
- continue to improve our operational, clinical, financial, management and regulatory compliance controls and reporting systems and procedures.

We are highly dependent on our management and scientific personnel, including our executive officers, certain other key employees and consultants, and the members of our Board. If we lose the services of any of these individuals, we might not be able to find suitable replacements on a timely basis or at all, and our business could be harmed as a result. All of our employees, including our executive officers with whom we have employment agreements, are employed on an at-will basis and their employment can be terminated by us or them at any time. In addition, as part of our reduction in force announced on February 16, 2023, the majority of our clinical operations team was terminated, which would further increase our need to attract additional personnel and/or our reliance on third parties in any future developments efforts.

We may also be unable to attract or retain qualified management and other key personnel in the future due to the intense competition among biotechnology, pharmaceutical, and other businesses. There may be a limited number of persons with the requisite skills to serve in these positions, and we cannot assure you that we will be able to identify or employ qualified personnel for any such position on acceptable terms, if at all, and the high levels of competition within the industry may mean that we will be required to expend significant financial resources in our employee recruitment and retention efforts. Many of the other pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. If we are not able to attract and retain the necessary personnel to accomplish our business objectives, we may experience constraints that will harm our ability to implement our business strategy and achieve our business objectives. Furthermore, as we currently have no marketed products, we currently have no sales or marketing personnel or capabilities. To commercialize any our other product candidates, if approved, we will need to build our marketing, sales, distribution, and other related capabilities or arrange with third parties to perform these services, and we may not be successful in doing so.

In addition, we have historically utilized the services of certain outside independent contractors to perform a number of critical functions for our company, including with respect to clinical development, regulatory matters, accounting, and human resources, a practice we expect to continue and may choose to expand in the future. We rely on these independent contractors and effectively managing our relationships with them is and will remain a priority. However, there can be no assurance that we will be able to manage these relationships effectively, that such contractors will be able or choose to continue working with us in the future, or that we will be able to find additional or replacement services if and as needed, on economically reasonable terms or at all.

If we are not able to effectively manage our growth and expand our organization through a combination of effectively retaining our existing employees and third-party contractors and successfully recruiting new employees and contractors, we may be unable to effectively execute on our product development and other strategic plans, which may adversely affect our business, financial condition, or results of operations.

Our ability to utilize our NOL carryforwards and other deferred tax assets may be limited as a result of past and future issuances of our common stock.

As of December 31, 2022, we had $34.2 million in federal and state NOL carryforwards available to reduce future taxable income, if any, for income tax purposes. If not utilized, the NOL carryforwards will begin expiring during the year ending December 31, 2034. Under Section 382 of the Tax Code, if a corporation undergoes an “ownership change,” generally defined as a greater than 50% change, measured by value, in its equity ownership over a three-year period, the corporation’s ability to use its pre-ownership change NOL carryforwards and other pre-ownership change tax attributes – such as research tax credits – to offset its post-ownership change income may be limited.

General Risks Related to Our Business, Financial Condition, Results of Operations, and Organizational Structure

Our business, financial condition, or results of operations may also be materially adversely affected by a number of general risks related thereto and to our organizational structure that are not specific to our Company, including:

- If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. Furthermore, our disclosure controls and procedures are subject to inherent limitations, human error, and other systematic breakdowns, and therefore may not prevent or detect all errors or acts of fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which could harm our business, financial condition, or results of operations.

- As our Company, the industry in which we operate, and the world-at-large become increasingly virtual, our acquisition and implementation of additional information technology solutions and our compliance with global privacy and data security requirements could result in additional costs and liabilities or inhibit our ability to collect and process data globally. Furthermore, any failure to comply with applicable requirements or best practices – as well as other events outside of our control – could result in a security breach or other disruption to our information technology systems, limit our capacity to effectively monitor and control our operations, compromise our or third parties' confidential information, or otherwise adversely affect our business, financial condition, or results of operations.

- We incur significant costs as a result of our public company status and devote substantial management time to operating as a public company, including complying with the applicable requirements of the Securities Act, the Exchange Act, the Dodd-Frank Act, SOX, and the rules and regulations of Nasdaq. If, in the future, we are required to include in our annual report an attestation of our independent registered public accounting firm regarding internal control over financial reporting, the amount of these compliance costs would increase significantly.

- Although we have in place business continuity and disaster recovery plans, our business, financial condition, or results of operations could be negatively affected by volatility, disruptions, or other uncertainty caused by market fluctuations, economic downturns or unfavorable global economic conditions, pandemics, natural disasters or other catastrophic events, events of war, terrorism, or other man-made problems, or other geopolitical events outside of our control, such as the ongoing war in Ukraine, the COVID-19 pandemic and Brexit.

- If we fail to comply with applicable laws and regulations, including the healthcare laws and regulations described under the heading, *Part I – Item 1. Business – Certain Other Legislation and Regulations – Current Healthcare Laws and Regulations* and applicable environmental, health, and safety laws and regulations, we could become subject to fines, penalties, or other consequences.

Risks Related to Ownership of Our Common Stock

Our stock price is volatile and any investment in our securities may suffer a decline in value, including as a result of our ongoing strategic review process. In addition, this volatility may subject our business to additional risks, such as an increased risk of securities litigation.

During the year ended December 31, 2022, the closing market price for our common stock as reported by Nasdaq varied between a high of $16.95 on March 23, 2022 and a low of $4.64 on November 10, 2022. As a result of fluctuations in the price of our common stock, you may be unable to sell shares or our common stock at or above the price you paid for them, even if your holding period is relatively short. 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 the outcome of our strategic review process and market, industry and other factors, including the degree of analyst coverage of our stock, their valuations and recommendations, and whether any such analysts publish inaccurate or unfavorable research about 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. Furthermore, despite this volatility, due to the fact that 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, we expect that only appreciation of the price of our common stock, if any, will provide a return to our stockholders for the foreseeable future.

Historically, the stock markets in general, and the markets for biotechnology stocks in particular, have experienced significant volatility that has at times 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 are able to sell any shares of our common stock that you own. In the past, following periods of volatility in the market or significant price declines in individual securities or the market as a whole, 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.

We have funded our operations to date through the issuance of securities, including common stock, warrants to purchase common stock, convertible preferred stock, and convertible debt securities, and we expect that in the future we will need to raise additional capital through similar means to fund our continued operations and liquidity needs. Assuming funding is available on acceptable terms, any future issuance of common stock or securities convertible for or exchangeable into common stock – including any stock issued to fund an acquisition, in connection with our strategic review process or otherwise, will result in dilution to our existing stockholders and could depress the market price of our common stock. Furthermore, the terms of future financing transactions may contain provisions that restrict our operations or require us to relinquish certain rights to our product candidates or other technologies.

Subject to the outcome of our strategic review process, we will likely need to raise additional funds in the future to continue our operations, fund research and development, and, if approved, commercialize our product candidates. We plan to continue to finance our operations with a combination of equity issuances, debt arrangements, and, potentially, licensing, or other partnering relationships. Our Board may determine at any time to raise additional capital if it believes the terms are in the best interests of our stockholders. In addition, we may also issue securities to counterparties as part of an acquisition, merger, or similar transaction, including as part of our strategic review process.

Accordingly, new issuances of a substantial number of shares of our common stock could occur at any time. Any issuance or sale of shares, or the perception in the market of an intent to issue or sell shares in the near-term, by the Company or holders of a large number of shares could reduce the market price of our common stock. We also cannot assure you that any such sale of common stock or other securities will be at a price per share that is equal to or greater than the price per share paid by you for our common stock. Furthermore, a depressed stock price could limit our ability to raise necessary capital through the sale of additional equity securities on terms that are acceptable.

We may also seek additional capital through other methods, either alone or in combination with the issuance of additional securities, including debt financings, receivables or royalty financings, strategic partnerships and alliances, and licensing arrangements, any of which could be coupled with an equity component, such as warrants to purchase stock. The incurrence of indebtedness could result in increased fixed payment obligations, liens and other security interests being placed on certain of our assets, and certain restrictive covenants being imposed on the operation of our business, such as limitations on our ability to incur additional debt or acquire intellectual property rights. We may also in the future raise additional funds through strategic partnerships, alliances, and licensing arrangements with third parties, any of which could require us to relinquish valuable rights to our product candidates or other assets. The restrictions imposed by any of these arrangements could materially decrease any potential returns on our investment in our product candidates, or otherwise materially and adversely affect our business, financial condition, or results of operations.

Our organizational documents impose certain anti-takeover provisions and make the Delaware Chancery Court the exclusive forum for certain stockholder actions, which could depress the trading price of our common stock.

Our certificate of incorporation, as amended, and our Bylaws contain provisions that may make the acquisition of our company, a proxy contest, or the nomination of a director candidate by a stockholder more difficult than such actions would be in the absence of such provisions, including that:

- only our Board has the right to fill a vacancy on the Board created by an expansion or by the resignation, death, or removal of a director, which prevents stockholders from being able to fill vacancies on our Board;
- only our Chairman of the Board, our Chief Executive Officer, or a majority of our directors are authorized to call a special meeting of stockholders;
- we may issue undesignated preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval (notwithstanding any requirements imposed by the SEC or any exchange on which our common stock may now or in the future trade), and which may include rights superior to the rights of the holders of common stock;
- our Board is expressly authorized to amend, restate, or repeal our Bylaws; and
- advance notice is required with respect to any nominations for election to our Board or for proposing matters that can be acted upon by stockholders at any meeting of stockholders.

In addition our Bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for certain actions, including derivative actions brought on the Company's behalf, stockholder actions claiming breaches of a fiduciary duty owed by any of our directors or officers, and claims arising under our organizational documents, in each case, subject to said Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein. Although this provision would not apply to any stockholder claims under the Exchange Act, there is uncertainty regarding whether a court would enforce such a forum selection provision as written to stockholder claims under the Securities Act. Nevertheless, this forum selection provision 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. The limitations on certain stockholder rights imposed by these provisions could also depress the trading price of our common stock.

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

Our common stock is currently listed on the NASDAQ Capital Market. To maintain the listing of our common stock on the NASDAQ Capital Market, we are required to meet certain listing requirements. In the event that our common stock is delisted from NASDAQ and is not eligible for quotation or listing on another market or exchange, trading of our common stock could be conducted only in the over-the-counter market or on an electronic bulletin board established for unlisted securities such as the Pink Sheets or the OTC Bulletin Board. In such event, it could become more difficult for us to raise capital and for our stockholders to dispose of, or obtain accurate price quotations for, our common stock, and there would likely also be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further.

Risks Related to Our Intellectual Property

In connection with our ongoing strategic review process and pending its conclusion, we have paused significant portions of our TSC development activities. If we choose to pursue further development of TSC or any other product candidate, we may not be able to obtain or enforce patent rights or other intellectual property rights that cover our product candidates and technologies that are of sufficient breadth to prevent third parties from competing against us.

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, and we face competition from a number of sources, such as pharmaceutical companies, generic drug companies, biotechnology companies and academic and research institutions. Accordingly, our ability to obtain and maintain patent protection in both the U.S. and non-U.S. jurisdictions will be critical to our ability to successfully develop, obtain regulatory approval for, and, in particular, commercialize TSC and our other product candidates. These protections are and will be essential to preserving and protecting our novel inventions, proprietary developments, and trade secrets and to preventing third parties from infringing upon them. In particular, our ability to protect any of our product candidates from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents in the U.S. and worldwide.

Our patent portfolio includes patents and patent applications in the U.S. and other major markets covering our technology with varying scope, including issued U.S. patents related to composition of matter, formulation, methods of delivery, and methods of use and the scope of coverage vary from country to country. Although we believe that our intellectual property position is strong and are currently assessing our operations and existing portfolio for additional intellectual property opportunities, we do not have – and may be unable to obtain – patent protection for every aspect of our technology. For aspects of our technology for which we do not have patent coverage, or in countries where we do not have granted patents, we may not have any ability to prevent the unauthorized use of our technologies or technologies substantially similar to ours, and any patents that we may obtain in the future may be narrow in scope and thus easily circumvented by competitors. Further, in countries where we do not have granted patents, third parties may be able to make, use or sell products identical to or substantially similar to, our product candidates.

Due to legal standards relating to patentability, validity, enforceability and claim scope of patents covering pharmaceutical inventions, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions. The patent application process, also known as patent prosecution, is expensive and time-consuming, and we may not be able to prepare, file, and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Despite any past and future efforts to obtain additional intellectual property and patent protections for product candidates, there is no assurance we will obtain such protections through our applications. Therefore, these and any of our patents and applications may not be prosecuted and enforced in an optimal manner. It is also possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as with respect to inadvertent prior public disclosures, proper priority claims, inventorship, claim scope, or patent term adjustments. If our current or future third party development partners are not fully cooperative or disagree with us as to the prosecution, maintenance, or enforcement of any patent rights, those patent rights could be compromised and we might not be able to prevent third parties from making, using and selling competing products. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Accordingly, we cannot guarantee that any patents will issue from any of our currently pending patent applications, which could impair our ability to prevent competition from third parties.

Even for aspects of our technology for which we have obtained, or obtain in the future, patent protection, the complexity of legal and factual questions underlying such claims means they may not provide us with sufficient protection for our product candidates to afford a commercial advantage against competitive products or processes, including those from branded and generic pharmaceutical companies. We cannot guarantee that the claims of these patents are or will be held valid or enforceable by the courts or will provide us with any significant protection against competitive products or otherwise be commercially valuable to us. Third parties may design around or challenge the validity, enforceability or scope of such issued patents or any other issued patents we own or license, which may result in such patents being narrowed, invalidated or held unenforceable. If the breadth or strength of protection provided by the patents we hold or pursue with respect to our product candidates is challenged, it could dissuade companies from collaborating with us to develop, or threaten our ability to commercialize, our product candidates. Changes in either the patent laws or in the interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property.

In addition, patents have a limited lifespan, presenting further challenges in effectively protecting our technologies and associated commercial position. In the U.S., the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available under a variety of legislative and regulatory avenues but often the life afforded by these extensions and the protections they afford are limited relative to full patent protection. The extensive period of time between patent filing and regulatory approval for a product candidate limits the time during which we can market a product candidate under patent protection, which may particularly affect the profitability of our early-stage product candidates. Even if patents covering our products are obtained, once the patent life has expired, we may be open to competition from competitive products. If one of our products requires extended development, testing and/or regulatory review, patents protecting such products might expire before or shortly after such products are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours, which could have a material adverse effect on our business, financial condition and results of operations.

For example, historically, our primary focus since the founding of Diffusion LLC in the early 2000s has been developing TSC and, as a result, portions of our patent portfolio, including certain patents related to TSC's composition of matter, have expired or will expire in the near future. While the Company actively engages in efforts to obtain additional patent protection covering our product candidates, there is no assurance that we will successfully obtain such patent protection.. Furthermore, if we are unable to obtain regulatory approval of and successfully commercialize our product candidates prior to the expirations of key underlying patents, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Furthermore, the laws of some foreign jurisdictions do not provide intellectual property rights to the same extent as in the United States and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally in those countries. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property in foreign jurisdictions, our business prospects could be substantially harmed.

Proprietary trade secrets and unpatented know-how are also very important to our business. Although we have taken steps to protect our trade secrets and unpatented know-how by entering into confidentiality agreements with third parties, and intellectual property protection agreements with certain employees, consultants and advisors, third parties may still obtain this information or we may be unable to protect our rights. We also have limited control over the protection of trade secrets used by our suppliers, manufacturers and other third parties. There can be no assurance that binding agreements will not be breached, that we would have adequate remedies for any breach or that our trade secrets and unpatented know-how will not otherwise become known or be independently discovered by our competitors. If trade secrets are independently discovered, we would not be able to prevent their use. Enforcing a claim that a third party illegally obtained and is using our trade secrets or unpatented know-how is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside the U.S. may be less willing to protect trade secret information.

If we are unable to adequately obtain or enforce our patent and other intellectual property rights for any reason, it could materially and adversely affect our business, financial condition, and results of operations. For more information about our intellectual property and our competition, see the information included under the heading, "Part I – Item 1. Business – Products, Product Development, and Our Competition – Our Intellectual Property" and "— Our Competition."

If we become involved in lawsuits to protect or enforce our patents or other intellectual property, or if we are sued for infringing intellectual property rights of third parties, it will be costly and time-consuming, and an unfavorable outcome in that litigation could have a material adverse effect on our business, financial condition, or results of operations.

Our ultimate commercial success depends upon our ability to develop, manufacture, market, and sell our product candidates and use our proprietary technologies in the U.S. and non-U.S. markets. In order to do so, it is critical that we prevent third parties from infringing on our intellectual property rights and that we operate our business without infringing on the intellectual property rights of others.

However, numerous U.S. and non-U.S. issued patents and pending patent applications owned by third parties exist in fields relating to our product candidates, their potential methods of delivery, potential indications they may be used to treat, and their other features, and, as more patents are issued over time, the risk increases that others may assert that our product candidates, technologies, or methods of delivery or use infringe their patent or other intellectual property rights, or that we discover a third party infringing on our rights. Moreover, it is not always clear to industry participants, including us, which patents cover various drugs, biologics, drug delivery systems, or their methods of use, which of these patents may be valid and enforceable, and what inventions or technologies may be claimed by non-public patent applications. Patent applications in the U.S. and many foreign jurisdictions are typically not published until 18 months after their first non-provisional filing and publications in the scientific literature often lag behind actual discoveries, meaning we cannot be certain whether others, including our competitors, have filed patent applications for technology covered by patents or our pending applications and whether any such filing has priority over our own applications or patents.

In the biopharmaceutical and pharmaceutical industries in particular, there is a substantial amount of litigation involving patent and other intellectual property rights. This type of litigation may occur unexpectedly but may also be prompted by specific events, such as a patent application being made public by the USPTO or a non-U.S. governmental authority or under Paragraph IV of the Hatch-Waxman Amendments. For more information regarding the Hatch-Waxman Amendments and Paragraph IV thereunder, see the information included under the heading, "*Part I – Item 1. Business – Government Regulation – The Hatch-Waxman Amendments*."

As of the date of this Annual Report, no litigation asserting infringement claims has been brought against us, nor have we filed such a claim against any third party. However, we cannot assure you that the development or future commercialization of any of our product candidates or other technologies will not result in claims that our activities infringe on the existing or future intellectual property rights of third parties. Furthermore, potential competitors may infringe our intellectual property, including our patents.

We may be required to file infringement claims to stop third-party infringement or unauthorized use or, if a third party claims we are infringing on their rights, respond to such claims. This process can be expensive and time consuming, and could result in a court deciding that a patent of ours is not valid or is unenforceable, that a third party is not required to stop using a technology we believe infringes on our rights, significant costs, or the diversion of management's time. An adverse determination in any litigation or other proceedings could put one or more of our patents at risk of being invalidated, interpreted narrowly, or amended such that they do not cover our product candidates in a manner sufficient to support our development and commercialization needs or that such product candidate needs to be significantly redesigned, or put our pending patent applications at risk of not issuing, or issuing with limited and potentially inadequate scope. Further, some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources.

In addition, interference, derivation, or other proceedings brought at the USPTO may be necessary to determine the priority or patentability of inventions with respect to our patents or patent applications. Litigation or USPTO proceedings brought by us may fail or may be invoked against us by third parties. Even if we are successful in these proceedings, domestic or foreign litigation or USPTO or foreign patent office proceedings may result in substantial costs and the diversion of management's time. We may not be able to prevent all misappropriation of our proprietary rights, particularly in countries with a legal framework that offers limited intellectual property protections or where the costs of enforcement outweigh the commercial and other benefits of maintaining intellectual property protections.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other proceedings, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings, including as a result of public announcements of the results of hearings, motions or other interim proceedings or developments, or public access to related documents. This type of disclosure could put us at a significant competitive disadvantage by disclosing important trade secrets or other proprietary information to our competitors and other third parties.

Any litigation or other challenge related to our intellectual property could materially and adversely affect our business, financial condition, and results of operations.

General Risks Related to Our Intellectual Property

Our business, financial condition, or results of operations may also be materially adversely affected by a number of general risks related to our intellectual property that are not specific to our Company, including:

- As is common in the biopharmaceutical and pharmaceutical industries, some of our employees were formerly employed by companies in the industry, including our competitors or potential competitors, and some of our consultants actively work for other companies in the industry. As a result, although we have in place policies which prohibit the use of third-party confidential information in violation of any obligation to a former employer or otherwise, we may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed to us alleged trade secrets of their former employers or their former or current customers. In addition, if any of our current employees or consultants are engaged by a competitor in the future, it is possible that they may appropriate or otherwise improperly use our proprietary and confidential information. Any of the foregoing events could result in significant costs and the diversion of time and resources.

- Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated as a result of any non-compliance with these requirements. We may also abandon certain intellectual property protections that we would otherwise maintain if we determine such protections are not expected to provide sufficient value relative to the cost of ongoing maintenance.

- Patent laws and other intellectual property protections available in the U.S., E.U., or other jurisdictions are subject to change. These changes may be unpredictable, weaken our overall intellectual property position, increase our costs related to maintenance and enforcement, or otherwise diminish the value of patents in general, thereby impairing our ability to protect our product candidates and maximize our return on investment thereon.

Risks Related to the Development, Regulatory Approval, and Commercialization of Our Product Candidates

The success of Diffusion is dependent on the successful development, regulatory approval, and, ultimately, commercialization of our product candidates. However, the drug development process is expensive, time-consuming and uncertain. Our efforts to develop, obtain regulatory approval for, and commercialize any of our product candidates could fail at any stage of the development process for a variety of reasons. Furthermore, because the results of preclinical studies and early-stage clinical trials are not necessarily predictive of future results, even if we are able to advance a product candidate into additional clinical trials, we may not continue to experience favorable results.

The success of Diffusion, including our ability to finance our operations and generate revenue in the future, will depend primarily on the successful development, regulatory approval, and, ultimately, commercialization of our product candidates. Historically, the majority of our product development resources have been dedicated to our most advanced product candidate, TSC, and for the foreseeable future, our planned expenditures are primarily related to our ongoing strategic review process and other costs associated with the conduct of certain preclinical studies and general research and development activities related to TSC. In the future, we may also seek to develop or commercialize additional product candidates, including product candidates that we may in-license or acquire to supplement our internally developed portfolio through our ongoing strategic process or otherwise.

The drug development process is very expensive, time-consuming, difficult to design and implement, and its outcome is inherently uncertain. Most product candidates that commence clinical trials are never approved by regulatory authorities for commercialization and success in early-stage clinical trials does not ensure that later clinical trials will demonstrate the efficacy and safety of an investigational drug in a manner adequate to support regulatory approval. Countless other companies, including many with greater resources and experience, have failed or suffered significant setbacks attempting to navigate the drug development process, and there can be no assurance that we will have success where others have failed.

Our current product candidates remain in early stages of the development process and, if further developed, we expect that the additional clinical trials necessary to support an NDA will take several years to complete. We do not know whether the clinical trials we may conduct will demonstrate adequate efficacy and safety or otherwise provide adequate information to result in regulatory approval to market any of our product candidates in any particular jurisdiction. Furthermore, the timeline for our clinical trials may be delayed in the future for a variety of reasons, including delays related to regulatory and IRB review and approval, slower than anticipated rates of enrollment in or early withdrawals from the trial, third party performance issues beyond our control including any CRO engaged in the conduct of the trial, discovery of series or unexpected toxicities or side effects, or a lack of effectiveness.

Whether we are able to successfully develop any of our product candidates will depend on a large number of factors, including the following:

- our ability to complete our planned and future clinical trials in a timely manner and our ability to fund such trials;
- our ability to demonstrate safety and efficacy to the satisfaction of the FDA and similar foreign regulatory authorities, and whether we are required by any such body to conduct additional clinical trials to support approval;
- the receipt of necessary regulatory approvals, including acceptance of our proposed indications and primary endpoint assessments, marketing approvals, and labeling claims;
- a continued acceptable safety profile during development and following approval, including the prevalence, duration and severity of potential side effects experienced; and
- our ability to commercialize successfully, including scaling our manufacturing capabilities, the development of sales and marketing capabilities internally or through a third party, acceptance by physicians and patients of the benefits, safety and efficacy of our treatments.

Any of these factors, many of which are beyond our control, could result in significant delays or an inability to develop, obtain regulatory approvals for, or commercialize our product candidates, and we may ultimately be able to receive regulatory approval or generate revenue from the sale of any product candidate.

A number of companies in the pharmaceutical and biopharmaceutical industry have suffered significant setbacks in later-stage Phase 3 clinical development even after promising results in earlier preclinical studies or clinical trials. If later-stage clinical trials do not produce favorable results for our product candidates, or we are unable to complete the necessary clinical trials for any reason (including a lack of funding), our ability to achieve regulatory approval or successfully commercialize may be compromised. At any time, we may decide or be forced by circumstance to delay or discontinue the development or commercialization of TSC or any of our other product candidates, including as a result of unfavorable results in later-stage clinical trials, changes in our internal product, technology or indication focus, the appearance of new technologies that make our product candidate obsolete, competition from a competing product, or changes in (or failure to comply with) applicable regulatory requirements. If we decide or are forced to terminate any development program in which we have invested significant resources, we may not receive any return on our investment despite the allocation of significant resources, we may not be able to execute on our business plan effectively, and our business, financial condition, results of operations may be materially and adversely affected.

Even if we are able to successfully complete the clinical trials and over development activities necessary to submit an NDA to the FDA or an application for marketing approval to an equivalent non-U.S. regulatory authority, we may be unable to obtain regulatory approval for any product candidates we may attempt to develop, for the indications for which we initially seek approval or at all. The FDA and similar non-U.S. regulatory authorities have significant discretion in the approval process, including the ability to delay, limit, or deny approval of product candidates. The delay, limitation, or denial of regulatory approval for any of our product candidates would limit or restrict altogether our ability to commercialize the product and generate revenue, which could materially and adversely impact our business, financial condition, and results of operations.

We currently have no products approved for sale, and we may never obtain regulatory approval to commercialize any product candidates we may attempt to develop. The research, testing, manufacturing, safety surveillance, efficacy, quality control, recordkeeping, labeling, packaging, storage, approval, sale, marketing, distribution, import, export, and reporting of safety and other post-market information related to drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and abroad, which often differ from country to country. We will not be permitted to market any of our product candidates in the U.S. until we receive approval of an NDA or other applicable regulatory filing from the FDA, and we will not be permitted to market in any non-U.S. countries until we receive the requisite approval from the applicable regulatory authorities.

To gain approval to market a new drug, the FDA and similar non-U.S. regulatory authorities require the submission of an NDA (or similar application) that contains preclinical and clinical data adequately demonstrating the safety, purity, potency, efficacy, and compliant manufacturing of the product for the intended indication. The FDA and their non-U.S. counterparts have substantial discretion in the drug approval process, including the ability to delay, limit, or deny approval of applications for many reasons, including:

- deemed issues with the design or execution of one or more clinical trials;
- deemed deficiencies in the formulation, quality control, labeling, or specifications of the product candidate;
- deemed issues in our manufacturing processes or in the controls or facilities of third-party manufacturers or testing labs with which we contract;
- a determination that the data from preclinical studies and clinical trials included in the application is not sufficient to support approval, or do not meet a required level of statistical or clinical significance, including as a result of a differing interpretation of the data than that presented by the Company in our application;
- a determination that the perceived risks of approving the product candidate outweigh the clinical and other benefits of approval;
- a determination that additional preclinical studies or clinical trials are required, either prior to or as a contingency to approval, and, for certain target indications such as pediatric populations, in the targeted sub-population;
- a determination that a product candidate may only be approved on a contingent basis or for a more limited indication or patient population than we request;
- a determination that labeling we believe is necessary or desirable for successful commercialization cannot be approved; or
- unanticipated future changes to the approval process and related regulations.

Historically, of the large number of drugs in development at any given time, only a small percentage successfully complete the regulatory approval processes and are ultimately commercialized. Our product candidates may not be approved for sale and marketing by the FDA or any other governmental authority, even if they meet specified endpoints in our clinical trials. The FDA or applicable foreign regulatory agencies may ask us to conduct additional costly and time-consuming clinical trials in order to obtain marketing approval or approval to enter into a further phase of clinical development, or may change the requirements for approval even after such agency has reviewed and commented on the design for the clinical trials.

Any delay in obtaining, or inability to obtain, the regulatory approvals necessary to market and sell our product candidates would delay or prevent commercialization and would materially and adversely affect our business, financial condition, and result of operations. Furthermore, if we determine in the future that the development, approval, or commercial prospects of any product candidate are insufficient to justify our continued expenditure of the associated development and other costs, we may choose to delay, suspend, or abandon our development or commercialization efforts with respect thereto, which would reduce or eliminate our potential return on investment for those product candidates.

Our ability to develop our product candidates depends, and, if any of our product candidates are approved, our ability to successfully commercialize our products will depend, in part on our ability to successfully obtain sufficient quantities of the necessary APIs, other component substances and materials, and finished drug product for our product candidates. We are currently entirely dependent on third parties for the manufacture and supply of our product candidates and their component parts, including, with respect to our product candidate TSC, a sole supplier. We may be unable to continue to develop or commercialize our product candidates or face significant delays in that process if we are unable to successfully obtain these materials or manufacture drug product in sufficient quantities.

Maintaining an adequate supply of our product candidates to meet our needs is critical to the success of our business. However, manufacturing and supply of APIs, other substances and materials and finished drug products is a complex and technically challenging process, and changes beyond our direct control can impact the quality, volume, price, and successful delivery of our product candidates or impede, delay, limit or prevent the successful development and commercialization of our product candidates. Mistakes and mishandling are not uncommon in the biopharmaceutical and pharmaceutical industry and can affect successful production and supply significantly.

As of the date of this Annual Report, we have no internal manufacturing capabilities and therefore we do not have direct control over our ability to maintain drug supply sufficient to serve our needs for our ongoing and planned clinical trials or, if any of our product candidates are approved, commercialization. Although we are ultimately responsible for ensuring compliance with regulatory requirements such as cGMPs, we are dependent on our third party CMOs and other contract suppliers and manufacturers for the manufacture of our drug product, including both APIs and finished products, as well as day-to-day compliance with cGMPs and certain other manufacturing-related regulatory requirements. Facilities used by our contract suppliers and manufacturers to produce the APIs and other substances and materials or finished products for commercial sale must pass inspection, provide regulators with certain technical information, and be approved by the FDA and other relevant regulatory authorities to confirm compliance with cGMP requirements and other regulatory requirements. If the safety of TSC or any of our other product candidates (or any component thereof) is found in the future to be compromised, we may not be able to successfully commercialize or obtain regulatory approval for the product candidate, and we may be held liable for injuries sustained as a result.

Any disruption in our relationship with these third parties or their ability to manufacture the APIs and finished drug product we need for our clinical trials and other development activities could result in significant delays in our anticipated development timelines and/or significant additional supply costs. Such a disruption could be the result of any number of reasons, including contractual disputes with our partners, regulatory issues with our partners or at their facilities (whether or not related to Diffusion or our drug product), financial issues faced by our partners (including bankruptcy or insolvency), damages to our partners' facilities or equipment, communication breakdowns, or acts of God. For example, during 2021 we faced certain delays in the manufacturing process for planned, new batches of TSC drug product due to the fact that, in connection with the U.S. federal government's Operation Warp Speed initiative in response to the COVID-19 pandemic, the facility at which our former, primary CMO partner conducts significant portions of the TSC manufacturing process had been mandated to devote the majority of the facility's available resources to the manufacture of components of the COVID-19 vaccine.

Amplifying this risk is the fact that, notwithstanding the improvements made to our supply chain during 2021 described under, "*Business - Product Development - Chemistry, Manufacturing, and Controls,"* we currently depend upon a sole source to manufacture our API for TSC and other aspects of our manufacturing process, limiting our available options to troubleshoot these issues. Although we actively manage this third-party relationship to ensure continuity, quality, and compliance with regulations and we intend to identify and develop alternative manufacturing and supply alternatives in the future, this process remains ongoing, will take time, and will involve significant costs. Even with these efforts, some events beyond our control, including global instability due to political unrest or from an outbreak of pandemic or contagious disease, such as COVID-19, could result in supply chain disruptions or the complete or partial failure of these manufacturing services. Any such failure or disruptions could materially adversely affect our business, financial condition, cash flows, and results of operations. Furthermore, due to the significant regulatory oversight of the pharmaceutical manufacturing process, any changes in the identity of our third-party partners or in our manufacturing processes – even if in the best interests of the Company and successful – could result in regulatory and other delays, as well as significant additional costs. In addition, if our current supplier terminated our arrangement or failed to meet our supply needs for any reason prior to the time we are able to identify sufficient alternative manufacturing capacity, we may be forced to delay our development plans significantly.

Our CMO and other manufacturing and supply partners are also engaged to supply and manufacture materials or products for other biopharmaceutical and pharmaceutical companies, exposing them to regulatory risks unrelated to the work they are doing for Diffusion but which may nevertheless impact their ability to meet their contractual requirements to us or otherwise impede their ability to supply us with sufficient quantities of drug product. Failure to meet the regulatory requirements for the production of those materials and products may also affect the regulatory clearance of a contract supplier's or manufacturer's facility. If the FDA or a comparable foreign regulatory agency does not approve these facilities for the supply or manufacture of our product candidates or if it withdraws its approval in the future, even if such lack of approval is unrelated to Diffusion or our product candidates, we may need to find alternative supply or manufacturing facilities.

In addition, to date we have only manufactured TSC and our other product candidates in relatively small quantities for preclinical studies and clinical trials. As we prepare for additional, later-stage clinical trials and potential commercialization, we will need to take steps to substantially increase the scale at which we are able to produce TSC, its API, and its other component parts. In order to meet these needs, our CMOs and suppliers will need to produce our API, other components, and finished product in larger quantities, more cost effectively and, in certain cases, at higher yields than they currently achieve. These third-party contractors may not be able to successfully increase the manufacturing capacity for any of such drug substance and product candidates in a timely or cost-effective manner or at all. Even if such a scale up is possible, it may require additional processes, technologies, and validation studies, which are costly, may not be successful, and which the FDA and foreign regulatory authorities would need to review and approve prior to any commercial sale of TSC or any other product candidate. In addition, quality issues may arise during those scale-up activities because of the inherent properties of a product candidate itself or in combination with other components added during the process of manufacturing, packaging, shipping, or storage.

Our reliance on contract manufacturers and suppliers further exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may misappropriate our trade secrets or other proprietary information. In addition, the manufacturing facilities of certain of our suppliers are located outside of the United States. This may give rise to difficulties in importing our product candidates or their components into the United States or other countries as a result of, among other things, regulatory agency approval requirements or import inspections, incomplete or inaccurate import documentation or defective packaging.

Any of these factors could cause a delay or termination of preclinical studies, clinical trials, other development activities, regulatory submissions or approvals of our product candidates, or, if any of our product candidates is approved, commercial supply, and could result in significant, unanticipated costs or an inability to effectively develop our products candidates or commercialize our approved products on a timely basis, or at all, which could materially and adversely affect our business, financial condition, and results of operations.

We expect to rely on third-party CROs and other third parties to conduct and oversee our clinical trials and other aspects of our development process for our product candidates. If these third parties do not meet our requirements or otherwise conduct the trials or perform the other services for which they are engaged, we may not be able to successfully develop, obtain regulatory approval for, or commercialize our product candidates when expected or at all. Furthermore, if we are not able to establish and maintain the necessary collaborative relationships with our CROs and other third party partners, we may have to alter our development and commercialization plans.

Conducting our clinical trials in a safe, compliant, and timely manner is critical to our success. We have historically relied on third-party CROs to conduct and oversee our clinical trials and other aspects of our product development, as well as various medical institutions, clinical investigators, contract laboratories, consultants, and other third parties to design and conduct our trials, to analyze the results therefrom, and to ensure that the trials are conducted in accordance with our clinical protocols and all applicable regulatory requirements, including the FDA's regulations and GCPs. These CROs and other third parties play a significant role in the conduct of these trials and the subsequent collection and analysis of data therefrom, as we control only certain aspects of their activities and rely heavily on them to execute our trials in a safe, compliant, and timely manner. Although we may internalize portions of these functions if and as our organization grows, we expect to continue to rely on these third parties to a significant degree in the future.

If any of our CROs, clinical trial sites, or other third party partners terminates their involvement in one of our clinical trials (or with Diffusion entirely) for any reason, we may not be able to enter into alternative arrangements sufficient to meet our needs, on a timely basis, on commercially reasonable terms, or at all. In addition, if our relationship with clinical trial sites is terminated, we may incur significant additional costs or experience the loss of follow-up information on patients enrolled in our ongoing clinical trials, unless we are able to transfer the care of those patients to another qualified clinical trial site.

We, as well as the CROs and other third-party contractors acting on our behalf, are required to comply with GCP and GLP requirements in all of our clinical trials, which are enforced through periodic inspections of trial sponsors, principal investigators, and trial sites. If we or any of these third parties fail to comply with applicable GCP, GLP, or other regulatory requirements, the clinical data generated in our clinical trials may be deemed unreliable and we may be required to perform additional clinical trials to supplement or replace such data before receiving approval of a product candidate from the FDA foreign regulatory authority. Our clinical trials must also generally be conducted with product produced under cGMP regulations. Our and our partners' compliance with these various regulations may be reviewed by regulatory inspections at any time, processes over which we will have very little control or immediate visibility, and a failure to comply with these regulations and policies by us, our CROs, or any of our other third party partners may result in significant delays in our development programs. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and could receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, the integrity of the data generated at the applicable clinical trial site may be questioned by the FDA.

In addition, in order to fund or otherwise further development of our current or future product candidates, we may collaborate with other pharmaceutical and biotechnology companies on their development and potential commercialization of those product candidates. We would face significant competition in seeking appropriate partners and whether we reach a definitive agreement for a collaboration will depend on many factors, including, our assessment of a partner's resources and experience, the terms and conditions of the proposed collaboration, the likelihood of approval by the FDA or other regulatory authorities; the potential market for the subject product candidate; uncertainty with respect to our ownership of our intellectual property; and industry and market conditions generally. These types of collaborations are complex and time-consuming to negotiate and document and could ultimately result in lower returns on investment for our stockholders than would have been achieved developing the product candidate without a partner. Further, if we were to breach our obligations under the agreements governing any such future collaboration, we may face substantial consequences, including potential termination of the collaboration, and our rights to our partners' product candidates, in which we have invested substantial time and money, would be lost.

Any failure to successfully enter into and maintain the necessary relationships with CROs and our other current and future third party partners and collaborators could materially and adversely affect our business, financial condition, and results of operations.

General Risks Related to the Development, Regulatory Approval, and Commercialization of Our Product Candidates

Our business, financial condition, or results of operations may also be materially adversely affected by a number of general risks related to the development and regulatory approval of our product candidates that are not specific to our Company, including:

- Our COVID Trial, which we completed in February 2021, was conducted in Bucharest, Romania and we may in the future conduct additional clinical trials for TSC or our other product candidates outside the U.S. In connection with an application for marketing approval, the FDA may determine not to accept data from clinical trials conducted outside of the U.S. if they determine the data presented therefrom cannot be considered valid without further inspection of the clinical trial site, are not applicable to the U.S. population and U.S. medical practice, or as a result of certain other factors. There can be no assurance that the FDA will accept any data we obtain from trials we have conducted or may in the future conduct outside the U.S.

- We face a number of risks related to the potential for one or more of our future product candidates to cause undesirable side effects, have other unexpected properties, contain manufacturing defects, or be subject to misuse or abuse. The occurrence of one or more of these events with respect to a product candidate or product could delay or prevent its regulatory approval, limit its commercial potential, result in additional pre- or post-approval regulatory requirements, or subject us to product liability exposure to consumers, health care providers, or others. Product liability claims could be brought in the future even if a product candidate is ultimately approved for commercial sale and manufactured in facilities licensed and regulated by the appropriate governmental authorities, and if product liability claims brought against us in the future were to be successful, we could incur substantial liability if our insurance coverage for those claims proved to be inadequate.

- Our employees, independent contractors, principal investigators, consultants, vendors, CROs, and other third parties we work with in the course of our development activities may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, during the course of their employment or other engagement with us. Any such misconduct or improper activities, whether intentional or negligent, could result in regulatory sanctions or other penalties against the Company, exclusion from federal healthcare programs such as Medicare and Medicaid, the incurrence of substantial defense costs, and serious harm to our reputation.

In addition, although we currently have no marketed products, in the event any of our product candidates are approved for marketing and commercial sale by the FDA or any other regulatory authority, our business, financial condition, or results of operations may be materially adversely affected by a number of general risks related to the commercialization of such products that are not specific to our Company, including:

- Even if our product candidates obtain regulatory approval, they may fail to achieve the broad degree of physician and patient adoption and use necessary for commercial success. The degree and rate of physician and patient adoption will depend on a number of factors, including the clinical indications for which a product candidate is approved and its effectiveness compared to other therapies, cost and the availability of reimbursement and other coverage from third party payors, our ability to educate patients and healthcare providers regarding a new therapy, and the effectiveness of our sales and marketing efforts. Furthermore, we will face significant competition, often from products sold and marketed by companies with far greater resources than Diffusion, and our failure to effectively compete may prevent us from achieving significant market penetration.

- With respect to any such future products available only by prescription, if we are unable to achieve and maintain coverage and adequate levels of reimbursement from third party payors – including governmental health programs such as Medicare and Medicaid and private insurance companies – and access to such third party payors' drug formularies, the commercial success of those products may be severely hindered. If any such products do not demonstrate attractive efficacy profiles, they may not qualify for coverage and reimbursement and, even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate, may require co-payments that patients find unacceptably high, and may vary from payor to payor, and there is no assurance that coverage and reimbursement levels necessary to achieve commercial success will be obtained..

- Any such future products candidates that we commercialize will be subject to ongoing and continued regulatory review, including rules and regulations of the FDA and similar non-U.S. governmental authorities relating to advertising, marketing and labeling (including restrictions on the promotion of off-label use), potential REMS requirements, routine manufacturing and other review, and required compliance with GLP. If we or a regulatory agency discovers previously unknown problems with any such product, or any facility at or process by which it is manufactured, we may face restrictions on the sale or distribution of such product or on our Company as a whole, including regulatory actions requiring us to modify marketing or sales materials, suspend manufacturing or ongoing trials, initiate a recall or withdraw the product from the market entirely, enter into a consent decree, or submit to other civil or criminal investigations and penalties. If we are not able to achieve and maintain regulatory compliance, we may not be permitted to market our product candidates, which would adversely affect our ability to generate revenue and achieve or maintain profitability.

- The biopharmaceutical and pharmaceutical industries are highly regulated and the potential for future legislative reform provides uncertainty and potential threats to our business and our potential future revenue and profitability of any such future products. In the U.S., there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system intended to contain or reduce the costs of medical products and medical services including those described under the heading *Part I – Item 1. Business – Certain Other Legislation and Regulations – Current Healthcare Laws and Regulations*. Additional state and federal healthcare reform measures may be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures. We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative or executive action, whether in the U.S. or other market territories we may pursue.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We do not own any real property. As of December 31, 2022, we had short-term agreements to utilize membership-based co-working space in both Charlottesville, Virginia and Philadelphia, Pennsylvania. Rent expense related to our short-term agreements for the years ended December 31, 2022 and 2021 was approximately $18,000 and $5,000, respectively.

ITEM 3. LEGAL PROCEEDINGS

The information in *Note 6, Commitments and Contingencies — Legal Proceedings* to our consolidated financial statements set forth in, *Part II — Item 8 — Financial Statements* of this Annual Report is incorporated herein by reference.

In addition, from time to time, we are subject to various pending or threatened legal actions and proceedings, including those that arise in the ordinary course of its business, which may include employment matters, breach of contract disputes and stockholder litigation. Such actions and proceedings are subject to many uncertainties and to outcomes that are not predictable with assurance and that may not be known for extended periods of time. We record a liability in our consolidated financial statements for costs related to claims, including future legal costs, settlements and judgments, when we have assessed that a loss is probable and an amount can be reasonably estimated. If the reasonable estimate of a probable loss is a range, we record the most probable estimate of the loss or the minimum amount when no amount within the range is a better estimate than any other amount. We disclose a contingent liability even if the liability is not probable or the amount is not estimable, or both, if there is a reasonable possibility that a material loss may have been incurred. In the opinion of management, as of the date hereof, the amount of liability, if any, with respect to these matters, individually or in the aggregate, will not materially affect our consolidated results of operations, financial position or cash flows.

ITEM 4. MINE SAFETY DISCLOSURES

None.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock trades publicly on the Nasdaq Capital Market under the symbol "DFFN."

Holders

As of March 14, 2023, there were 103 record holders of our common stock. This does not include beneficial owners of our common stock whose stock is held in nominee or "street name".

Dividends

To date, we have not declared or paid any cash dividends on our common stock and do not intend to do so in the near future.

Securities Authorized for Issuance Under Equity Compensation Plans

The information set forth in, *Part III — Item 12 (Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters)* of this Annual Report is incorporated herein by reference to the extent required by Item 201(d) of Regulation S-K.

Recent Unregistered Sales of Equity Securities and Use of Proceeds

None

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

ITEM 6. SELECTED FINANCIAL DATA

The information required by Item 6 of Form 10-K has been omitted from this Annual Report pursuant to the amendments to Regulation S-K adopted by the SEC on November 19, 2020.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Introduction

This discussion and analysis contains information related to historical and prospective events intended to enable you to assess our financial condition and results of operations. The information contained in this discussion and analysis should be read in conjunction with our consolidated financial statements and the related notes contained elsewhere in this Annual Report, as well as the risks and uncertainties discussed under the headings, "*Item 1A — Risk Factors*" and "*Note Regarding Forward-Looking Statements*."

Overview

Diffusion is a biopharmaceutical company that has historically focused on developing novel therapies that may enhance the body's ability to deliver oxygen to the areas where it is needed most. Our most advanced product candidate, TSC, has been investigated and 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, including hypoxic solid tumors like GBM.

Ongoing Evaluation of Strategic Opportunities

In early 2022, we identified the pursuit of an opportunistic transaction with the potential to complement and diversify our portfolio of product candidates as one of our key strategic objectives for the year. The intended purpose is to reduce the Company's overall risk profile as an investment and enhance long-term value for our stockholders. In pursuit of this objective, during the fourth quarter of 2021 and first half of 2022, our management team held conversations with several potential counterparties and, in July 2022, we engaged Canaccord Genuity LLC as our financial advisor to support the ongoing evaluation. In October 2022, following further deterioration of the public capital markets throughout 2022, and the corresponding increase in the cost of capital for small biopharmaceutical companies, we publicly announced our Board's authorization of an expanded evaluation and review of potential transactions, including a joint venture, licensing, merger, reverse merger, sale or divestiture of some of the Company's proprietary technologies or a sale of the Company, among others. Since that time, our management team has been increasingly focused on advancing this strategic review process through conversations about potential deal constructs with multiple companies. In connection with our strategic review process and pending its conclusion, we have paused significant portions of our TSC development activities, including initiation of our previously announced Phase 2 study of TSC in newly diagnosed GBM patients.

There is no assurance the Board's review will result in any transaction being consummated. Any further comments or disclosures regarding the strategic review process will be made from time to time as and when we determine an update is appropriate.

Financial Summary

As of December 31, 2022, we had cash, cash equivalents, and marketable securities of $22.5 million. We have incurred operating losses since inception, have not generated any product sales revenue, and have not achieved profitable operations. We incurred net losses of $15.6 million and $24.1 million for the years ended December 31, 2022 and 2021, respectively. To date, we have funded our operations and short-term liquidity needs primarily through the issuance and sale of common stock, warrants to purchase common stock, convertible debt, and convertible preferred stock. We expect to continue funding our operations through similar means for the foreseeable future, assuming the availability of additional capital, though we may enter into strategic partnerships or other alternative transactions in order to fund our ongoing capital requirements.

Our accumulated deficit as of December 31, 2022, was $145.6 million and we expect to continue to incur substantial losses in future periods for the foreseeable future, including any costs related to:

- our ongoing strategic review process;
- any additional studies we may undertake to evaluate our current or future product candidates, including other preclinical and clinical studies to support the filing of any NDA with the FDA;
- other research, development, and manufacturing activities designed to develop and optimize formulation, manufacturing processes, dosage, dose forms, and other characteristics prior to regulatory approval;
- the maintenance, expansion, and protection our global intellectual property portfolio;
- the hiring of additional clinical, manufacturing, scientific, sales, or other personnel;
- research and development related to any other product candidates we may acquire or in-license in the future; and
- investments in operational, financial, and management information systems.

Subject to the outcome and timing of our ongoing strategic review process, we currently expect that our existing cash, cash equivalents and marketable securities as of December 31, 2022 are sufficient to fund its current operations for at least 12 months following the issuance of these financial statements.

Financial Operations Overview

Revenues

We have not yet generated any revenue from product sales. We do not expect to generate revenue from product sales for the foreseeable future.

Research and Development Expense

R&D expenses include, but are not limited to, third-party CRO arrangements and employee-related expenses, including salaries, benefits, stock-based compensation, and travel expense reimbursement. R&D activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical studies.

General and Administrative Expense

G&A expenses consist principally of salaries and related costs for executive and other personnel, including stock-based compensation, other employee benefit costs, expenses associated with investment bank and other financial advisory services, and travel expenses. Other G&A expenses include, facility-related costs, communication expenses and professional fees for legal, patent prosecution and maintenance, consulting, accounting, and other professional services.

Interest Income

Interest income consists of interest earned from our cash, cash equivalents and marketable securities

Income Tax Benefit

The Company recorded no income tax benefit or expense during the year ended December 31, 2022. The Company maintains a full valuation allowance against its deferred tax assets due to the Company's history of losses as of December 31, 2022. The Company maintains a full valuation allowance against its deferred tax assets due to the Company's history of losses as of December 31, 2022.

Our NOLs and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL and tax credit carryforwards may become subject to an annual limitation in the event of a greater than 50.0% cumulative change in the ownership interest of significant stockholders over a three year period, as defined under Sections 382 and 383 of the Internal Revenue Code as well as similar state provisions. The amount of the annual limitation is determined based on the Company's value immediately prior to the ownership change, and subsequent ownership changes may further affect the limitation in future years. In 2019, due to the significant changes to our stockholder base as a result of the equity financing we completed during that year, we performed an analysis under Section 382 of the Internal Revenue Code and, as a result, reduced the magnitude of our NOL carryforwards to account for the ownership changes. In addition, the cumulative benefit of our NOLs was remeasured, resulting in tax expense recognized during the year ended December 31, 2019. We have not yet performed an analysis to determine whether or not ownership changes that have occurred in the year ended December 31, 2022 (or otherwise subsequent to the 2019 analysis) give rise to any further limitations.

Results of Operations for Year Ended December 31, 2022 Compared to Year Ended December 31, 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021:

	Year ended December 31,		
	2022	2021	Change
Operating expenses:			
Research and development	$ 7,237,165	$ 8,499,414	$ (1,262,249)
Intangible asset impairment charge	—	8,639,000	$ (8,639,000)
General and administrative	8,735,015	7,445,277	1,289,738
Depreciation	—	93,416	(93,416)
Loss from operations	(15,972,180)	(24,677,107)	(8,704,927)
Interest income	380,752	137,487	243,265
Loss from operations before income taxes	(15,591,428)	(24,539,620)	8,948,192
Income tax benefit	—	443,893	(443,893)
Net loss	$ (15,591,428)	$ (24,095,727)	$ 8,504,299

Research and development expenses were $7.2 million during the year ended December 31, 2022 compared to $8.5 million during the year ended December 31, 2021, a decrease of 15%. This decrease was due to lower project spending due to the completion and/or wind-down of certain CMC-related activities and clinical studies evaluating TSC in Covid-19, GBM, and our Oxygenation Trials.

The decrease in intangible asset impairment charge is related to the nonrecurring $8.6 million non-cash impairment charge related to the write down of our DFN-529 IPR&D asset during the year ended December 31, 2021.

General and administrative expenses were $8.7 million during the year ended December 31, 2022 compared to $7.4 million during the year ended December 31, 2021, an increase of 17%. The increase was primarily due to increased headcount resulting in higher compensation expense and other costs associated with the hiring of new employees as well as an increase in professional fees related to ongoing business development activity.

The decrease in depreciation for the year ended December 31, 2022 compared to the year ended December 31, 2021 is related to the disposal of property and equipment during the year-ended December 31, 2021 resulting in no remaining property and equipment remaining during the year ended December 31, 2022 for depreciating.

Interest income was $0.4 million for the year ended December 31, 2022 compared to $0.1 million for the year ended December 31, 2021 primarily as a result of investing a significant portion of our cash balance in marketable securities during the second half of the year ended December 31, 2021 and rising interest rates during 2022.

The decrease in income tax benefit of $0.4 million during the year ended December 31, 2022 compared to the year ended December 31, 2021 is due to the tax effect of the reduction in the deferred tax liability associated with the basis differences from the DFN-529 IPR&D intangible asset that was written down in the third quarter of 2021.

Liquidity and Capital Resources

Working Capital

The following table summarizes our working capital as of December 31, 2022 and 2021:

	December 31,	
	2022	2021
Cash and cash equivalents	$ 10,113,706	$ 37,313,558
Marketable securities	12,408,940	—
Prepaid expenses, deposits and other assets	112,406	510,015
Total current liabilities	2,417,336	2,927,684
Working capital	$ 20,217,716	$ 34,895,889

We expect to continue to incur net losses for the foreseeable future. We intend to use our existing cash and cash equivalents for working capital purposes, to support our ongoing strategic review process and, subject to the outcome thereof, to fund the research and development of our product candidates.

Cash Flows

The following table sets forth our cash flows for the years ended December 31, 2022 and 2021:

	December 31,	
Net cash (used in) provided by:	2022	2021
Operating activities	$ (14,969,114)	$ (14,501,789)
Investing activities	(12,235,738)	4,000
Financing activities	5,000	33,295,752
Net (decrease) increase in cash and cash equivalents	$ (27,199,852)	$ 18,797,963

Operating Activities

For the year ended December 31, 2022, net cash used in operating activities increased $0.5 million, or 3% compared to the year ended December 31, 2021.

Net cash used in operating activities of $15.0 million during the year ended December 31, 2022 was primarily attributable to our net loss of $15.6 million. These amounts were partially offset by our net change in operating assets and liabilities of $0.1 million, and non-cash charges comprised of $0.9 million of stock-based compensation expense, as well as $0.2 million for the amortization of premium and discount on marketable securities.

Net cash used in operating activities of $14.5 million during the year ended December 31, 2021 was primarily attributable to our net loss of $24.1 million and a $0.4 million change in deferred income taxes. These amounts were partially offset by a $8.6 million non cash impairment charge in connection with the write down of our DFN-529 IPR&D asset, our net change in operating assets and liabilities of $0.4 million, and non-cash charges comprised of $0.9 million of stock-based compensation expense and the loss on the write-off of property and equipment of $0.1 million and depreciation expense of $0.1 million.

Investing Activities

Net cash used in investing activities during the year ended December 31, 2022 was attributable to the purchase of $38.0 million of marketable securities and maturities of $25.8 million of marketable securities. During the year ended December 31, 2021, we received $4,000 from the sale of property and equipment.

Financing Activities

For the year ended December 31, 2022, net cash provided by financing activities decreased $33.3 million, or 100% compared to the year ended December 31, 2021.

Net cash provided by financing activities of $5,000 during the year ended December 31, 2022 was attributable to net proceeds received from the sale of our Series C Preferred Stock.

Net cash provided by financing activities of $33.3 million during the year ended December 31, 2021 which was attributable to net proceeds of $31.1 received from the sale of our common stock in connection with the February 2021 Offering and $2.2 million in proceeds received from the exercise of previously issued common stock warrants.

Capital Requirements

Historically, including during the year ended December 31, 2022, we have incurred substantial expenses and generated significant operating losses pursuing our business strategy of developing TSC. As of the date of this Annual Report and for the foreseeable future, most of our cash resources are dedicated to, and our planned expenditures are primarily related to, our ongoing strategic review process, as well as other costs associated with the conduct of certain preclinical studies and general research and development activities related to TSC.

While we currently believe we have adequate cash resources to fund our current operations for at least 12 months following the issuance of our financial statements included in this Annual Report (subject to the outcome and timing of our ongoing strategic review process), we anticipate that we will likely need additional funding in the future to support our research and development activities and other operations which, if available, could be obtained through additional capital raising transactions, entry into strategic partnerships or collaborations, or alternative financing arrangements.

In July 2022, we entered into the 2022 Sales Agreement with BTIG. The 2022 Sales Agreement is an "at-the-market" sales agreement pursuant to which we may, from time to time and through BTIG as our agent, sell up to an aggregate of $20.0 million in shares of common stock by any permissible method deemed an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act. As of the date of this Annual Report, however, we have not sold any shares pursuant to the 2022 Sales Agreement.

In the future, we may seek to raise additional funds through various sources. However, we can give no assurances that we will be able to secure additional sources of funds to support our operations, or if such funds are available to us, that such additional financing will be sufficient or be on terms acceptable to us. This risk may increase if economic and market conditions continue to be challenging or deteriorate. If we are unable to obtain additional financing when needed, we may need to curtail portions of our operations, terminate, significantly modify, or delay the development our product candidates, or obtain funds on terms that may require us to relinquish rights to our technologies, product candidates or other assets that we might otherwise seek to develop or commercialize independently or receive superior value. If we are unable to raise adequate additional capital as and when required in the future, we could be forced to cease development activities and terminate our operations, and you could experience a complete loss of your investment.

To the extent that we raise additional capital in the future through the sale of our common stock or securities convertible or exchangeable for common stock such as common stock warrants, convertible preferred stock, or convertible debt instruments, or fund acquisitions or other transactions through the issuance of such securities, the interests of our current stockholders may be diluted or otherwise impacted. In particular, specific rights granted to future holders of preferred stock or convertible debt securities may include voting rights, preferences as to dividends and liquidation, conversion and redemption rights, sinking fund provisions, and restrictions on our ability to merge with or sell our assets to a third party. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements, as defined by the rules and regulations of the SEC that have or are reasonably likely to have a material effect on our financial condition, changes in financial condition, revenue or expenses, results of operations, liquidity, capital expenditures or capital resources. As a result, we are not materially exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in these arrangements.

Recently Issued Accounting Pronouncements

The information in *Note 3, Basis of Presentation and Summary of Significant Accounting Policies* to our consolidated financial statements set forth in, *"Part II — Item 8 — Financial Statements*" of this Annual Report is incorporated herein by reference.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK

As a "smaller reporting company" (as such term is defined in Rule 12b-2 of the Exchange Act), we are not required to provide the information described in Item 305 of Regulation S-K and, accordingly, the information required by Item 6 of Form 10-K has been omitted from this Annual Report.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Diffusion Pharmaceuticals Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Diffusion Pharmaceuticals Inc. and subsidiaries (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

Critical audit matters are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ KPMG LLP

We have served as the Company's auditor since 2015.

McLean, Virginia
March 24, 2023

DIFFUSION PHARMACEUTICALS INC.

CONSOLIDATED BALANCE SHEETS

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 10,113,706	$ 37,313,558
Marketable securities	12,408,940	—
Prepaid expenses and other current assets	112,406	510,015
Total current assets	22,635,052	37,823,573
Other assets	—	15,578
Total assets	$ 22,635,052	$ 37,839,151
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,127,782	$ 947,495
Accrued expenses and other current liabilities	1,289,554	1,980,189
Total liabilities	2,417,336	2,927,684
Commitments and Contingencies (Note 9)		
Stockholders' Equity:		
Common stock, $0.001 par value: 1,000,000,000 shares authorized: 2,039,557 and 2,038,185 shares issued and outstanding at December 31, 2022 and 2021, respectively	2,040	2,038
Additional paid-in capital	165,847,590	164,914,540
Accumulated other comprehensive loss	(35,375)	—
Accumulated deficit	(145,596,539)	(130,005,111)
Total stockholders' equity	20,217,716	34,911,467
Total liabilities and stockholders' equity	$ 22,635,052	$ 37,839,151

See accompanying notes to consolidated financial statements.

DIFFUSION PHARMACEUTICALS INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Year Ended December 31,	
	2022	**2021**
Operating expenses:		
Research and development	$ 7,237,165	$ 8,499,414
Intangible asset impairment charge	—	8,639,000
General and administrative	8,735,015	7,445,277
Depreciation	—	93,416
Loss from operations	(15,972,180)	(24,677,107)
Other income:		
Interest income	380,752	137,487
Loss before income taxes	(15,591,428)	(24,539,620)
Income tax benefit	—	443,893
Net loss	$ (15,591,428)	$ (24,095,727)
Share information:		
Net loss per share of common stock, basic and diluted	$ (7.65)	$ (12.38)
Weighted average shares outstanding, basic and diluted	2,038,891	1,946,859
Comprehensive loss:		
Net loss	$ (15,591,428)	$ (24,095,727)
Unrealized loss on marketable securities	(35,375)	—
Comprehensive loss	$ (15,626,803)	$ (24,095,727)

See accompanying notes to consolidated financial statements.

DIFFUSION PHARMACEUTICALS INC.

CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY

	Series C Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balance at January 1, 2022	—	$ —	2,038,185	$ 2,038	$ 164,914,540	$ —	$ (130,005,111)	$ 34,911,467
Sale of Series C preferred stock to related parties	10,000	5,000	—	—	—	—	—	5,000
Conversion of Series C preferred stock to common stock	(10,000)	(5,000)	200	—	5,000	—	—	—
Stock-based compensation expense and vesting of restricted stock units	—	—	1,172	2	928,050	—	—	928,052
Unrealized loss on marketable securities	—	—	—	—	—	(35,375)	—	(35,375)
Net loss	—	—	—	—	—	—	(15,591,428)	(15,591,428)
Balance at December 31, 2022	—	$ —	2,039,557	$ 2,040	$ 165,847,590	$ (35,375)	$ (145,596,539)	$ 20,217,716

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount			
Balance at January 1, 2021	1,280,207	$ 1,280	$ 130,722,286	$ (105,909,384)	$ 24,814,182
Vesting of restricted stock units	207	—	—	—	—
Sale of common stock	673,171	673	31,093,629	—	31,094,302
Issuance of common stock upon exercise of warrants	84,600	85	2,201,365	—	2,201,450
Stock-based compensation expense	—	—	897,260	—	897,260
Net loss	—	—	—	(24,095,727)	(24,095,727)
Balance at December 31, 2021	2,038,185	$ 2,038	$ 164,914,540	$ (130,005,111)	$ 34,911,467

See accompanying notes to consolidated financial statements.

DIFFUSION PHARMACEUTICALS INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,	
	2022	**2021**
Cash flows from operating activities:		
Net loss	$ (15,591,428)	$ (24,095,727)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	—	93,416
Loss on disposal of property and equipment	—	51,782
Stock-based compensation expense	928,052	897,260
Abandonment of in-process research and development intangible asset	—	8,639,000
Change in deferred income taxes	—	(443,893)
Amortization of premium and discount on marketable securities	(208,577)	—
Changes in operating assets and liabilities:		
Prepaid expenses, deposits and other assets	413,187	(248,997)
Accounts payable, accrued expenses and other current liabilities	(510,348)	605,370
Net cash used in operating activities	(14,969,114)	(14,501,789)
Cash flows from investing activities:		
Cash received from sale of property and equipment	—	4,000
Purchases of marketable securities	(37,985,738)	—
Maturities of marketable securities	25,750,000	—
Net cash (used in) provided by investing activities	(12,235,738)	4,000
Cash flows from financing activities:		
Proceeds from the sale of common stock, net of issuance cost	—	31,094,302
Proceeds from the sale of common stock warrants	—	2,201,450
Proceeds from the sale of preferred stock	5,000	—
Net cash provided by financing activities	5,000	33,295,752
Net (decrease) increase in cash and cash equivalents	(27,199,852)	18,797,963
Cash and cash equivalents at beginning of year	37,313,558	18,515,595
Cash and cash equivalents at end of year	$ 10,113,706	$ 37,313,558
Supplemental disclosure of non-cash investing and financing activities:		
Conversion of Series C preferred stock to common stock	$ 5,000	$ —
Unrealized loss on marketable securities	$ 35,375	$ —
Vesting of restricted stock units	$ 1,361	$ 207

See accompanying notes to consolidated financial statements.

1. Organization and Description of Business

Diffusion Pharmaceuticals Inc., a Delaware corporation, is a biopharmaceutical company historically focused on developing novel therapies that enhance the body's ability to deliver oxygen to areas where it is needed most. The Company's most advanced product candidate, TSC, has been investigated and 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, including GBM..

On April 18, 2022, the Company effected a 1-for-50 reverse split of its common stock. Any references in the consolidated financial statements and related notes to share or per share amounts give retroactive effect to this reverse stock split.

2. Liquidity

The Company has not generated any revenues from product sales and has historically funded operations primarily from the proceeds of public and private offerings of equity, convertible debt, and convertible preferred stock.

In July 2022, the Company entered into an at-the-market sales agreement (the "2022 Sales Agreement") with BTIG pursuant to which the Company may, from time to time and through BTIG as its agent, sell up to an aggregate of $20.0 million in shares of the Company's common stock by any method permitted that is deemed an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act. To date, the Company has not sold any shares pursuant to the 2022 Sales Agreement.

On October 25, 2022, the Company announced that its Board authorized a thorough review and evaluation of a range of potential strategic opportunities in the interest of enhancing stockholder value, including transactional opportunities such as a merger, joint venture, licensing, sale, or divestiture of assets. As of the date of this Annual Report, the Board's review and evaluation remains ongoing and there is no assurance the Board's review will result in any transaction being consummated. Depending on the outcome of the Board's strategic review process, the Company may in the future, among other things, (i) pursue a strategic transaction and, if consummated, dedicate its resources primarily to research and development activities related to the transactional counterparty's product candidates, (ii) dedicate its resources primarily to research and development activities related to the Company's existing product candidates, or (iii) elect to pursue a dissolution and liquidation of the Company.

On February 16, 2023, in connection with the ongoing strategic review process and efforts to utilize and preserve assets in a manner that maximizes value for its stockholders, the Company committed to a reduction in force that is expected to impact six of the Company's thirteen current employees. The reduction is a cash preservation measure and impacts employees primarily in the Company's clinical operations function. In connection with the strategic review process and pending its conclusion, the Company has paused significant portions of its TSC development activities, including initiation of the Company's previously announced Phase 2 study of TSC in newly diagnosed GBM patients.

Substantial additional financing will be required by the Company to fund any research and development activities related to the Company's existing or future product candidates. The Company regularly explores alternative means of financing its operations and seeks funding through various sources, including public and private securities offerings, collaborative arrangements with third parties, and other strategic alliances and business transactions. However, as of the date of this Annual Report, the Company does not have any commitments to obtain additional funds and no assurance can be given that any such financing will be available in the future — when needed, in sufficient amounts, on acceptable terms, or at all. If the Company cannot obtain the necessary funding, it may need to, among other things, delay, continue to scale back or eliminate research and development programs, modify its overall development strategy for one or more product candidates (or the Company as a whole) in a manner it would not if sufficient cash resources were available, or cease operations altogether.

Operations of the Company are subject to certain additional risks and uncertainties as well, and any one or more of these factors could materially affect the Company's financial condition, future operations and liquidity needs. Many of these risks and uncertainties are outside of the Company's control, including the outcome of its ongoing strategic review process and various internal and external factors that may affect the success or failure of the Company's research and development efforts, the length of time and cost of developing and commercializing the Company's current or future product candidates, whether and when any such product candidates become approved drugs, and how significant a drug's market share will be, if approved, among others.

Subject to the outcome and timing of its ongoing strategic review process, the Company currently expects that its existing cash, cash equivalents and marketable securities as of December 31, 2022 are sufficient to fund its current operations for at least 12 months following the issuance of these financial statements.

3. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements of the Company have been prepared in accordance with Generally Accepted Accounting Principles. Any reference in these notes to applicable guidance is meant to refer to GAAP as found in the Accounting Standards Codification and Accounting Standards Updates of the Financial Accounting Standards Board.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires the Company to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period.

On an ongoing basis, the Company evaluates its estimates using historical experience and other factors, including the current economic environment. Significant items subject to such estimates are assumptions used for purposes of determining stock-based compensation and accounting for research and development activities. Management believes its estimates to be reasonable under the circumstances. Actual results could differ significantly from those estimates.

Fair Value of Financial Instruments

The carrying amounts of the Company's financial instruments, including cash, cash equivalents, marketable securities, and accounts payable approximate fair value due to the short-term nature of those instruments.

Concentration of Credit Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist principally of cash on deposit with multiple financial institutions, the balances of which frequently exceed federally insured limits.

Cash and Cash Equivalents

The Company considers any highly-liquid investments, such as money market funds, with an original maturity of three months or less to be cash equivalents.

Marketable Securities

The Company classifies its marketable securities as available-for-sale, which include commercial paper and U.S. government debt securities with original maturities of greater than three months from date of purchase. The Company considers its marketable securities as available for use in current operations, and therefore classifies these securities as current assets on the consolidated balance sheet. These securities are carried at fair value, with unrealized gains and losses reported in comprehensive loss and accumulated other comprehensive loss within stockholders' equity. Gains or losses on marketable securities sold will be based on the specific identification method.

Reverse Stock Split

On April 18, 2022, the Company filed a Certificate of Amendment to its Certificate of Incorporation, as amended, with the Secretary of State of the State of Delaware to implement the Reverse Stock Split at a ratio of 1-to-50. No fractional shares were issued in connection with the Reverse Stock Split. Stockholders who otherwise would have been entitled to receive fractional shares of common stock became entitled to receive an amount in cash (without interest or deduction) equal to the fraction of one share to which such stockholder would otherwise be entitled multiplied by $12.93, representing the split-adjusted average closing price of the Company's common stock on the Nasdaq Capital Market for the five consecutive trading days immediately preceding the effective date of the Reverse Stock Split. Proportional adjustments were made to the Company's outstanding warrants, stock options, and other equity securities, as well as to the reserve of shares available for future issuance under the 2015 Equity Plan, to reflect the Reverse Stock Split, in each case, in accordance with the respective terms thereof.

Intangible Asset

In the third quarter of 2021, the Board of Directors made a determination to no longer dedicate financial resources to the Company's DFN-529 intangible asset and any future internal development efforts were abandoned. In connection with this decision, the Company concluded that DFN-529 was impaired in its entirety and as such, the Company recognized a non-cash impairment charge of $8.6 million in 2021. The abandonment also resulted in an income tax benefit of $0.4 million due to the tax effect of the reduction in the deferred tax liability associated with the asset.

Research and Development

Major components of research and development costs include internal research and development (such as salaries and related employee benefits, equity-based compensation, supplies and allocated facility costs) and contracted services (research and development activities performed on the Company's behalf). Costs incurred for research and development are expensed as incurred.

At the end of the reporting period, the Company compares payments made to third-party service providers to the estimated progress toward completion of the research or development objectives. Such estimates are subject to change as additional information becomes available. Depending on the timing of payments to the service providers and the progress that the Company estimates has been made as a result of the services provided, the Company may record net prepaid or accrued expenses relating to these costs.

Upfront payments made to third parties who perform research and development services on the Company's behalf are expensed as services are rendered.

Patent Costs

Patent costs, including related legal costs, are expensed as incurred and are recorded within general and administrative expenses in the consolidated statements of operations and comprehensive loss.

Income Taxes

As a corporation, the Company uses the asset and liability method of accounting for income taxes. Deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. The Company recognizes the benefit of an uncertain tax position that it has taken or expects to take on its income tax return it files, if such a position is more likely than not to be sustained.

FASB ASC Subtopic 740-10, *Accounting for Uncertainty of Income Taxes*, ("ASC 740-10") defines the criterion an individual tax position must meet for any part of the benefit of the tax position to be recognized in financial statements prepared in conformity with GAAP. The Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not such tax position will be sustained on examination by the taxing authorities, based solely on the technical merits of the respective tax position. The tax benefits recognized in the financial statements from such a tax position should be measured based on the largest benefit having a greater than 50% likelihood of being realized upon ultimate settlement with the tax authority. In accordance with the disclosure requirements of ASC 740-10, the Company's policy on income statement classification of interest and penalties related to income tax obligations is to include such items as part of total interest expense and other expense, respectively. The Company adopted ASU No. 2019-12 in the first quarter of 2021 and the adoption did not have a material impact on the Company's consolidated financial statements.

Stock-based Compensation

The Company measures stock-based awards at grant-date fair value and records compensation expense on a straight-line basis over the vesting period of the award. The Company uses the Black-Scholes Model to value its stock option awards. Estimating the fair value of stock option awards requires management to apply judgment and make estimates, including the volatility of the Company's common stock, the expected term of the Company's stock options, the expected dividend yield and the fair value of the Company's common stock on the measurement date. As a result, if factors change and management uses different assumptions, stock-based compensation expense could be materially different for future awards.

For certain stock option grants, the expected term was estimated using the "simplified method" for employee options as the Company has limited historical information to develop reasonable expectations about future exercise patterns and post vesting employment termination behavior for its stock option grants. The simplified method is based on the average of the vesting tranches and the contractual life of each grant. During the year ended December 31, 2022, the Company uses the simplified method to estimate the expected term.

For stock price volatility, the Company uses a combination of its own historical stock price and comparable public companies as a basis for its expected volatility to calculate the fair value of option grants. The Company assumes no dividend yield because dividends are not expected to be paid in the near future, which is consistent with the Company's history of not paying dividends. The risk-free interest rate is based on U.S. Treasury notes with a term approximating the expected term of the option. The Company accounts for forfeitures in the periods they occur.

Net Loss Per Common Share

Basic net loss per share is computed by dividing net loss by the weighted average number of shares of common stock outstanding during each period. Diluted net loss per share includes the effect, if any, from the potential exercise or conversion of securities, such as common stock warrants, stock options and unvested restricted stock that would result in the issuance of incremental shares of common stock. In computing the basic and diluted net loss per share applicable to common stockholders, the weighted average number of shares remains the same for both calculations due to the fact that when a net loss exists, dilutive shares are not included in the calculation as the impact is anti-dilutive.

The following potentially dilutive securities outstanding have been excluded from the computation of diluted weighted average shares outstanding, as they would be anti-dilutive:

	December 31,	
	2022	2021
Common stock warrants	111,891	129,989
Stock options	140,040	72,454
Unvested restricted stock units	3,652	5,509
	255,583	207,952

Recently Issued But Not Yet Adopted Accounting Pronouncements

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments—Credit Losses, Measurement of Credit Losses on Financial Instruments* (Topic 326). The standard amends the impairment model by requiring entities to use a forward-looking approach based on expected losses to estimate credit losses for most financial assets and certain other instruments that aren't measured at fair value through net income. For available-for-sale debt securities, entities will be required to recognize an allowance for credit losses rather than a reduction in carrying value of the asset. Entities will no longer be permitted to consider the length of time that fair value has been less than amortized cost when evaluating when credit losses should be recognized. This new guidance is effective for the Company as of January 1, 2023. The Company is currently evaluating the impact of this ASU and does not expect that adoption of this standard will have a material impact on its consolidated financial statements and related disclosures.

4. Cash, cash equivalents and marketable securities

The following is a summary of the Company's cash and cash equivalents as of the dates indicated:

	December 31,	
	2022	2021
Cash in banking institutions	$ 1,586,920	$ 30,308,075
Money market funds	8,526,786	7,005,483
Total	$ 10,113,706	$ 37,313,558

The following is a summary of the Company's marketable securities as of December 31, 2022:

	Amortized cost	Unrealized gains	Unrealized losses	Fair Value
Commercial paper	$ 9,445,220	$ 263	$ (21,313)	$ 9,424,170
U.S. treasury bonds	2,999,095	—	(14,325)	2,984,770
Total	$ 12,444,315	$ 263	$ (35,638)	$ 12,408,940

The Company did not have any marketable securities as of December 31, 2021. The Company's marketable securities generally have contractual maturity dates between 3 and 12 months. All but one of the Company's marketable securities are in an unrealized loss position at December 31, 2022. Unrealized losses on marketable securities as of December 31, 2022 were $35,638 and were primarily due to changes in interest rates, and not due to increased credit risks associated with specific securities. Accordingly, no other-than-temporary impairment was recorded for the year ended December 31, 2022 and there were no realized gains or losses recorded during the year ended December 31, 2022.

5. Fair Value of Financial Instruments

Fair value is the price that could be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. Fair value determination in accordance with applicable accounting guidance requires that a number of significant judgments be made. Additionally, fair value is used on a nonrecurring basis to evaluate assets for impairment or as required for disclosure purposes by applicable accounting guidance on disclosures about fair value of financial instruments. Depending on the nature of the assets and liabilities, various valuation techniques and assumptions are used when estimating fair value. The carrying amounts of certain of the Company's financial instruments, including prepaid expense and accounts payable are shown at cost, which approximates fair value due to the short-term nature of these instruments. The Company follows the provisions of FASB ASC Topic 820, *Fair Value Measurement*, for financial assets and liabilities measured on a recurring basis. The guidance requires fair value measurements be classified and disclosed in one of the following three categories:

- Level 1: Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities.
- Level 2: Quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liabilities.
- Level 3: Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

The following table presents the Company's assets that are measured at fair value on a recurring basis:

	Fair value measurement at reporting date		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
December 31, 2022			
Cash equivalents:			
Money market funds	$ 8,526,786	$ —	$ —
Commercial paper	—	—	—
Total cash and cash equivalents	$ 8,526,786	$ —	$ —
Marketable securities:			
Commercial paper	$ —	$ 9,424,170	$ —
US treasury	—	2,984,770	—
Total marketable securities	$ —	$ 12,408,940	$ —
Total financial assets	$ 8,526,786	$ 12,408,940	$ —

The fair values of the Company's Level 2 marketable securities are estimated primarily based on benchmark yields, reported trades, market-based quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers, and reference data including market research publications, which represent a market approach. In general, a market approach is utilized if there is readily available and relevant market activity for an individual security. This valuation technique may change from period to period, based on the relevance and availability of market data.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	December 31,	
	2022	2021
Accrued payroll and payroll related expenses	$ 131,777	$ 879,971
Accrued professional fees	552,785	247,704
Accrued clinical studies expenses	475,141	786,579
Other	129,851	65,935
Total	$ 1,289,554	$ 1,980,189

7. Stockholders' Equity and Common Stock Warrants

Common Stock Warrants

As of December 31, 2022, the Company had the following warrants outstanding to acquire shares of its common stock:

	Outstanding	Range of exercise price per share	Expiration dates
Common stock warrants issued in 2018 related to the January 2018 Offering	23,639	$599.71 - $749.76	January 2023
Common stock warrants issued related to the May 2019 Offering	27,648	$250.09 - $306.04	May and December 2024
Common stock warrants issued related to the November 2019 Offering	4,269	$17.51	November 2024
Common stock warrants issued related to the December 2019 Offering	6,264	$21.68 - $34.92	December 2024 and June 2025
Common stock warrants issued related to the May 2020 Offering	11,424	$65.65	March 2025
Common stock warrants issued related to the May 2020 Investor Warrant Exercise	4,998	$29.70	November 2025
Common stock warrants issued related to the February 2021 Offering	33,649	$64.08	February 2026
	111,891		

During the years ended December 31, 2022 and 2021, 18,077 and 1,071 warrants expired, respectively.

8. Stock-Based Compensation

2015 Equity Plan

The 2015 Equity Plan provides for increases to the number of shares reserved for issuance thereunder each January 1 equal to 4.0% of the total shares of the Company’s common stock outstanding as of the immediately preceding December 31, unless a lesser amount is stipulated by the Compensation Committee of the Company's board of directors. Accordingly, 81,582 shares were added to the reserve as of January 1, 2023, which shares may be issued in connection with the grant of stock-based awards, including stock options, restricted stock, restricted stock units, stock appreciation rights and other types of awards as deemed appropriate, in each case, in accordance with the terms of the 2015 Equity Plan. As of December 31, 2022, there were 24,953 shares available for future issuance under the 2015 Equity Plan.

The Company recorded stock-based compensation expense in the following expense categories of its consolidated statements of operations and comprehensive loss for the periods indicated:

	December 31,	
	2022	2021
Research and development	$ 215,904	$ 154,041
General and administrative	712,148	743,219
Total stock-based compensation expense	$ 928,052	$ 897,260

The following table summarizes the activity related to all stock options:

	Number of Options	Weighted average exercise price per share	Weighted average remaining contractual term (in years)	Aggregate Intrinsic Value
Balance at January 1, 2021	44,738	$ 407.60		
Granted	36,310	44.66		
Expired	(8,594)	68.48		
Balance at December 31, 2021	72,454	265.91		
Granted	77,088	9.87		
Forfeited	(8,892)	147.28		
Expired	(610)	1,562.92		
Outstanding at December 31, 2022	140,040	126.75	8.5	—
Exercisable at December 31, 2022	74,086	$ 226.95	7.9	—
Vested and expected to vest at December 31, 2022	140,040	$ 126.75	8.5	—

The weighted average grant date fair value of stock option awards granted was $9.87 and $44.66 during the years ended December 31, 2022 and 2021, respectively. The total fair value of options vested during the years ended December 31, 2022 and 2021 were $0.8 million and $0.8 million, respectively. No options were exercised during any of the periods presented. At December 31, 2022, there was $0.9 million of unrecognized compensation cost related to unvested options that will be recognized as expense over a weighted-average period of 1.5 years.

The grant date fair value of employee stock options is determined using the Black-Scholes Model. The following assumptions were used during the years ended December 31, 2022 and 2021:

	2022	2021
Expected term (in years)	5.5 — 5.7	10
Risk-free interest rate	1.7% — 3.9%	1.3% — 1.7%
Expected volatility	121.4% — 137.1%	122.6% — 125.8%
Dividend yield	— — —	— — —

Restricted Stock Unit Awards

The Company issues restricted stock ("RSU") to newly elected, non-executive members of the board of directors that vest in six, tri-monthly installments beginning 18 months after the respective grant date. The fair value of an RSU is equal to the fair market value price of the Company's common stock on the date of grant. RSU expense is recorded on a straight-line basis over the service period.

The following table summarizes activity related to RSU stock-based payment awards:

	Number of Units	Weighted average grant date fair value
Balance at January 1, 2022	5,509	$ 34.78
Vested[1]	(1,857)	31.41
Outstanding at December 31, 2022	3,652	36.49

(1) The RSUs vested during the year ended December 31, 2022 were settled on a hybrid basis. The Company withheld 685 shares of common stock and, in lieu of delivering such shares, paid the RSU holder an amount in cash equal to the fair market value of such shares on the vesting date, representing the holder's approximate tax liability associated with the vesting.

The Company recognized approximately $65,000 and $54,000 in expense related to these units during the years ended December 31, 2022 and 2021, respectively. At December 31, 2022, there was approximately $0.1 million of unrecognized compensation cost that will be recognized over a weighted average period of 1.3 years.

9. Commitments and Contingencies

Office Space Lease Commitment

As of December 31, 2022, the Company had short-term agreements to utilize membership-based co-working space in both Charlottesville, Virginia and Philadelphia, Pennsylvania. Rent expense related to the Company's short-term agreements for the years ended December 31, 2022 and 2021 was approximately $18,000 and $5,000, respectively.

Research and Development Arrangements

In the course of normal business operations, the Company enters into agreements with universities and contract research organizations, or CROs, to assist in the performance of research and development activities and contract manufacturers to assist with chemistry, manufacturing, and controls related expenses. Expenditures to CROs represent a significant cost in clinical development for the Company. The Company could also enter into additional collaborative research, contract research, manufacturing, and supplier agreements in the future, which may require upfront payments and long-term commitments of cash.

Defined Contribution Retirement Plan

The Company has established a 401(k) defined contribution plan that covers all employees who qualify under the terms of the plan. Eligible employees may elect to contribute to the 401(k) Plan up to 90% of their compensation, limited by the IRS-imposed maximum. The Company provides a safe harbor match with a maximum amount of 4% of the participant’s compensation. The Company made matching contributions under the 401(k) Plan of approximately $97,000 and $75,000 for the years ended December 31, 2022 and 2021, respectively.

Legal Proceedings

On August 7, 2014, a complaint was filed in the Superior Court of Los Angeles County, California by Paul Feller, the former Chief Executive Officer of the Company's legal predecessor under the caption Paul Feller v. RestorGenex Corporation, Pro Sports & Entertainment, Inc., ProElite, Inc. and Stratus Media Group, GmbH (Case No. BC553996). The complaint asserts various causes of action, including, among other things, promissory fraud, negligent misrepresentation, breach of contract, breach of employment agreement, breach of the covenant of good faith and fair dealing, violations of the California Labor Code and common counts. The plaintiff is seeking, among other things, compensatory damages in an undetermined amount, punitive damages, accrued interest and an award of attorneys' fees and costs. On December 30, 2014, the Company filed a petition to compel arbitration and a motion to stay the action. On April 1, 2015, the plaintiff filed a petition in opposition to the Company's petition to compel arbitration and a motion to stay the action. After a related hearing on April 14, 2015, the court granted the Company's petition to compel arbitration and a motion to stay the action. On January 8, 2016, the plaintiff filed an arbitration demand with the American Arbitration Association. On November 19, 2018 at an Order to Show Cause Re Dismissal Hearing, the court found sufficient grounds not to dismiss the case and an arbitration hearing was scheduled, originally for November 2020 but later postponed due to the COVID-19 pandemic and related restrictions on gatherings in the State of California. In addition, following the November 2018 hearing, an automatic stay was placed on the arbitration in connection with the plaintiff filing for personal bankruptcy protection. On October 22, 2021, following a determination by the bankruptcy trustee not to pursue the claims and release them back to the plaintiff, the parties entered into a stipulation to abandon arbitration and return the matter to state court. A case management conference was held on February 23, 2022 at which an initial trial date of May 24, 2023 was set, and the parties have agreed to stipulate to mediation in advance of the trial. On October 20, 2022, the parties filed a joint stipulation to continue the trial and certain deadlines related to the mediation in order to allow plaintiff's counsel to continue to seek treatment for an ongoing medical issue. On November 1, 2022, based on the parties joint stipulation, the court entered an order continuing the trial date to October 25, 2023.

The Company believes the claims in this matter are without merit and is defending itself vigorously. However, at this stage, the Company is unable to predict the outcome and possible loss or range of loss, if any, associated with its resolution or any potential effect the matter may have on the Company's financial position. Depending on the outcome or resolution of this matter, it could have a material effect on the Company's consolidated financial position, results of operations and cash flows.

10. Income Taxes

Income tax expense is summarized as follows:

	December 31, 2022	December 31, 2021
Federal	$ —	$ (362,150)
State	—	(81,743)
Total	—	(443,893)

Deferred tax assets and liabilities are determined based on the differences between the financial statement carrying amounts and tax bases of assets and liabilities using enacted tax rates in effect for years in which differences are expected to reverse.

Significant components of the Company's deferred tax assets for federal income taxes consisted of the following:

Deferred tax assets	**December 31, 2022**	**December 31, 2021**
Net operating loss carryforwards	$ 8,650,404	$ 6,033,726
Stock option compensation	1,754,906	1,641,354
Orphan Drug credits	1,306,682	647,937
Capitalized start-up costs and other	12,788,834	12,403,925
Valuation allowance	(24,471,392)	(20,726,942)
Deferred tax assets	$ —	$ —

The Company does not have unrecognized tax benefits as of December 31, 2022 or December 31, 2021. The Company recognizes interest and penalties accrued on any unrecognized tax benefits as a component of income tax expense.

The Company had NOL carryforwards for federal and state income tax purposes at December 31, 2022 and 2021 of approximately:

Combined NOL Carryforwards:	**December 31, 2022**	**December 31, 2021**
Federal	$ 34,116,553	$ 23,442,045
State	30,727,733	23,436,624

The pre-2018 net operating loss carryforwards have begun to expire for both federal and state income tax purposes. Net operating loss carryforwards post Tax Cuts and Jobs Act of 2017 have an indefinite life. In November 2019, the Company increased the number of shares outstanding resulting in a change of ownership, under the provisions of Internal Revenue Code Section 382 and similar state provisions. These provisions limit the Company’s ability to utilize these net operating loss carryforwards to offset future income. The amounts above reflect the amount of NOLs that the Company expects to be able to utilize as a result of the limitation. The Company recorded a 100% valuation allowance of the deferred tax assets as of December 31, 2022 because of the uncertainty of their realization.

A reconciliation of income tax benefit at the statutory federal income tax rate and income taxes as reflected in the consolidated financial statements is as follows:

Rate reconciliation:	**December 31, 2022**	**December 31, 2021**
Federal tax benefit at statutory rate	(21.0)%	(21.0)%
State tax, net of Federal benefit	(3.9)%	(4.7)%
Orphan drug credit	(4.5)%	(0.4)%
Change in valuation allowance	29.0%	24.3%
Stock compensation	0.4%	—%
Other	—%	—%
Total provision	—%	(1.8)%

The Company files income tax returns in the U.S. federal jurisdiction and various state jurisdictions. The Company’s 2018 to 2022 tax years remain open and subject to examination. All net operating losses and credits remain subject to review until utilized.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

The term "disclosure controls and procedures" means our controls and other procedures that are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

We carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, of the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a – 15(e) and 15d – 15(e)). Based upon that evaluation, our principal executive officer and principal financial officer concluded that, as of the end of the period covered in this report, our disclosure controls and procedures were effective to ensure that information required to be disclosed in reports filed under the Exchange Act is recorded, processed, summarized and reported within the required time periods and is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

Our principal executive officer and principal financial officer do not expect that our disclosure controls or internal controls will prevent all error and all fraud. Although our disclosure controls and procedures were designed to provide reasonable assurance of achieving their objectives, a control system, no matter how well conceived and operated, can provide only reasonable, not absolute assurance that the objectives of the system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within our company have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented if there exists in an individual a desire to do so. There can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, our management conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in *Internal Control—Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on that evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2022.

Attestation Report of the Independent Registered Public Accounting Firm

This report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting. As a "smaller reporting company" (as such term is defined in Rule 12b-2 of the Exchange Act), pursuant to Section 989G of the Dodd-Frank Act, we are exempt from the requirement subjecting management's report to attestation by our independent registered public accounting firm.

Change in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting that occurred during our fourth quarter ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

CORPORATE GOVERNANCE

Introduction

Our common stock is currently listed for quotation on the Nasdaq Capital Market under the symbol "DFFN." As required by the Listing Rules of the Nasdaq Capital Market, the Board has adopted certain governance standards, including its standard of independence.

Corporate Governance Guidelines

Our Board has adopted Corporate Governance Guidelines, a copy of which can be found on the Investor Relations—Corporate Governance section of our corporate website at www.diffusionpharma.com. Among the topics addressed in our Corporate Governance Guidelines are:

- Board size, composition and qualifications;
- Retirement, term limits, and resignation policy;
- Selection of directors;
- Board compensation;
- Board leadership;
- Loans to directors and executive officers;
- Board committees;
- Chief Executive Officer evaluation;
- Board and committee meetings;
- Board and committee evaluations;
- Executive sessions of outside directors;
- Director continuing education;
- Meeting attendance by directors and non-directors;
- Succession planning;
- Appropriate information and access;
- Related person transactions;
- Ability to retain advisors;
- Communication with directors;
- Conflicts of interest and director independence;
- Director attendance at annual meetings of stockholders; and
- Board interaction with corporate constituencies;
- Change of principal occupation and board memberships.
- Stock ownership by directors and executive officers;

Directors & Director Independence

The Board has determined that five of our six current directors — Robert Adams, Mark T. Giles, Jane H. Hollingsworth, Diana Lanchoney, and Alan Levin — are "independent directors" under the Listing Rules of the Nasdaq Capital Market.

Board Leadership Structure

The Board believes that our stockholders are best served if the Board retains the flexibility to adapt its leadership structure to applicable facts and circumstances, which necessarily change over time. Accordingly, under our Corporate Governance Guidelines, the office of Chairman of the Board and Chief Executive Officer may or may not be held by one person. The Board believes it is best not to have a fixed policy on this issue and that it should be free to make this determination based on what it believes is best under the circumstances.

Currently, Jane H. Hollingsworth serves as the Chair of the Board and Robert J. Cobuzzi, Jr. serves as our Chief Executive Officer. The Board believes that it is currently in the best interests of the Company's stockholders to separate these offices. This separation allows for our Board Chair to act as a bridge between the Board and the operating organization, while our Chief Executive Officer focuses on running the Company's business. The Board believes that this separation allows for a more effective utilization of the proven leadership capabilities, breadth of industry experience, and business success of the individuals holding both positions, and that the Company and its stockholders are best currently served by this leadership structure.

Executive Sessions

Generally, at regular meetings of the Board, our independent directors meet in executive session with no company management present during a portion of each meeting. Ms. Hollingsworth typically presides over these executive sessions and serves as a liaison between the independent directors and our Chief Executive Officer.

Board Meetings and Attendance

During 2022, the Board held 28 meetings. Each of our directors attended 75 percent or more of the meetings of the Board and all committees on which he or she served during 2022.

Board Committees

The Board has three standing committees: the Audit Committee, the Compensation Committee, and the Nominating and Corporate Governance Committee. Each of these committees has the composition and responsibilities described below. The Board, from time to time, may establish other committees to facilitate the management of the Company and may change the composition and the responsibilities of the existing committees. Each of the three standing committees has a charter which can be found on the Investor Relations—Corporate Governance section of our corporate website at www.diffusionpharma.com.

Audit Committee

Responsibilities

The primary responsibilities of the Audit Committee include:

- overseeing our accounting and financial reporting processes, systems of internal control over financial reporting and disclosure controls and procedures on behalf of the Board and reporting the results or findings of its oversight activities to the Board;
- having sole authority to appoint, retain and oversee the work of our independent registered public accounting firm and establishing the compensation to be paid to the independent registered public accounting firm;
- establishing procedures for the receipt, retention and treatment of complaints regarding accounting, internal accounting controls and/or auditing matters and for the confidential, anonymous submission by our employees of concerns regarding questionable accounting or auditing matters;

- reviewing and pre-approving all audit services and permissible non-audit services to be performed for us by our independent registered public accounting firm as provided under the federal securities laws and rules and regulations of the SEC; and
- overseeing our system to monitor and manage risk, and legal and ethical compliance programs, including the establishment and administration (including the grant of any waiver from) a written code of ethics applicable to each of our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions.

The Audit Committee has the authority to engage the services of outside experts and advisors as it deems necessary or appropriate to carry out its duties and responsibilities.

Composition and Audit Committee Financial Expert

The current members of the Audit Committee are Mr. Giles, Mr. Levin, and Ms. Hollingsworth. Mr. Levin is the chair of the Audit Committee.

Each current member of the Audit Committee qualifies as "independent" for purposes of membership on audit committees under the Listing Rules of the Nasdaq Capital Market and the rules and regulations of the SEC and is "financially literate" under the Listing Rules of the Nasdaq Capital Market. In addition, the Board has determined that Mr. Levin qualifies as an "audit committee financial expert" as defined by the rules and regulations of the SEC and meets the qualifications of "financial sophistication" under the Listing Rules of the Nasdaq Capital Market as a result of his experience in senior financial positions. Stockholders should understand that these designations related to the Audit Committee members' experience and understanding with respect to certain accounting and auditing matters are disclosure requirements of the SEC and the Nasdaq Capital Market and do not impose upon any of them any duties, obligations or liabilities that are greater than those generally imposed on a member of the Audit Committee or of the Board.

Meetings

The Audit Committee met four times during 2022.

Processes and Procedures for Complaints

The Audit Committee has established procedures for the receipt, retention and treatment of complaints the Company receives regarding accounting, internal accounting controls, or auditing matters, and the submission by our employees, on a confidential and anonymous basis, of concerns regarding questionable accounting or auditing matters. Our personnel with such concerns are encouraged to discuss their concerns with their supervisor first, who in turn will be responsible for informing our Chief Executive Officer of any concerns raised. If an employee prefers not to discuss a particular matter with his or her own supervisor, the employee may instead discuss such matter with our Chief Executive Officer. If an individual prefers not to discuss a matter with the Chief Executive Officer or if the Chief Executive Officer is unavailable and the matter is urgent, the individual is encouraged to contact the Chair of the Audit Committee, Mr. Levin.

Compensation Committee

Responsibilities

The primary responsibilities of the Compensation Committee include:

- determining the annual salaries, incentive compensation, long-term incentive compensation, special or supplemental benefits or perquisites and any and all other compensation applicable to our Chief Executive Officer and other executive officers;

- determining any revisions to corporate goals and objectives with respect to compensation for our Chief Executive Officer and other executive officers and establishing and leading a process for the full Board to evaluate the performance of our Chief Executive Officer and other executive officers in light of those goals and objectives;
- administering our equity-based compensation plans, including determining specific grants of options and other awards for executive officers and other employees under our equity-based compensation plans; and
- establishing and leading a process for determination of the compensation applicable to the non-employee directors on the Board.

The Compensation Committee has the authority to engage the services of outside experts and advisors as it deems necessary or appropriate to carry out its duties and responsibilities.

Composition

The current members of the Compensation Committee are Mr. Adams, Ms. Hollingsworth, and Dr. Lanchoney. Mr. Adams is the chair of the Compensation Committee. Each of the three current members of the Compensation Committee is an "independent director" under the Listing Rules of the Nasdaq Capital Market and a "non-employee director" within the meaning of Rule 16b-3 under the Exchange Act.

Meetings

The Compensation Committee met five times during 2022.

Processes and Procedures for Consideration and Determination of Executive Compensation

The Compensation Committee has authority to determine all compensation applicable to our executive officers. In setting executive compensation for our executive officers, the Compensation Committee considers, among other things, the following primary factors: each executive's position within the Company and the level of responsibility; the ability of the executive to affect key business initiatives; the executive's individual experience and qualifications; compensation paid to executives of comparable positions by companies similar to our Company; Company and individual performance; and the executive's current and historical compensation levels. The Compensation Committee has also from time to time – including, most recently, during 2021 – retained the services of its independent consulting firm, Radford, to provide advice with respect to executive compensation, such as developing a group of comparable peer companies and reviewing executive and director compensation levels. In making decisions regarding the form and amount of compensation to be paid to our executives, the Compensation Committee may consider information gathered by, and the recommendations of, Radford, when necessary and appropriate.

In making decisions regarding the form and amount of compensation to be paid to our executive officers (other than our Chief Executive Officer), the Compensation Committee considers and gives weight to the recommendations of our Chief Executive Officer recognizing that due to his reporting and otherwise close relationship with each executive, the Chief Executive Officer often is in a better position than the Compensation Committee to evaluate the performance of each executive (other than himself). In making decisions regarding the form and amount of compensation to be paid to our Chief Executive Officer, the Compensation Committee considers the recommendation of the Chief Executive Officer with respect to his own compensation and the Compensation Committee's own assessment of the Chief Executive Officer's annual performance and input from other Board members. The Compensation Committee meets in executive session regularly and makes all executive compensation decisions about the Chief Executive Officer without the presence of the Chief Executive Officer or any executive or employee of our company.

Processes and Procedures for Consideration and Determination of Director Compensation

The Board has delegated to the Compensation Committee the responsibility, among other things, to establish and lead a process for determining compensation payable to our non-employee directors. The Compensation Committee makes recommendations regarding compensation payable to our non-employee directors to the entire Board, which then makes the final decision.

In making decisions regarding compensation to be paid to our non-employee directors, the Board considers factors such as its own views as to the form and amount of compensation to be paid, the current and anticipated time demands placed on non-employee directors and other factors that may be relevant, including the recommendations of Radford, when necessary and appropriate.

Nominating and Corporate Governance Committee

Responsibilities

The primary responsibilities of the Nominating and Corporate Governance Committee are:

- identifying individuals qualified to become Board members;
- recommending director nominees for each annual meeting of our stockholders and director nominees to fill any vacancies that may occur between meetings of stockholders;
- general management and director succession planning;
- being aware of best practices in corporate governance, and developing and recommending to the Board a set of corporate governance standards to govern the Board, its committees, the Company, and our employees in the conduct of our business and affairs;
- developing and overseeing a Board and Board committee evaluation process; and
- reviewing and discussing with our Chief Executive Officer and reporting periodically to the Board plans for executive officer development and succession plans for the Chief Executive Officer and other key executive officers and employees.

The Nominating and Corporate Governance Committee has the authority to engage the services of outside experts and advisors as it deems necessary or appropriate to carry out its duties and responsibilities.

Composition

The current members of the Nominating and Corporate Governance Committee are Messrs. Adams, Giles, and Levin and Dr. Lanchoney. Mr. Giles is the chair of the Nominating and Corporate Governance Committee. Each of the four current members of the Nominating and Corporate Governance Committee is an "independent director" within the meaning of the Listing Rules of the Nasdaq Capital Market.

Meetings

The Nominating and Corporate Governance Committee met three times during 2022.

Processes and Procedures for Consideration Director Nominations

In selecting nominees for the Board, the Nominating and Corporate Governance Committee first determines whether the incumbent directors are qualified to serve, and wish to continue to serve, on the Board. The Nominating and Corporate Governance Committee believes that our Company and stockholders benefit from the continued service of certain qualified incumbent directors because those directors have familiarity with and insight into our Company's affairs that they have accumulated during their tenure with Diffusion. Appropriate continuity of Board membership also contributes to the Board's ability to work as a collective body. Accordingly, it is the practice of the Nominating and Corporate Governance Committee, in general, to re-nominate an incumbent director at the upcoming annual meeting of stockholders if the director wishes to continue his or her service with the Board, the director continues to satisfy the Nominating and Corporate Governance Committee's criteria for membership on the Board, the Nominating and Corporate Governance Committee believes the director continues to make important contributions to the Board and there are no special, countervailing considerations against re-nomination of the director.

In identifying and evaluating new candidates for election to the Board, the Nominating and Corporate Governance Committee from time to time solicits recommendations from persons with whom the Nominating and Corporate Governance Committee is familiar and who are knowledgeable about the Company and the biotech industry generally for nominees likely to have the qualifications, skills and characteristics required for Board nominees. Such persons may include members of the Board and senior management of Diffusion. In addition, the Nominating and Corporate Governance Committee may engage a search firm to assist it in identifying qualified candidates. The Nominating and Corporate Governance Committee would typically review and evaluate each candidate whom it believes merits serious consideration, taking into account available information concerning the candidate, any qualifications or criteria for Board membership established by the Nominating and Corporate Governance Committee, the existing composition of the Board (including with respect to diversity), and other factors that it deems relevant. In conducting its review and evaluation, the Nominating and Corporate Governance Committee may solicit the views of our management, other Board members and any other individuals it believes may have insight into a candidate. The Nominating and Corporate Governance Committee may designate one or more of its members and/or other Board members to interview any proposed candidate. The Nominating and Corporate Governance Committee also, in general, considers recommendations for the nomination of directors submitted by our stockholders in the same manner.

In addition, in connection with our ongoing strategic review process, potential counterparties are likely to seek representation and/or the right to nominate specific individuals to the Board in connection with a proposed transaction.

There are no formal requirements or minimum qualifications that a candidate must meet in order for the Nominating and Corporate Governance Committee to recommend the candidate to the Board. The Nominating and Corporate Governance Committee believes that each nominee should be evaluated based on his or her merits as an individual, taking into account the needs of the Company and the Board. However, in evaluating candidates, there are a number of criteria that the Nominating and Corporate Governance Committee generally views as relevant and is likely to consider. Some of these factors include:

- whether the candidate is an "independent director" under applicable independence tests under the federal securities laws and rules and regulations of the SEC;
- whether the candidate is "financially sophisticated" and otherwise meets the requirements for serving as a member of an audit committee;
- whether the candidate is an "audit committee financial expert" under the rules and regulations of the SEC for purposes of serving as a member of the Audit Committee;
- the needs of the Company with respect to the particular talents and experience of our directors;
- the personal and professional integrity and reputation of the candidate;
- the candidate's level of education and business experience;
- the candidate's business acumen;
- the candidate's level of understanding of our business and industry and other industries relevant to our business;
- the candidate's ability and willingness to devote adequate time to the work of the Board and its committees;
- the fit of the candidate's skills and personality with those of other directors and potential directors in building a board of directors that is effective, collegial and responsive to the needs of our company;
- whether the candidate possesses strategic thinking and a willingness to share ideas;
- the candidate's diversity of experiences, expertise and background, in general and as compared to other directors on the Board; and
- the candidate's ability to represent the interests of all stockholders and not a particular interest group.

While we do not have a stand-alone diversity policy, in considering whether to recommend any director nominee, including candidates recommended by stockholders, the Nominating and Corporate Governance Committee will consider the factors described above. The Nominating and Corporate Governance Committee seeks nominees with a broad diversity of experience, expertise, and backgrounds. The Nominating and Corporate Governance Committee does not assign specific weights to particular criteria and no particular criterion is necessarily applicable to all prospective nominees. We believe that the backgrounds and qualifications of the directors, considered as a group, should provide a significant mix of experience, knowledge and abilities that will allow the Board to fulfill its responsibilities.

Code of Business Conduct and Ethics

Our Code of Business Conduct and Ethics applies to all of our directors, executive officers and other employees, and meets the requirements of the SEC. A copy of our Code of Business Conduct and Ethics is available on the Investor Relations—Corporate Governance—Code of Business Conduct and Ethics section of our corporate website at www.diffusionpharma.com.

Process Regarding Stockholder Communications with Board

Stockholders may communicate with the Board or any one particular director by sending correspondence, to our General Counsel & Corporate Secretary via e-mail to info@diffusionpharma.com or via mail to 300 East Main Street, Suite 201, Charlottesville, Virginia 22902, with an instruction to forward the communication to the Board or one or more particular directors. Our General Counsel & Corporate Secretary will forward promptly all such stockholder communications to the Board or the one or more particular directors, with the exception of any advertisements, solicitations for periodical or other subscriptions and other similar communications.

LifeSci Settlement Agreement

In December 2022, we entered into a binding settlement agreement with LifeSci Special Opportunities Master Fund Ltd. ("LifeSci"), a stockholder of the Company, and certain of its affiliates following LifeSci's submission of a letter in November 2022 seeking to nominate an alternative slate of directors (collectively, the "LifeSci Nominees") at our 2022 Annual Meeting of Stockholders. Upon the terms and subject to the conditions set forth in the settlement agreement, (i) LifeSci agreed to irrevocably withdraw its notices nominating the LifeSci Nominees for election to the Board and to vote its shares of the Company's common stock in favor of the election of the nominees recommended by the Board and (ii) the Company agreed that, in the event it has not completed an Extraordinary Transaction (as defined in the settlement agreement) prior to July 1, 2023 and so long as LifeSci Special Opportunities and its named affiliates collectively own at least 96,976 of the Company's outstanding shares of common stock, the Company will promptly appoint one of the LifeSci Nominees to the Board.

DIRECTORS

Number of Directors

Our Bylaws provide that the Board will consist of at least one member, or such other number as may be determined by the Board or our stockholders. The Board has currently fixed the number of directors at six.

Information About Our Directors

The table below sets forth, as of March 15, 2023, certain information that has been furnished to us by our current directors.

Name	Age	Director Since
Robert Adams	72	2016
Robert J. Cobuzzi, Jr., Ph.D.	58	2020
Mark T. Giles	68	2016
Jane H. Hollingsworth	64	2020
Diana Lanchoney, M.D.	56	2021
Alan Levin	60	2016

In addition, the paragraphs below provide further information about each current director, including all positions he or she holds, his or her principal occupation and business experience for the past five years, and the names of other publicly held companies of which he or she currently serves as a director or served as a director during the past five years. We believe that all of our directors and director nominees display personal and professional integrity; satisfactory levels of education and/or business experience; broad-based business acumen; an appropriate level of understanding of our business and its industry and other industries relevant to our business; the ability and willingness to devote adequate time to the work of the Board and its committees; a fit of skills and personality with those of our other directors that helps build a board of directors that is effective, collegial and responsive to the needs of our company; strategic thinking and a willingness to share ideas; a diversity of experiences, expertise and background; and the ability to represent the interests of all of our stockholders. The information presented below regarding each director and nominee for director also sets forth specific experience, qualifications, attributes and skills that led the Board to the conclusion that he or she should serve as a director in light of our business and structure.

Robert Adams — Mr. Adams has served as a director since January 2016 and as a director of Diffusion LLC since 2002. Prior to his retirement in 2015, Mr. Adams was a partner in the intellectual property law firm of Nixon & Vanderhye P.C, where he had practiced for over 25 years, focusing on patent litigation and international patent licensing and negotiations. During that time period, Mr. Adams was lead litigation counsel in more than 50 major intellectual property lawsuits, where he directly handled, for example, all intellectual property valuations and settlements on behalf of his U.S. and foreign clients. Moreover, Mr. Adams served as the head negotiator for a well-known Japanese consumer products company for 15 years in various complicated licensing situations. Those negotiations typically involved the cross-licensing of up to hundreds of U.S. and foreign patent rights. His lead licensing activities on behalf of that client included, among other things, multi-year negotiations with Texas Instruments, Advanced Micro Devices and Freescale. Mr. Adams received a B.A. from the University of Maryland and a J.D. from George Washington University (with honors), and is a member of the Virginia State Bar.

The Board believes Mr. Adams' perspective and experience as a director of Diffusion, as well as the depth and breadth of his intellectual property experience, provide him with the qualifications to serve as a director.

Robert J. Cobuzzi, Jr., Ph.D. – Dr. Cobuzzi has served as a director since January 2020 and as our President and Chief Executive Officer since September 2020. Dr. Cobuzzi also currently serves as a Venture Partner and Chairman of the Business Development Board for Sunstone Life Science Ventures, an independent European venture capital investment firm focused on life science therapeutic innovations. Previously, Dr. Cobuzzi served as an Advisor to the Mitochondrial Disease Research Program at the Children's Hospital of Philadelphia, an internationally recognized hospital and research center devoted to children, from January 2019 to April 2020, and as President and Chief Executive Officer of MitoCUREia, Inc., an affiliated company, from July 2019 to July 2020. From 2005 to 2018, Dr. Cobuzzi served in various roles at Endo International PLC, a specialty branded and generic pharmaceuticals manufacturer, most recently serving as President of Endo Ventures Limited. Dr. Cobuzzi received his Bachelor of Arts in Biochemistry and Art History from Colby College and his Ph.D. in Molecular and Cellular Biochemistry from Loyola University Chicago. He served as a Post-doctoral Fellow in Experimental Therapeutics at Roswell Park Cancer Institute.

The Board believes Dr. Cobuzzi's experience and insight with drug development and business development and funding, both in the U.S. and abroad, as well as his experience and background as our Chief Executive Officer, provide him with the qualifications to serve as a director.

Mark T. Giles — Mr. Giles has served as a director since January 2016 and as a director of Diffusion LLC since 2008. Since July 2007, Mr. Giles has been the sole managing member of Panda Holdings, LLC, which engages in the investment and management of private capital. Since February 2015, Mr. Giles has been a general partner of Anchormark Holdings, LLC, which engages in the investment and management of private capital. Prior to joining Panda Holdings and Anchormark Holdings, Mr. Giles served as the Chief Executive Officer of Virginia National Bank from July 1998 until June 2007 and thereafter continued to serve as the non-executive Chairman until December 2011. Prior to joining Virginia National Bank, Mr. Giles also served as the president of two publicly traded bank holding companies and subsidiary banks in Texas and practiced law with the banking group of a Houston law firm. He chairs the board of Expedition Trust Company. Mr. Giles received a B.S. from the McIntire School of Commerce at the University of Virginia and a J.D. from the University of Virginia School of Law.

The Board believes Mr. Giles' perspective and experience as a director of Diffusion, as well as the depth and breadth of his business and legal experience, provide him with the qualifications to serve as a director.

Jane H. Hollingsworth – Ms. Hollingsworth has served as a director since September 2020. She currently serves as the founding Managing Partner of Militia Hill Ventures, an organization that creates, builds, and invests in life sciences companies, a role she has held since 2013. While at Militia Hill, Jane co-founded and currently serves as Executive Chair of Eliksa Therapeutics, a regenerative medicine company, co-founded and served as Executive Chair of Spirovant Sciences, a gene therapy company sold to Sumitomo Dainippon Pharma, and served as Executive Chair and CEO of Immunome Inc., a cancer immunotherapy company. Prior to founding Militia Hill, Ms. Hollingsworth co-founded and served as Chief Executive Officer of NuPathe, Inc., a neuroscience focused biopharmaceutical company. She also co-founded and served as EVP of Auxilium Pharmaceuticals, a urology and rare disease focused biopharmaceutical company. Ms. Hollingsworth also currently serves on the boards of the life science companies Afimmune Ltd. and Ribonova, and various industry and community organizations, including the University City Science Center, the Kimmel Center for the Performing Arts and Breatcancer.Org. Ms. Hollingsworth received her B.A. from Gettysburg College and her J.D. from Villanova University.

The Board believes Ms. Hollingsworth's industry perspective and experience, including as chief executive officer and director of a publicly-traded biopharmaceutical company, as well as her depth of her other operating and senior management experience in our industry and educational background, provide her with the qualifications to serve as a director.

Diana Lanchoney, M.D. – Dr. Lanchoney has served as a director since June 2021. Since 2014, Dr. Lanchoney has served as a Vice President of CSL Behring, Inc., a global biopharmaceutical company manufacturing plasma-derived and recombinant therapeutic products, since October 2021 as Vice President, R&D Strategy Implementation, from January 2018 to October 2021 as Vice President, Clinical Pharmacology and Translational Development and prior to that as Vice President, R&D Project Management, from October 2014 to December 2017. Prior to joining CSL, Dr. Lanchoney served in positions of increasing responsibility with Merck & Co., a global pharmaceutical company, most recently as Associate Vice President, Corporate Strategy. Dr. Lanchoney received her B.A. in Economics and German Studies from Tufts University and her M.D. from the University of Pennsylvania.

The Board believes Dr. Lanchoney's professional and academic background and experience provide her with the qualifications to serve as a director, including the depth and breadth of her experience with clinical development, corporate strategy, and pharmaceutical industry partnering.

Alan Levin — Mr. Levin has served as a director since January 2016 and as a director of Diffusion LLC since June 2015. He previously served as Executive Vice President and Chief Financial Officer of Endo Health Solutions Inc., a global specialty healthcare company, from June 2009 until his retirement in September 2013. Prior to joining Endo, Mr. Levin worked with Texas Pacific Group, a leading private equity firm, and one of their start-up investments. Before that, he was Senior Vice President & Chief Financial Officer of Pfizer, Inc. where he worked for 20 years in a variety of executive positions of increasing responsibility, including Treasurer and Senior Vice President of Finance & Strategic Management for the company's research and development organization. Mr. Levin received a bachelor's degree from Princeton University and a master's degree from New York University's Stern School of Business. Mr. Levin is a certified public accountant. Mr. Levin currently serves as a member of the board of directors of Biocryst Pharmaceuticals, Inc., a Nasdaq-traded biopharmaceuticals company. He is also a member of the Advisory Board of Auven Therapeutics, a private equity fund; and the Critical Path Institute, a nonprofit collaboration between the Food and Drug Administration and pharmaceutical industry participants focused on streamlining and accelerating the development and regulatory pathways for innovative medicines. From December 2013 to July 2019, he was a member of the board of directors of Aceto Corporation, a Nasdaq-traded company specialized in generics and pharmaceutical intermediate products.

The Board believes that the combination of Mr. Levin's perspective and experience as a director of Diffusion; his experience in financial reporting, treasury and corporate finance (including his prior positions as chief financial officer of Endo and Pfizer, Inc.); and his executive-level experience in the pharmaceutical industry all provide him with the qualifications and skills to serve as a director.

Overview of Non-Employee Director Compensation Program

As described in more detail under the heading "Corporate Governance—Compensation Committee—Responsibilities," the Board has delegated to the Compensation Committee the responsibility, among other things, to establish and lead a process for the determination of compensation payable to our non-employee directors. The Compensation Committee makes recommendations regarding compensation payable to our non-employee directors to the entire Board, which then makes final decisions regarding such compensation. Dr. Cobuzzi, our Chief Executive Officer, is not compensated separately for serving on the Board while also serving as an employee.

As further described below, the principal elements of our non-employee director compensation program have historically included cash compensation in the form of annual cash retainers and long-term equity-based incentive compensation, in the form of stock options and restricted stock units.

Cash Compensation

The cash compensation paid to our non-employee members of the Board consists of the following cash retainers:

Description	Annual Cash Retainer
Board Member	$ 40,000
Chairman of the Board	$ 25,000
Audit Committee Chair	$ 15,000
Compensation Committee Chair	$ 10,000
Nominating and Corporate Governance Committee Chair	$ 8,000
Audit Committee Member (other than Chair)	$ 7,500
Compensation Committee Member (other than Chair)	$ 5,000
Nominating and Corporate Governance Committee Member (other than Chair)	$ 4,000

The annual cash retainers are paid in regular installments and otherwise in accordance with the Company's standard payroll practices. The Compensation Committee has also reserved the right to make a portion of such payments in the form of equity rather than cash under certain conditions. During the fiscal year 2022, all retainers were paid in cash.

Long-Term Equity-Based Incentive Compensation

In addition to cash compensation, our non-employee directors have historically received long-term equity-based incentive compensation in the form of options to purchase shares of our common stock and restricted stock units. Upon a non-employee director's initial appointment to the Board, he or she shall receive a stock option award to purchase a number of shares of common stock equal to 0.114% of our shares of common stock outstanding on the grant date, vesting in 18 equal monthly installments following his or her appointment to the Board. In addition, upon appointment he or she also receives a restricted stock unit award for an equivalent number of shares, vesting in six tri-monthly installments commencing on the 18-month anniversary of his or her appointment to the Board. Directors appointed prior to January 1, 2020 received the entirety of this initial appointment award in the form of an option.

In addition, each non-employee director historically received an annual stock option award to purchase a number of shares of common stock equal to 0.114% of our shares of common stock outstanding on the grant date, vesting in equal monthly installments over one year, unless otherwise provided by the Compensation Committee. In consideration of, among other things, uncertainties regarding with the Company's long-term focus pending the completion of the Board's strategic review process, the Compensation Committee made the determination that no equity-based compensation would be awarded to the Company's non-employee directors during 2022 (other than the continued vesting of awards granted prior to 2022).

All option awards granted to our non-employee directors have a ten-year term and an exercise price equal to the fair market value of our common stock on the grant date.

Director Compensation Table for 2022

The table below provides summary information concerning the compensation of each individual who served as a non-employee director of the Company during the year ended December 31, 2022:

Name	Fees Earned or Paid in Cash	Stock Awards	Option Awards	All Other Compensation	Total
Robert Adams	$ 54,000	$ -	$ -	$ -	$ 54,000
Robert J. Cobuzzi, Jr., Ph.D. (1)	$ -	$ -	$ -	$ 691,787	$ 691,787
Eric Francois (2)	$ 50,481	$ -	$ -	$ -	$ 50,481
Mark T. Giles	$ 55,500	$ -	$ -	$ -	$ 55,500
Jane H. Hollingsworth	$ 77,500	$ -	$ -	$ -	$ 77,500
Diana Lanchoney	$ 49,000	$ -	$ -	$ -	$ 49,000
Alan Levin	$ 59,000	$ -	$ -	$ -	$ 59,000

1) Reflects compensation for Dr. Cobuzzi's service as our President and Chief Executive Officer. See "*Item 11. Executive Compensation -- Summary Compensation Table*" for additional information. Dr. Cobuzzi does not receive any additional compensation for his service as a director.

2) Mr. Francois resigned from the Board and all Board committees of which he was a member effective December 16, 2022.

EXECUTIVE OFFICERS

Information About Our Executive Officers

The table below sets forth, as of March 15, 2023, certain information concerning our current executive officers. Biographical information for Dr. Cobuzzi is included above under the heading, "Directors — Information About Our Directors," and incorporated herein by reference.

Name	Age	Position with Diffusion
Robert J. Cobuzzi, Jr., Ph.D.	58	President and Chief Executive Officer
William K. Hornung	54	Chief Financial Officer
William R. Elder	40	General Counsel & Corporate Secretary

In addition, the paragraphs below provide further information about each current director, including all positions he or she holds, his or her principal occupation and business experience for the past five years, and the names of other publicly held companies of which he or she currently serves as a director or served as a director during the past five years.

William K. Hornung – Mr. Hornung serves as our Chief Financial Officer, a position he has held since September 2018. Prior to his appointment as Chief Financial Officer, Mr. Hornung served as the Chief Business Officer at Diffusion from July 2017 through September 2018. Previously, Mr. Hornung served as Chief Financial Officer of Contravir Pharmaceuticals from June 2014 to November 2015 and helped the company up-list to Nasdaq and raise nearly $30 million. Prior to Contravir, from 2002 through 2014 Mr. Hornung held positions of increasing responsibility with PTC Therapeutics, most recently serving as Vice President of Finance from April 2012 to March 2014. While at PTC Therapeutics, he oversaw the initial public offering process and raised more than $1 billion. From 1998 through 2002, Mr. Hornung was with Elan Pharmaceuticals (formerly The Liposome Company) in various financial roles. At Liposome and Elan he was responsible for strategic planning and operations of the company's UK-based European headquarters. Earlier in his career, Mr. Hornung worked for a clinical research organization where he was responsible for project management and nearly all financial aspects of the company. Mr. Hornung holds a Bachelor of Science in Accounting from the William Paterson State University of New Jersey.

William R. Elder – Mr. Elder has served as our General Counsel & Corporate Secretary since September 2020. Prior to joining Diffusion, Mr. Elder principally served as president and chief executive officer of BillyVonElds, LLC, a season-long and daily fantasy sports company, where he managed all corporate, legal, and operational aspects of the business from April 2019 to September 2020. From July 2020 to September 2020, Mr. Elder also served as a part-time consultant to Diffusion. From 2011 to February 2019, Mr. Elder served as a corporate and securities associate for Dechert LLP, an international law firm, where Mr. Elder's practice focused primarily on counseling public companies on securities laws and regulatory requirements, corporate governance matters, and financial transactions in the equity and debt markets. He received his J.D. from the University of Pennsylvania Law School, an M.S. in finance from Villanova University, and a B.A. in economics from Tufts University.

ITEM 11. EXECUTIVE COMPENSATION

Summary Compensation Table

The table below provides summary compensation information concerning compensation awarded for service during the years ended December 31, 2022 and December 31, 2021 to the individuals that served as our named executive officers during the year ended December 31, 2022:

Name and Principal Position	Year	Salary (1)	Bonus Compensation (2)	Stock Awards	Option Awards (3)	All Other Compensation (4)	Total
Robert J. Cobuzzi, Jr., Ph.D.	2022	$ 450,000	$ 202,500	$ --	$ --	$ 39,287	$ 691,787
Chief Executive Officer	2021	$ 410,000	$ 164,000	$ --	$ 170,735	$ 38,617	$ 783,352
William K. Hornung	2022	$ 339,551	$ 90,915	$ --	$ --	$ 29,660	$ 460,126
Chief Financial Officer	2021	$ 324,929	$ 96,667	$ --	$ 84,838	$ 29,084	$ 535,518
William R. Elder	2022	$ 292,782	$ 115,283	$ --	$ --	$ 5,858	$ 413,923
General Counsel	2021	$ 256,250	$ 76,234	$ --	$ 66,246	$ 5,877	$ 404,607
Christopher D. Galloway, M.D. (5)	2022	$ 391,875	$ 126,968	$ --	$ --	$ 37,374	$ 556,217
Former Chief Medical Officer	2021	$ 375,000	$ 127,500	$ --	$ 86,393	$ 37,092	$ 625,985

1. Represents cash portion of base salary.

2. Represents the annual cash incentive bonuses for service during the applicable year by our named executive officers.

3. The amounts shown in this column reflect the grant date fair value of option awards granted for service during the applicable year, calculated in accordance with the provisions of ASC Topic 718 and determined without regard to forfeitures. Amounts shown for 2021 include the full grant date fair value of (i) time-based awards granted in January 2022 and (ii) milestone-based, performance awards granted in March 2021. Pursuant to the terms of the award agreements for the performance awards, two-thirds of the underlying shares originally granted were automatically forfeited due to the first patient in the ILD-DLCO Trial not being dosed on or before September 30, 2021. The Company subsequently announced dosing of the first patients in the ILD-DLCO Trial on December 16, 2021.

4. The amounts reported in this column for 2021 represent (w) with respect to Dr. Cobuzzi, (i) $11,600 in 401(k) Plan matching contributions by the Company and (iii) $27,017 in Company-paid health insurance premiums, (x) with respect to Mr. Hornung, (i) $11,600 in 401(k) Plan matching contributions by the Company and (ii) $17,484 in Company-paid health insurance premiums, (y) with respect to Dr. Galloway, (i) $11,600 in 401(k) Plan matching contributions by the Company and (ii) $25,492 in Company-paid health insurance premiums, and (z) with respect to Mr. Elder, $5,877 in Company-paid health insurance premiums. The amounts reported in this column for 2022 represent (w) with respect to Dr. Cobuzzi, (i) $11,600 in 401(k) Plan matching contributions by the Company and (ii) $39,287 in Company-paid health insurance premiums, (x) with respect to Mr. Hornung, (i) $11,600 in 401(k) Plan matching contributions by the Company and (ii) $29,660 in Company-paid health insurance premiums, (y) with respect to Dr. Galloway, (i) $11,600 in 401(k) Plan matching contributions by the Company and (ii) $37,374 in Company-paid health insurance premiums, and (z) with respect to Mr. Elder, $5,858 in Company-paid health insurance premiums.

5. As part of our reduction in force announced on February 16, 2023, Dr. Galloway departed Diffusion effective March 1, 2023 and no longer serves as our Chief Medical Officer. In accordance with the terms of his employment agreement as described in the 2021 Annual Report and his separation agreement filed as Exhibit 10.14 to this Annual Report and described in our Current Report on Form 8-K filed with the SEC on February 16, 2023, Dr. Galloway received separation benefits in connection with his departure, including a lump-sum payment of nine months (75%) of his current annual base salary and a pro-rated annual cash bonus for the current calendar year based on the number of days served as Chief Medical Officer during 2023.

Employment Agreements

Robert J. Cobuzzi, Jr., Ph.D., President & Chief Executive Officer

Effective September 8, 2020, we entered into an employment agreement with Dr. Cobuzzi pursuant to which he serves as our President & Chief Executive Officer. The employment agreement has an indefinite term. Dr. Cobuzzi is currently entitled to an initial annual base salary of $410,000, subject to increase at the discretion of the Board. Dr. Cobuzzi has the opportunity to earn a target annual bonus of 50 percent of his base salary. The Board may, in its discretion, pay a portion of Dr. Cobuzzi' annual salary and annual bonus in the form of equity or equity-based compensation, provided that commencing with the year following the year in which a "change of control" (as defined in the employment agreement) occurs, Dr. Cobuzzi's entire base salary and annual bonus will be paid in cash. For 2022, Dr. Cobuzzi's entire pro-rated base salary was paid in cash. The employment agreement contains certain severance and change of control provisions as described in more detail under the heading "—Post-Termination Severance and Change in Control Arrangements." The employment agreement also contains certain non-competition and non-solicitation provisions (each applicable during employment and for 24 months thereafter), as well as confidentiality and non-disparagement provisions (each applicable during employment and at all times thereafter).

William K. Hornung, Chief Financial Officer

Effective September 21, 2018, we entered into an amended and restated employment agreement with Mr. Hornung pursuant to which he serves as our Chief Financial Officer. The employment agreement has an indefinite term. Mr. Hornung was entitled to an annual base salary of $298,100 during 2020, subject to increase at the discretion of the Board. Mr. Hornung has the opportunity to earn a target annual bonus of 35 percent of his base salary. The Board may, in its discretion, pay a portion of Mr. Hornung's annual salary and annual bonus in the form of equity or equity-based compensation, provided that commencing with the year following the year in which a "change of control" (as defined in the employment agreement) occurs, Mr. Hornung's entire base salary and annual bonus will be paid in cash. For 2022, Mr. Hornung's entire base salary was paid in cash. The employment agreement contains certain severance and change of control provisions as described in more detail under the heading "—Post-Termination Severance and Change in Control Arrangements." The employment agreement also contains certain non-competition and non-solicitation provisions (each applicable during employment and for 18 months thereafter), as well as confidentiality and non-disparagement provisions (each applicable during employment and at all times thereafter).

William R. Elder, General Counsel & Corporate Secretary

Effective September 23, 2020, we entered into an employment agreement with Mr. Elder pursuant to which he serves as our General Counsel & Corporate Secretary. The employment agreement has an indefinite term. Mr. Elder is entitled to an initial annual base salary of $250,000, subject to increase at the discretion of the Board. Mr. Elder has the opportunity to earn a target annual bonus of 30 percent of his base salary. The Board may, in its discretion, pay a portion of Mr. Elder's annual salary and annual bonus in the form of equity or equity-based compensation, provided that commencing with the year following the year in which a "change of control" (as defined in the employment agreement) occurs, Mr. Elder's entire base salary and annual bonus will be paid in cash. For 2022, Mr. Elder's entire pro-rated base salary was paid in cash. The employment agreement contains certain severance and change of control provisions as described in more detail under the heading "—Post-Termination Severance and Change in Control Arrangements." The employment agreement also contains certain non-competition and non-solicitation provisions (each applicable during employment and for 24 months thereafter), as well as confidentiality and non-disparagement provisions (each applicable during employment and at all times thereafter).

Long-Term Equity Incentive Compensation and Other Compensatory Arrangements

The Compensation Committee administers the 2015 Equity Plan in which our named executive officers participate, the bonus payments made to our named executive officers provided for in the employment agreements described under the heading "—Employment Agreements," and any other compensation-related matters as they otherwise determine in their discretion.

In the first quarter of 2021, the Compensation Committee granted 50% of the annual long-term equity incentive awards granted to our named executive officers at the outset of the year in the form of performance-based options the vesting of which was dependent on the achievement of specified performance metrics during calendar year 2021. The remaining 50 percent were granted in the form of option awards subject to time-based vesting in accordance with the Company's past practice.

In the first quarter of 2022, the Compensation Committee returned to the Company's historic practice of granting all such awards as options subject to time-based vesting.

In consideration of, among other things, uncertainties regarding with the Company's long-term focus pending the completion of the Board's strategic review process, the Compensation Committee made the determination that no equity-based compensation would be awarded to the Company's named executive officers or other employees in the first quarter of 2023 (other than the continued vesting of previously granted awards).

2022 Bonus Compensation

Executive bonuses are determined by the Compensation Committee. The Compensation Committee determines whether bonuses are earned and the amounts of the bonus payout by considering a number of factors, the principal factor being based upon the performance goals developed by the Compensation Committee. Other important factors include clinical trial progress, business development activities, status of public filings, capital raising transactions, and stock price performance.

Outstanding Equity Awards at Fiscal Year End

Option Awards

The table below provides information regarding unexercised stock option awards held by each of our named executive officers that remained outstanding as of December 31, 2022. Unless otherwise indicated, each grant was awarded under our 2015 Equity Plan.

Name	Award Type	Grant Date	Shares Underlying Unexercised Options Exercisable	Shares Underlying Unexercised Options Unexercisable	Exercise Price	Expiration Date
Robert J. Cobuzzi, Jr., Ph.D.	NQO	1/7/2020	2,372	—	$ 25.50	1/7/2030
	NQO	6/17/2020	1,226	—	$ 50.00	6/17/2030
	NQO	9/8/2020	7,128	2,372	$ 39.50	9/8/2030
	NQO	3/1/2021	660	414	$ 55.50	3/1/2031
	NQO**	3/1/2021	719	355	$ 55.50	3/1/2031
	NQO	1/27/2022	5,100	10,187	$ 12.00	1/7/2023
William K. Hornung	NQO	1/2/2018	120	—	$ 885.00	1/2/2028
	NQO	1/2/2019	326	—	$ 105.00	1/2/2029
	NQO	1/2/2020	1,052	—	$ 23.00	1/2/2030
	NQO	3/1/2021	1,503	952	$ 55.50	3/1/2031
	NQO**	3/1/2021	358	175	$ 55.50	3/1/2031
	NQO	1/27/2022	2,040	4,074	$ 12.00	1/27/2023
William R. Elder	NQO*	9/22/2020	1,053	347	$ 41.00	9/22/2030
	NQO	3/1/2021	1,078	675	$ 55.50	3/1/2031
	NQO**	3/1/2021	283	133	$ 55.50	3/1/2031
	NQO	1/27/2022	2,040	4,074	$ 12.00	1/27/2023

* - Non-plan based equity award grant made as an inducement to the individual's acceptance of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).

** - Pursuant to the terms of the corresponding award agreements, two-thirds of the underlying shares originally granted were automatically forfeited on October 1, 2021 due to non-achievement of certain specified performance metrics.

Restricted Stock Unit Awards

The table below provides information regarding restricted stock unit awards held by each of our named executive officers that remained outstanding as of December 31, 2022, if any. Each grant was awarded under our 2015 Equity Plan.

Name	Award Type	Grant Date	Number of Shares That Have Not Vested	Market Value of Shares That Have Not Vested*
Robert J. Cobuzzi, Jr., Ph.D.	RSU	1/7/2020	327	$ 1,655

* - Based on a price per share of $5.06, the closing price of our common stock on December 30, 2022, as reported by Nasdaq. The award was granted to Dr. Cobuzzi in connection with his appointment as a non-employee director in January 2020 and vested in six tri-monthly installments. The first such installment vested on October 31, 2021 and the final installment vested on January 31, 2023.

401(k) Retirement Plan

We maintain our 401(k) Plan pursuant to which all eligible employees are entitled to make pre-tax and after-tax contributions of their compensation. In addition, the Company makes discretionary matching contributions at a rate of 100% for contributions up to 3% of the participant's eligible compensation and 50% for any additional contributions up to 5% of the participant's eligible compensation. The matching contributions received by our named executive officers in 2022 and 2021 are reported in the "All Other Compensation" column of the Summary Compensation Table above.

Post-Termination Severance and Change in Control Arrangements

As described under the heading "—Employment Agreements," we have entered into employment agreements with each of Dr. Cobuzzi and Messrs. Hornung and Elder that provide for certain severance and change of control benefits, subject to the execution and non-revocation of a release of claims by the executive or his estate (as applicable).

Under Dr. Cobuzzi's employment agreement, if his employment is terminated by us other than for "cause," death or "disability," or by Dr. Cobuzzi for "good reason" (as such terms are defined in the employment agreement), Dr. Cobuzzi will be entitled to any unpaid bonus earned in the year prior to the termination, a pro-rata portion of the bonus earned during the year of termination, continuation of base salary for 12 months, plus 12 months of COBRA premium reimbursement, provided that if such termination occurs within 60 days before or within 24 months following a "change of control" (as defined in the employment agreement), then Dr. Cobuzzi will be entitled to receive the same severance benefits as described above, except that he will receive (a) a payment equal to two times the sum of his base salary and the higher of his target annual bonus opportunity and the bonus payment he received for the year immediately preceding the year in which the termination occurred instead of 12 months of base salary continuation, and (b) a payment equal to 36 times the monthly COBRA premium for him and his eligible dependents instead of 12 months of COBRA reimbursements (the payments in clauses (a) and (b) are paid in a lump sum in some cases and partly in a lump sum and partly in installments over 12 months in other cases). In addition, if Dr. Cobuzzi's employment is terminated by us without cause or by Dr. Cobuzzi for good reason, in either case, upon or within 24 months following a change of control, then Dr. Cobuzzi will be entitled to full vesting of all equity awards received by him from us (with any equity awards that are subject to the satisfaction of performance goals deemed earned at not less than target performance, and with any equity award that is in the form of a stock option or stock appreciation right to remain outstanding and exercisable for 24 months following the termination date (but in no event beyond the expiration date of the applicable option or stock appreciation right)).

Under the employment agreements for each of Messrs. Hornung and Elder (and, prior to his separation, Dr. Galloway), in the event that the executive's employment is terminated by us other than for "cause", death or "disability" or upon the executive's resignation for "good reason" (as such terms are defined in the applicable employment agreement), the applicable executive will be entitled to any unpaid bonus earned in the year prior to the termination, a pro-rata portion of the bonus earned during the year of termination, continuation of base salary for nine months, plus 12 months of COBRA premium reimbursement, provided that if such termination occurs within 60 days before or within 24 months following a "change of control" (as defined in the applicable employment agreement), then the executive will be entitled to receive the same severance benefits as described above, except that the executive will receive (a) a payment equal to 1.5 times the sum of the executive's base salary and the higher of the executive's target annual bonus opportunity and the bonus payment the executive received for the year immediately preceding the year in which the termination occurred instead of nine months of base salary continuation and (b) a payment equal to 18 times the monthly COBRA premium for the executive and any eligible dependents instead of 12 months of COBRA reimbursements (the payments in clauses (a) and (b) are paid in a lump sum in some cases and in installments over nine or 12 months in other cases). In addition, if the applicable executive's employment is terminated by the Company without cause or by the applicable executive for good reason, in either case, upon or within 24 months following a change of control, then the applicable executive will be entitled to full vesting of all equity awards received by the executive from us (with any equity awards that are subject to the satisfaction of performance goals deemed earned at not less than target performance, and with any equity award that is in the form of a stock option or stock appreciation right to remain outstanding and exercisable for 24 months following the termination date (but in no event beyond the expiration date of the applicable option or stock appreciation right)).

Under the employment agreements for each of our current named executive officers (and, prior to his separation, Dr. Galloway), in the event that the executive's employment is terminated due to his or her death or disability, the executive (or the executive's estate) will be entitled to any unpaid bonus earned in the year prior to the termination, a pro-rata portion of the bonus earned during the year of termination, 12 months of COBRA premium reimbursement and accelerated vesting of (a) all equity awards received in payment of base salary or an annual bonus and (b) with respect to any other equity award, the greater of the portion of the unvested equity award that would have become vested within 12 months after the termination date had no termination occurred and the portion of the unvested equity award that is subject to accelerated vesting (if any) upon such termination under the applicable equity plan or award agreement (with performance goals deemed earned at not less than target performance, and with any equity award that is in the form of a stock option or stock appreciation right to remain outstanding and exercisable for 12 months following the termination date or, if longer, such period as provided under the applicable equity plan or award agreement (but in no event beyond the expiration date of the applicable option or stock appreciation right)).

Further, under the terms of the stock option agreements with our named executive officers, upon a completion of a "change of control" (as defined in the 2015 Equity Plan), options held by our named executive officers will become immediately vested and remain exercisable through their expiration date regardless of whether the holder remains in the employment or service of the Company after the change of control. Alternatively, in connection with a change of control, the Compensation Committee may, in its sole discretion, cash out the options.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

Based on information available to us and filings with the SEC, the following table sets forth certain information regarding the beneficial ownership (as defined by Rule 13d-3 under the Exchange Act) of our outstanding common stock as of March 15, 2023 for (i) each person or group of affiliated persons known by us to be the beneficial owner of more than 5% of our common stock, if any, (ii) each of our current directors; (iii) each of our current named executive officers (as defined in Item 402(a)(3) of Regulation S-K under the Exchange Act); and (iv) all of our current directors and named executive officers as a group. As of March 15, 2023, to our knowledge, no beneficial owner owned 5% or more of the shares of common stock then outstanding.

Beneficial ownership and percentage ownership are determined in accordance with the rules of the SEC and include voting or investment power with respect to shares of stock. This information does not necessarily indicate beneficial ownership for any other purpose. Under these rules, shares of common stock issuable under restricted stock units, stock options or warrants that are exercisable or convertible within 60 days of March 15, 2023 are deemed outstanding for the purpose of computing the beneficial ownership percentage of the holder thereof, but are not deemed outstanding for the purpose of computing the beneficial ownership percentage of any other person. Ownership is based upon information provided by each respective director and officer and public documents filed with the SEC, including Forms 3 and 4, Schedules 13D and 13G and certain other documents, which information may not be accurate as of the Record Date.

Unless otherwise indicated and subject to applicable community property laws, to our knowledge, each stockholder named in the following table possesses sole voting and investment power over their shares of common stock, except for those jointly owned with that person's spouse. Unless otherwise indicated below, the address of each person listed on the table is c/o Diffusion Pharmaceuticals Inc., 300 East Main Street, Suite 201, Charlottesville, Virginia 22902.

Name and Address of Beneficial Owner	Shares of Common Stock Beneficially Owned (1)	Common Stock Beneficial Ownership Percentage (2)
Current Directors		
Robert Adams (3)	3,585	*
Robert J. Cobuzzi, Jr., Ph.D. (4)	21,817	1.1%
Mark T. Giles (5)	4,589	*
Jane H. Hollingsworth (6)	4,130	*
Diana Lanchoney, M.D. (7)	3,564	*
Alan Levin (8)	3,535	*
Current Named Executive Officers		
William R. Elder (9)	5,934	*
William K. Hornung (10)	6,411	*
All Current Directors, Director Nominees, and Named Executive Officers as a Group (eight persons) (11)	53,365	**2.6%**

* Indicates less than 1.0%

1. Includes shares of common stock held as of March 15, 2023 plus shares of common stock that may be acquired upon exercise of options, warrants and other rights exercisable within 60 days of the March 15, 2023.
2. Based on 2,039,878 shares of common stock issued and outstanding as of March 15, 2023. The percentage ownership and voting power for each person (or all directors and executive officers as a group) is calculated by assuming (i) the exercise or conversion of all options, RSUs and other convertible securities exercisable or convertible within 60 days of March 15, 2023 held by such person and (ii) the non-exercise and non-conversion of all outstanding options, RSUs and other convertible securities held by all other persons (including our other directors and executive officers).
3. Consists of (a) 34 shares held directly by Mr. Adams, (b) 12 shares held jointly with Mr. Adams' wife, (c) 25 shares held for the benefit of Mr. Adams in his 401(k) retirement account, and (d) 3,514 shares of common stock issuable upon the exercise of options exercisable within 60 days of March 15, 2023.
4. Consists of (a) 1,616 shares held directly by Dr. Cobuzzi and (b) 20,201 shares of common stock issuable upon the exercise of options exercisable within 60 days of March 15, 2023.

5. Consists of (a) 5 shares held for the benefit of Mr. Giles in his individual retirement account, (b) 1,070 shares held by MTG Investment Holdings, LLC, and (c) 3,514 shares of common stock issuable upon the exercise of options exercisable within 60 days of March 15, 2023. Mr. Giles is the sole member of MTG Investment Holdings, LLC and may be deemed to be the beneficial owner of such securities. Mr. Giles disclaims beneficial ownership of such securities except to the extent of his pecuniary interest therein.
6. Consists of (a) 1,116 shares held directly by Ms. Hollingsworth, and (b) 3,014 shares of common stock issuable upon the exercise of options exercisable within 60 days of March 15, 2023.
7. Consists of (a) 3,332 shares of common stock issuable upon the exercise of options exercisable within 60 days of March 15, 2023 and (b) 232 shares of common stock issuable upon the vesting of RSUs expected to vest within 60 days of March 15, 2023.
8. Consists of (a) 33 shares held by Mr. Levin directly and (b) 3,502 shares of common stock issuable upon the exercise of options exercisable within 60 days of March 15, 2023.
9. Consists of (a) 400 shares held directly by Mr. Elder and (b) 5,534 shares of common stock issuable upon the exercise of options exercisable within 60 days of March 15, 2023.
10. Consists of 6,411 shares of common stock issuable upon the exercise of options exercisable within 60 days of March 15, 2023.
11. Includes (a) 49,022 shares of common stock issuable upon the exercise of options exercisable within 60 days of March 15, 2023 and (b) 232 shares of common stock issuable upon the vesting of RSUs expected to vest within 60 days of March 15, 2023.

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors and executive officers and all persons who beneficially own more than 10 percent of the outstanding shares of our common stock to file with the SEC initial reports of ownership and reports of changes in ownership of our common stock. Directors, executive officers and greater than 10 percent beneficial owners also are required to furnish us with copies of all Section 16(a) forms they file.

To our knowledge, based on a review of the copies of such reports and amendments to such reports furnished to us with respect to the year ended December 31, 2021, and based on written representations by our directors and executive officers, all required Section 16 reports under the Exchange Act, for our directors, executive officers and beneficial owners of greater than 10 percent of our common stock were filed on a timely basis during the year ended December 31, 2021, except for the following, each of which were not timely filed: a Form 3 relating to Ms. Raven Jaeger's appointment as Chief Regulatory Officer on May 18, 2022, filed on August 26, 2022; and a Form 4 relating to a June 7, 2022 option grant to Ms. Raven Jaeger in connection with such appointment, also filed on August 26, 2022.

Equity Compensation Plan Information

The following table summarizes our equity compensation plan information as of December 31, 2022:

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights		Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (1)
Equity compensation plans approved by security holders (2)	138,292	$	130.14(3)	24,953(4)
Equity compensation plans not approved by security holders (5)	5,400	$	42.11	0
Total	143,692	$	126.75(3)	24,953(4)

1. Excludes securities reflected under, “Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights.

2. Consists of options to purchase 134,640 shares of common stock and 3,652 restricted stock units, in each case, awarded pursuant to the 2015 Equity Plan.

3. Reflects the weighted-average exercise price of outstanding stock options and does not include restricted stock units.

4. The 2015 Equity Plan provides for increases to the number of shares reserved for issuance thereunder each January 1 equal to 4.0% of the total shares of the Company’s common stock outstanding as of the immediately preceding December 31, unless a lesser amount is stipulated by the Compensation Committee of the Company's board of directors. Accordingly, 81,582 shares were added to the reserve as of January 1, 2023.

5. Consists of options to purchase shares awarded as an inducement to an individual’s acceptance of employment with the Company in accordance with Nasdaq Listing Rule 5635(c)(4).

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

Certain Relationships and Related Party Transactions

Our Audit Committee is charged with the responsibility of reviewing and approving or ratifying all related person transactions in accordance with the Listing Rules of the Nasdaq Capital Market and other applicable law, rules and regulations and any related policies and procedures adopted by or on behalf of the Company and then in effect.

Since January 1, 2021, the following are the only transactions to which we have been a party in which (i) the amount involved in the transaction

exceeds $120,000 and (ii) any of our directors, nominees for director, former directors, executive officers, to our knowledge, beneficial owners of more than 5% of our capital stock, or any members of their immediate family or any entities affiliated with any of the foregoing persons had or will have a direct or indirect material interest: The Company's former Senior Director of Information Technologies, who is the son of the former Chairman of the Board/Chief Executive Officer of the Company, received total compensation for 2022 and 2021 of approximately $196,606 and $151,250, respectively.

No family relationships exist among any of our directors or executive officers.

Director Independence

The information required by Item 13 of Form 10-K with respect to director independence included above under the heading, "Item 10. Directors, Executive Officers and Corporate Governance — Corporate Governance," is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

Independent Registered Public Accounting Firm

The Audit Committee selected KPMG LLP as our independent registered public accounting firm for the fiscal year ended December 31, 2022. The Audit Committee's selection of KPMG LLP was ratified by our stockholders at our 2022 annual meeting of stockholders.

Independent Registered Public Accounting Firm's Fees

The table below presents fees billed to us for professional services rendered by KPMG LLP for the years ended December 31, 2022 and December 31, 2021.

	Aggregate Amount Billed	
	2022	2021
Audit Fees	$ 505,000	$ 365,000
Audit-Related Fees	$ —	$ —
Tax Fees	$ —	$ —
All Other Fees	$ —	$ —
Total	$ 505,000	$ 365,000

Pre-Approval Policies and Procedures

The Audit Committee has adopted procedures pursuant to which all audit, audit-related, and tax services and all permissible non-audit services provided by our independent registered public accounting firm must be pre-approved by the Audit Committee. All services rendered by KPMG during 2022 and 2021 were permissible under applicable laws and regulations and were approved in advance by the Audit Committee in accordance with the rules adopted by the SEC in order to implement requirements of SOX.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

1. Our financial statements are included in Part II, Item 8 of this Annual Report.

2. All financial statement schedules have been omitted from this Item 15 as the required information is not applicable, is not present in amounts sufficient to require submission of such schedules, or because the information required is included in our financial statements or the related notes included in Part II, Item 8 of this Annual Report.

3. The exhibits set forth in the following "Index to Exhibits" are filed with, furnished with, and/or incorporated by reference into this Annual Report, as set forth therein. A copy of any of such exhibit will be furnished at a reasonable cost, upon receipt from any person of a written request for any such exhibit. Such request should be sent to Diffusion Pharmaceuticals Inc., 300 East Main Street, Suite 201, Charlottesville, Virginia 22902, Attention: General Counsel.

INDEX TO EXHIBITS

Exhibit No.	Description	Method of Filing
3.1	Certificate of Incorporation of Diffusion Pharmaceuticals Inc., as amended	Filed herewith
3.2	Bylaws of Diffusion Pharmaceuticals Inc., as amended	Filed herewith
3.3	Certificate of Designation of Preferences, Rights, and Limitations of Series C Convertible Preferred Stock	Incorporated by reference to Exhibit 3.1 to the registrant's Current Report on Form 8-K filed on March 18, 2022
4.1	Form of 2018 Common Stock Warrant	Incorporated by reference to Exhibit 4.1 to the registrant's Current Report on Form 8-K filed on January 19, 2018
4.2	Form of 2018 Underwriter's Warrant	Incorporated by reference to Exhibit 4.2 to the registrant's Current Report on Form 8-K filed on January 22, 2018
4.3	Form of May 2019 Common Stock Warrant	Incorporated by reference to Exhibit 4.1 to the registrant's Current Report on Form 8-K filed on May 28, 2019
4.4	Form of May 2019 Placement Agent's Warrant	Incorporated by reference to Exhibit 4.2 to the registrant's Current Report on Form 8-K filed on May 28, 2019
4.5	Form of November 2019 Series I Common Stock Warrant	Incorporated by reference to Exhibit 4.1 to the registrant's Current Report on Form 8-K filed on November 13, 2019
4.6	Form of November 2019 Series II Common Stock Warrant	Incorporated by reference to Exhibit 4.2 to the registrant's Current Report on Form 8-K filed on November 13, 2019
4.7	Form of December 2019 Common Stock Warrant	Incorporated by reference to Exhibit 4.1 to the registrant's Current Report on Form 8-K filed on December 13, 2019
4.8	Form of December 2019 Placement Agent's Warrant	Incorporated by reference to Exhibit 4.2 to the registrant's Current Report on Form 8-K filed on December 13, 2019
4.9	Form of May 2020 Placement Agent's Warrant (In Respect of Exercise Transaction)	Incorporated by reference to Exhibit 4.2 to the registrant's Current Report on Form 8-K filed on May 8, 2020
4.10	Form of May 2020 Placement Agent's Warrant (In Respect of Offering Transaction)	Incorporated by reference to Exhibit 4.3 to the registrant's Current Report on Form 8-K filed on May 20, 2020
4.11	Form of February 2021 Underwriter's Warrant	Incorporated by reference to Exhibit 4.1 to the registrant's Current Report on Form 8-K filed on February 18, 2021
4.12	Description of Securities	Incorporated by reference to Exhibit 4.12 to the registrant's Annual Report on 10-K for the year ended December 31, 2019
10.1	Employment Agreement dated as of September 8, 2020 by and between Robert J. Cobuzzi, Jr., Ph.D. and Diffusion Pharmaceuticals Inc.*	Incorporated by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K filed on September 9, 2020
10.2	Amended and Restated Employment Agreement, dated as of September 21, 2018, by and between William Karl Hornung and Diffusion Pharmaceuticals Inc. *	Incorporated by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K filed September 27, 2018

10.3	Employment Agreement, dated as of October 19, 2020, by and between Christopher D. Galloway, M.D. and Diffusion Pharmaceuticals Inc. *	Incorporated by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K filed October 20, 2020
10.4	Employment Agreement, dated as of September 23, 2020, by and between William Elder and Diffusion Pharmaceuticals Inc. *	Incorporated by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K filed September 25, 2020
10.5	Employment Agreement, effective as of May 18, 2022, by and between Raven Jaeger and Diffusion Pharmaceuticals Inc.*	Incorporated by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K filed June 28, 2022
10.6	Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan*	Incorporated by reference to Appendix C to the registrants definitive proxy statement on Schedule 14A filed on June 10, 2016
10.7	Amendment No. 1 to Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan*	Incorporated by reference to Appendix B to the registrants definitive proxy statement on Schedule 14A filed on June 10, 2016
10.8	Form of Stock Option Award Agreement under 2015 Equity Incentive Plan*	Incorporated by reference to Exhibit 10.7 to the registrant's Annual Report on Form 10-K for the year ended December 31, 2021
10.9	Form of Director RSU Agreement under 2015 Equity Incentive Plan*	Incorporated by reference to Exhibit 10.8 to the registrant's Annual Report on Form 10-K for the year ended December 31, 2021
10.10	Form of Diffusion Pharmaceuticals LLC Stock Option Award Agreement*	Incorporated by reference to Exhibit 10.24 to the registrant's annual report on Form 10-K for the year ended December 31, 2015
10.11	Form of Indemnification Agreement between Diffusion Pharmaceuticals Inc. and each of its Directors and Officers*	Incorporated by reference to Exhibit 10.3 to the registrant's annual report on Form 10-K for the year ended December 31, 2015
10.12	Form of Subscription Agreement between Diffusion Pharmaceuticals Inc. and the investors named there, dated March 18, 2022	Incorporated by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K filed March 18, 2022
10.13	Settlement Agreement, dated as of December 15, 2022, by and among Diffusion Pharmaceuticals Inc, LifeSci Special Opportunities Master Fund Ltd., LifeSci Special Opportunities Partners L.P., LifeSci Special Opportunities Offshore Fund, Ltd., LifeSci Special Opportunities Partners GP, LLC, LifeSci Management Company LLC, Pirate Cove Capital Ltd. and David Dobkin.	Incorporated by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K filed December 16, 2022
10.14	Separation Agreement and General Release, effective as of March 8, 2023, by and between Diffusion Pharmaceuticals and Christopher D. Galloway, M.D.	Filed herewith
10.15	Separation Agreement and General Release, effective as of March 8, 2023, by and between Diffusion Pharmaceuticals and Raven Jaeger	Filed herewith
10.16	At-The-Market Sales Agreement, dated as of July 22, 2022, by and between Diffusion Pharmaceuticals Inc. and BTIG, LLC	Incorporated by reference to Exhibit 1.1 to the registrant's Current Report on Form 8-K filed on July 22, 2022
21.1	Subsidiaries of Diffusion Pharmaceuticals Inc.	Filed herewith
23.1	Consent of KPMG LLP, independent registered public accounting firm	Filed herewith
31.1	Certification of Chief Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 and SEC Rule 13a-14(a)	Filed herewith
31.2	Certification of Principal Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 and SEC Rule 13a-14(a)	Filed herewith
32.1	Certification of Chief Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	Filed herewith
101	The following materials from the registrant's annual report on Form 10-K for the year ended December 31, 2022, formatted in iXBRL (Inline Extensible Business Reporting Language): (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations and Comprehensive Loss, (iii) Consolidated Statements of Cash Flows, and (iv) Notes to Consolidated Financial Statements	Filed herewith
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and contained in Exhibit 101).	
*	Indicates a management contract or compensatory plan or arrangement.	

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Dated: March 24, 2023

DIFFUSION PHARMACEUTICALS INC.
By: /s/ Robert J. Cobuzzi, Jr., Ph.D.
Robert J. Cobuzzi, Jr., Ph.D.
President, Chief Executive Officer, and Director
(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Name and Signature	Title	Date
/s/ Robert J. Cobuzzi, Jr., Ph.D. Robert J. Cobuzzi, Jr., Ph.D.	President, Chief Executive Officer, and Director (Principal Executive Officer)	March 24, 2023
/s/ William K. Hornung William K. Hornung	Chief Financial Officer (Principal Financial and Accounting Officer)	March 24, 2023
/s/ Jane H. Hollingsworth Jane H. Hollingsworth	Chair of the Board	March 24, 2023
/s/ Robert Adams Robert Adams	Director	March 24, 2023
/s/ Mark T. Giles Mark T. Giles	Director	March 24, 2023
/s/ Diana Lanchoney Diana Lanchoney	Director	March 24, 2023
/s/ Alan Levin Alan Levin	Director	March 24, 2023

EXHIBIT 3.1

CERTIFICATE OF INCORPORATION
OF
DIFFUSION PHARMACEUTICALS INC.
(AS AMENDED)

ARTICLE I
NAME

The name of the corporation is Diffusion Pharmaceuticals Inc. (the "Corporation").

ARTICLE II
REGISTERED OFFICE AND AGENT

The address of the registered office of the Corporation in the State of Delaware is 615 South Dupont Hwy., in the City of Dover, Zip Code of 19901, County of Kent. The name of the registered agent of the Corporation at that address is National Corporate Research, Ltd.

ARTICLE III
PURPOSE

The purpose of the Corporation is to engage in any lawful act or activity for which a corporation may be organized under the General Corporation Law of the State of Delaware ("DGCL").

ARTICLE IV
CAPITAL STOCK

A. The total number of shares of common stock which the Corporation shall have authority to issue is 1,000,000,000, at a par value of $0.001 per share ("Common Stock"), and the total number of shares of preferred stock which the Corporation shall have authority to issue is 30,000,000, at a par value of $0.001 per share ("Preferred Stock").

1. Common Stock. All preferences, voting powers, relative, participating, optional or other special rights and privileges, and qualifications, limitations, or restrictions of the Common Stock are expressly made subject and subordinate to those that may be fixed with respect to any shares of the Preferred Stock. Except as otherwise required by law or this Certificate of Incorporation, each share of Common Stock shall entitle the holder thereof to one (1) vote, in person or by proxy, on each matter submitted to a vote of stockholders of the Corporation. Subject to the preferential rights of the Preferred Stock, the holders of shares of Common Stock shall be entitled to receive, when and if declared by the Board of Directors, out of the assets of the Corporation which are by law available therefor, dividends payable either in cash, in property or in shares of capital stock. In the event of any dissolution, liquidation or winding up of the affairs of the Corporation, after distribution in full of the preferential amounts, if any, to be distributed to the holders of shares of the Preferred Stock, holders of Common Stock shall be entitled, unless otherwise provided by law or this Certificate of Incorporation, to receive all of the remaining assets of the Corporation of whatever kind available for distribution to stockholders ratably in proportion to the number of shares of Common Stock held by them respectively.

2. Preferred Stock. The Preferred Stock may be issued from time to time in one or more series, as determined by the Board of Directors of the Corporation (the "Board of Directors"). The Board of Directors is expressly authorized to provide for the issue, in one or more series, of all or any of the remaining shares of Preferred Stock and, in the resolution or resolutions providing for such issue, to establish for each such series the number of its shares, the voting powers, full or limited, of the shares of such series, or that such shares shall have no voting powers, and the designations, preferences and relative, participating, optional or other special rights, if any, of the shares of such series, and any qualifications, limitations or restrictions thereof. The powers, preferences and relative, participating, optional and other special rights of each series of preferred stock and the qualifications, limitations or restrictions thereof, if any, may differ from those of any and all other series at any time outstanding. The Board of Directors is further expressly authorized to increase or decrease (but not below the number of shares of any such series then outstanding) the number of shares of any series, the number of which was fixed by it, subsequent to the issuance of shares of such series then outstanding, subject to the powers, preferences and rights, and the qualifications, limitations and restrictions thereof stated in this Certificate of Incorporation or the resolution of the Board of Directors originally fixing the number of shares of such series. If the number of shares of any series is so decreased, then the shares constituting such decrease shall resume the status which they had prior to the adoption of the resolution originally fixing the number of shares of such series.

Effective upon the effective time of the Certificate of Amendment of the Certificate of Incorporation filed on August 17, 2016 with the Secretary of State of the State of Delaware (the "Effective Time"), each ten (10) shares of Common Stock issued and outstanding immediately prior to the Effective Time shall, automatically and without the necessity for any further action, be changed, reclassified and combined into one (1) share of Common Stock (the "Reverse Stock Split"). No fractional shares shall be issued in connection with the Reverse Stock Split. Stockholders who otherwise would be entitled to receive fractional shares of Common Stock shall have that rounded up to one additional whole share. Each certificate that immediately prior to the Effective Time represented shares of Common Stock ("Old Certificates") shall thereafter represent that number of shares of Common Stock into which the shares of Common Stock represented by the Old Certificate shall have been combined, subject to the elimination of fractional shares as described above.

Effective upon the effective time of the Certificate of Amendment of the Certificate of Incorporation filed on December 13, 2018 with the Secretary of State of the State of Delaware (the "2018 Effective Time"), each fifteen (15) shares of Common Stock issued and outstanding immediately prior to the 2018 Effective Time shall, automatically and without the necessity of any further action, be changed, reclassified and combined into one (1) share of Common Stock (the "2018 Reverse Stock Split"). No fractional shares shall be issued in connection with the 2018 Reverse Stock Split. Stockholders who otherwise would be entitled to receive fractional shares of Common Stock shall have that rounded up to one additional whole share. Each certificate that immediately prior to the 2018 Effective Time represented shares of Common Stock ("2018 Old Certificates"), shall thereafter represent that number of shares of Common Stock into which the shares of Common Stock represented by the 2018 Old Certificate shall have been combined, subject to the elimination of fractional shares as described above.

Effective upon April 18, 2022 at 5:59 p.m. Eastern Time, the effective time of this Certificate of Amendment of the Certificate of Incorporation with the Secretary of State of the State of Delaware (the "Effective Time"), each fifty (50) shares of Common Stock issued and outstanding immediately prior to the Effective Time shall, automatically and without the necessity of any further action, be changed, reclassified and combined into one (1) share of Common Stock (the "Reverse Stock Split"). No fractional shares shall be issued in connection with the Reverse Stock Split. Stockholders who otherwise would be entitled to receive fractional shares of Common Stock shall be entitled to receive cash (without interest and subject to applicable withholding taxes) in lieu of such fractional shares in an amount equal to the product obtained by multiplying such fractional share of Common Stock by the inverse of the Reverse Stock Split ratio times the average closing price per share of Common Stock on the securities trading market on which the shares were traded for the five consecutive trading days immediately preceding the date on which the Effective Time occurs. Each certificate that immediately prior to the Effective Time represented shares of Common Stock ("Old Certificates"), shall thereafter represent that number of shares of Common Stock into which the shares of Common Stock represented by the Old Certificate shall have been combined, subject to the elimination of fractional shares as described above.

ARTICLE V
EXCULPATION AND INDEMNIFICATION

A. Limitation of Liability. A director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except to the extent such exemption from liability or limitation thereof is not permitted under the DGCL as it presently exists or may hereafter be amended. Any amendment, modification or repeal of the foregoing sentence shall not adversely affect any right arising prior to the time of such amendment, modification or repeal.

B. Right of Indemnification. The Corporation shall indemnify and hold harmless, to the fullest extent permitted by applicable law as it presently exists or may hereafter be amended, any person (a "Covered Person") who was or is made or is threatened to be made a party or is otherwise involved in any action, suit or proceeding, whether civil, criminal, administrative or investigative (a "Proceeding"), by reason of the fact that he or she, or a person for whom he or she is the legal representative, is or was a director, officer, employee or agent of the Corporation or, while a director, officer, employee or agent of the Corporation, is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation or of a partnership, joint venture, trust, enterprise or nonprofit entity, including service with respect to employee benefit plans, against all liability and loss suffered and expenses (including attorneys' fees) reasonably incurred by such Covered Person. Notwithstanding the preceding sentence, except as otherwise provided in section D of this Article V, the Corporation shall not be required to indemnify a Covered Person in connection with a Proceeding (or part thereof) commenced by such Covered Person unless the commencement of such Proceeding (or part thereof) by the Covered Person was authorized in the specific case by the Board of Directors.

C. Prepayment of Expenses. The Corporation shall to the fullest extent not prohibited by applicable law pay the expenses (including attorneys' fees) incurred by a Covered Person in defending any Proceeding in advance of its final disposition, provided, however, that, to the extent required by law, such payment of expenses in advance of the final disposition of the Proceeding shall be made only upon receipt of an undertaking by the Covered Person to repay all amounts advanced if it should be ultimately determined that the Covered Person is not entitled to be indemnified under this Article V or otherwise.

D. Claims. If a claim for indemnification (following the final disposition of the Proceeding with respect to which indemnification is sought, including any settlement of such Proceeding) or advancement of expenses under this Article V is not paid in full within thirty (30) days after a written claim therefor by the Covered Person has been received by the Corporation, the Covered Person may file suit to recover the unpaid amount of such claim and, if successful in whole or in part, shall be entitled to be paid the expense of prosecuting such claim to the fullest extent permitted by applicable law. In any such action the Corporation shall have the burden of proving that the Covered Person is not entitled to the requested indemnification or advancement of expenses under this Article V and applicable law.

E. Non-Exclusivity of Rights. The rights conferred on any Covered Person by this Article V shall not be exclusive of any other rights which such Covered Person may have or hereafter acquire under any statute, any other provision of this Certificate of Incorporation, the Bylaws of the Corporation, or any agreement, vote of stockholders or disinterested directors or otherwise.

F. Insurance. The Corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation or of a partnership, joint venture, trust, enterprise or nonprofit entity, including service with respect to employee benefit plans, against any liability asserted against such person and incurred by such person in any such capacity, or arising out of such person's status as such, whether or not the Corporation would have the power to indemnify such person against such liability under this Article V, the DGCL or otherwise.

G. Amendment or Repeal. Any right to indemnification or to advancement of expenses of any Covered Person arising hereunder shall not be eliminated or impaired by an amendment to or repeal of this Article V after the occurrence of the act or omission that is the subject of the civil, criminal, administrative or investigative action, suit or proceeding for which indemnification or advancement of expenses is sought.

H. Other Indemnification and Advancement of Expenses. This Article V shall not limit the right of the Corporation, to the extent and in the manner permitted by law, to indemnify and to advance expenses to persons other than Covered Persons when and as authorized by appropriate corporate action.

ARTICLE VI
MANAGEMENT

For the management of the business and for the conduct of the affairs of the Corporation, and in further definition, limitation and regulation of the powers of the Corporation, of its directors and of its stockholders or any class thereof, as the case may be, it is further provided that:

A. The management of the business and the conduct of the affairs of the Corporation shall be vested in the Board of Directors. The Board of Directors shall fix the number of directors that constitute the whole Board of Directors in the manner provided in the Bylaws of the Corporation, subject to any restrictions that may be set forth in this Certificate of Incorporation.

B. In furtherance and not in limitation of the powers conferred by statute, the Board of Directors is expressly empowered to adopt, amend or repeal the Bylaws of the Corporation or adopt new Bylaws of the Corporation without any action on the part of the stockholders. Any adoption, amendment or repeal of the Bylaws of the Corporation by the Board of Directors shall require the approval of a majority of the directors then in office. The stockholders of the Corporation shall also have the power to adopt, amend or repeal the Bylaws of the Corporation; provided, however, that, in addition to any vote of the holders of any class or series of stock of the Corporation required by law or by this Certificate of Incorporation, the affirmative vote of the holders of at least sixty-six and two-thirds percent (66-2/3%) of the voting power of all of the then-outstanding shares of the capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required to adopt, amend or repeal any provision of the Bylaws of the Corporation.

C. The Corporation reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by the DGCL, and all rights conferred upon stockholders herein are granted subject to this reservation.

ARTICLE VII
STOCKHOLDER MEETINGS

Meetings of stockholders may be held within or without the State of Delaware, as the Bylaws of the Corporation may provide. Elections of directors need not be by written ballot unless and except to the extent that the Bylaws of the Corporation so provide. Any action required to or which may be taken at a meeting of stockholders of the corporation may be taken without a meeting if authorized by a writing signed by all of the holders of shares who would be entitled to vote upon the action at a meeting for such purpose.

ARTICLE VIII
INCORPORATOR

The name and mailing address of the incorporator of the Corporation are as follows:

Amy E. Culbert
Oppenheimer Wolff & Donnelly LLP
Campbell Mithun Tower, Suite 2000
222 South Ninth Street
Minneapolis, MN 55402

ARTICLE IX
EFFECTIVE TIME

This Certificate of Incorporation shall be effective as of 5:00 p.m. Eastern Time on June 18, 2015.

The undersigned, being the incorporator named above, for the purpose of forming a corporation pursuant to the DGCL, does hereby make this Certificate of Incorporation, hereby acknowledging, declaring and certifying that the foregoing Certificate of Incorporation is the undersigned's act and deed and the facts herein stated are true, and accordingly has hereunto set the undersigned's hand this 17th day of June, 2015.

INCORPORATOR:

By: /s/ Amy E. Culbert
Amy E. Culbert

Amended: January 8, 2016; August 17, 2016; January 23, 2017; March 13, 2017; August 13, 2018; December 13, 2018; April 18, 2022.

EXHIBIT 3.2

BYLAWS
OF
DIFFUSION PHARMACEUTICALS INC.
(AS AMENDED)

ARTICLE I
OFFICES

1.1 Registered Office. The address of the registered office of Diffusion Pharmaceuticals Inc. (the "Corporation") in the State of Delaware shall be 615 South Dupont Hwy., Dover, Kent County, Delaware 19901. The name of the registered agent of the Corporation at that address is National Corporate Research, Ltd.

1.2 Other Offices. The Corporation may have other offices, both within and without the State of Delaware, as the Board of Directors of the Corporation (the "Board of Directors"), from time to time shall determine or the business of the Corporation may require.

ARTICLE II
STOCKHOLDERS' MEETINGS

2.1 Place of Meetings. Meetings of the stockholders of the Corporation may be held at any place, either within or without the State of Delaware, as may be determined from time to time by the Board of Directors. The Board of Directors may, in its sole discretion, determine that a meeting of stockholders hall not be held at any place, but may instead be held solely by means of remote communication as authorized by Section 211(a)(2) of the General Corporation Law of the State of Delaware (as amended from time to time, the "DGCL"). In the absence of any such designation or determination, meetings of the stockholders of the Corporation shall be held at the Corporation's principal executive office.

2.2 Annual Meetings.

(a) The annual meeting of the stockholders of the Corporation, for the purpose of election of directors and for such other business as may lawfully come before it, shall be held on such date and at such time as may be designated from time to time by the Board of Directors. Nominations of persons for election to the Board of Directors of the Corporation and the proposal of business to be considered by the stockholders may be made at an annual meeting of stockholders: (i) pursuant to the Corporation's notice with respect to such meeting; (ii) by or at the direction of the Board of Directors; or (iii) by any stockholder of the Corporation who was a stockholder of record at the time of giving the stockholder's notice provided for in the following subsection (b), who is entitled to vote at the meeting and who complied with the notice procedures set forth below in this Section 2.2.

(b) At an annual meeting of the stockholders, only such business shall be conducted as shall have been properly brought before the meeting. For nominations or other business to be properly brought before an annual meeting by a stockholder pursuant to Section 2.2(a)(iii) above, (i) the stockholder must have given timely notice thereof in writing to the Secretary of the Corporation, (ii) such other business must be a proper matter for stockholder action under the DGCL, and (iii) if the stockholder, or the beneficial owner on whose behalf any such proposal or nomination is made, has provided the Corporation with a Solicitation Notice (as defined below in Section 2.2(d)(iii)(C)(2)), such stockholder or beneficial owner must, in the case of a proposal, have delivered a proxy statement and form of proxy to holders of at least the percentage of the Corporation's voting shares required under applicable law or the Corporation's Certificate of Incorporation (as the same may be amended and/or restated from time to time, the "Certificate of Incorporation") or these Bylaws (as the same may be amended and/or restated from time to time, the "Bylaws") to carry any such proposal, or, in the case of a nomination or nominations, have delivered a proxy statement and form of proxy to holders of a percentage of the Corporation's voting shares reasonably believed by such stockholder or beneficial owner to be sufficient to elect the nominee or nominees proposed to be nominated by such stockholder, and must, in either case, have included in such materials the Solicitation Notice.

(c) To be timely, a stockholder's notice shall be delivered to the Secretary at the principal executive offices of the Corporation not later than the close of business on the ninetieth (90th) day, nor earlier than the close of business on the one hundred twentieth (120th) day, prior to the first anniversary of the date of the proxy statement delivered to stockholders in connection with the preceding year's annual meeting; provided, however, that in the event (i) the date of the annual meeting is advanced more than thirty (30) days prior to or delayed by more than thirty (30) days after the anniversary of the preceding year's annual meeting, (ii) no proxy statement was delivered to stockholders in connection with the preceding year's annual meeting, or (iii) the Corporation did not hold an annual meeting in the preceding year, notice by the stockholder to be timely must be so delivered not earlier than the close of business on the ninetieth (90th) day prior to such annual meeting and not later than the close of business on the later of the sixtieth (60th) day prior to such annual meeting or the tenth (10th) day following the day on which public announcement of the date of such meeting is first made. In no event shall the public announcement of an adjournment of an annual meeting commence a new time period for the giving of a stockholder's notice as described above.

(d) Such stockholder's notice shall set forth:

(i) as to each person whom the stockholder proposes to nominate for election or reelection as a director, all information relating to such person that is required to be disclosed in solicitations of proxies for election of directors, or is otherwise required, in each case pursuant to Regulation 14A under the Securities Exchange Act of 1934, as amended (as amended from time to time, the "1934 Act") (including such person's written consent to being named in the proxy statement as a nominee and to serving as a director if elected);

(ii) as to any other business that the stockholder proposes to bring before the meeting, a brief description of the business desired to be brought before the meeting, the reasons for conducting such business at the meeting and any material interest in such business of such stockholder and the beneficial owner, if any, on whose behalf the proposal is made; and

(iii) as to the stockholder giving the notice and the beneficial owner, if any, on whose behalf the nomination or proposal is made:

(A) the name and address of such stockholder, as they appear on the Corporation's books, and of such beneficial owner;

(B) (1) the class and number of shares of the Corporation which are owned beneficially and of record by such stockholder and such beneficial owner; (2) any option, warrant, convertible security, stock appreciation right, or similar right with an exercise or conversion privilege or a settlement payment or mechanism at a price related to any class or series of shares of the Corporation or with a value derived in whole or in part from the value of any class or series of shares of the Corporation, whether such instrument or right shall be subject to settlement in the underlying class or series of capital stock of the Corporation or otherwise (a "Derivative Instrument") directly or indirectly owned beneficially by such stockholder and such beneficial owner and any other direct or indirect opportunity to profit or share in any profit derived from any increase or decrease in the value of shares of the Corporation; (3) any proxy, contract, arrangement, understanding, or relationship pursuant to which such stockholder has a right to vote any shares of any security of the Corporation; (4) any short interest in any security of the Corporation (for purposes of this Bylaw a person shall be deemed to have a short interest in a security if such person directly or indirectly, through any contract, arrangement, understanding, relationship or otherwise, has the opportunity to profit or share in any profit derived from any decrease in the value of the subject security) held directly or indirectly by such stockholder and such beneficial owner; (5) any rights to dividends on the shares of the Corporation owned beneficially and of record by such stockholder and such beneficial owner that are separated or separable from the underlying shares of the Corporation; (6) any proportionate interest in shares of the Corporation or Derivative Instruments held, directly or indirectly, by a general or limited partnership in which such stockholder or such beneficial owner is a general partner or, directly or indirectly, beneficially owns an interest in a general partner; and (7) any performance-related fees (other than an asset-based fee) that such stockholder or such beneficial owner is entitled to based on any increase or decrease in the value of shares of the Corporation or Derivative Instruments, if any, as of the date of such notice, in each case including without limitation any such interests held by members of such stockholder's or such beneficial owner's immediate family sharing the same household (which information shall be supplemented by such stockholder and beneficial owner, if any, not later than ten (10) days after the record date for the meeting to disclose such ownership as of the record date);

(C) any other information relating to such stockholder and beneficial owner, if any, that would be required to be disclosed in a proxy statement or other filings required to be made in connection with solicitations of proxies for, as applicable, the proposal and/or for the election of directors in a contested election pursuant to Section 14 of the 1934 Act and the rules and regulations promulgated thereunder, including without limitation:

(1) a description of all arrangements or understandings between the stockholder or beneficial owner and each proposed nominee and any other person or persons (including their names) pursuant to which the nomination(s) are to be made by such stockholder; and

(2) whether either such stockholder or beneficial owner intends to deliver a proxy statement and form of proxy to holders of, in the case of the proposal, at least the percentage of the Corporation's voting shares required under applicable law or the Certificate of Incorporation or these Bylaws to carry the proposal or, in the case of a nomination or nominations, a sufficient number of holders of the Corporation's voting shares to elect such nominee or nominees (an affirmative statement of such intent, a "Solicitation Notice").

(e) Notwithstanding anything in Section 2.2(c) of these Bylaws to the contrary, in the event that the number of directors to be elected to the Board of Directors of the Corporation is increased and there is no public announcement naming all of the nominees for director or specifying the size of the increased Board of Directors made by the Corporation at least seventy (70) days prior to the first anniversary of the preceding year's annual meeting (or, if the annual meeting is held more than thirty (30) days before or thirty (30) days after such anniversary date, at least seventy (70) days prior to such annual meeting) a stockholder's notice required by this Section 2.2 shall also be considered timely, but only with respect to nominees for any new positions created by such increase, if it shall be delivered to the Secretary at the principal executive offices of the Corporation not later than the close of business on the tenth (10th) day following the day on which such public announcement is first made by the Corporation.

(f) Only such persons who are nominated in accordance with the procedures set forth in this Section 2.2 shall be eligible to serve as directors and only such business shall be conducted at a meeting of stockholders as shall have been brought before the meeting in accordance with the procedures set forth in this Section 2.2. Except as otherwise provided by law, the chairman of the meeting shall have the power and duty to determine whether a nomination or any business proposed to be brought before the meeting was made, or proposed, as the case may be, in accordance with the procedures set forth in these Bylaws and, if any proposed nomination or business is not in compliance with these Bylaws, to declare that such defective proposal or nomination shall not be presented for stockholder action at the meeting and shall be disregarded.

(g) Notwithstanding the foregoing provisions of this Section 2.2, in order to include information with respect to a stockholder proposal in the proxy statement and form of proxy for a stockholders' meeting, stockholders must provide notice as required by the regulations promulgated under the 1934 Act. Nothing in these Bylaws shall be deemed to affect any rights of stockholders to request inclusion of proposals in the Corporation's proxy statement pursuant to Rule 14a-8 under the 1934 Act.

(h) For purposes of these Bylaws, "public announcement" shall mean disclosure in a press release reported by the Dow Jones News Service, Associated Press, PR Newswire, Reuters or comparable national news service or in a document publicly filed by the Corporation with the U.S. Securities and Exchange Commission pursuant to Section 13, 14 or 15(d) of the 1934 Act.

2.3 Special Meetings.

(a) Unless otherwise provided in the Certificate of Incorporation, special meetings of the stockholders of the Corporation may be called, for any purpose or purposes, only by (i) the Chairman of the Board of Directors, (ii) the Chief Executive Officer, or (iii) the Board of Directors pursuant to a resolution adopted by a majority of the directors then in office, and shall be held at such place, on such date and at such time as determined by the Board of Directors.

(b) If a special meeting is properly called by any person or persons other than the Board of Directors, the request shall be in writing, specifying the general nature of the business proposed to be transacted, and shall be delivered personally or sent by certified or registered mail, return receipt requested, to the Secretary of the Corporation. No business may be transacted at such special meeting otherwise than specified in such notice. The Board of Directors shall determine the time and place of such special meeting, which shall be held not less than thirty-five (35) nor more than one hundred twenty (120) days after the date of the receipt of the request. Upon determination of the time and place of the meeting, the Secretary shall cause notice to be given to the stockholders entitled to vote, in accordance with the provisions of Section 2.4 of these Bylaws. Nothing contained in this subsection (b) shall be construed as limiting, fixing or affecting the time when a meeting of stockholders called by action of the Board of Directors may be held.

(c) Nominations of persons for election to the Board of Directors may be made at a special meeting of stockholders at which directors are to be elected pursuant to the Corporation's notice of meeting (i) by or at the direction of the Board of Directors or (ii) by any stockholder of the Corporation who is a stockholder of record at the time of giving notice provided for in these Bylaws who shall be entitled to vote at the meeting and who complies with the notice procedures set forth in this Section 2.3(c). In the event the Corporation calls a special meeting of stockholders for the purpose of electing one or more directors to the Board of Directors, any such stockholder may nominate a person or persons (as the case may be), for election to such position(s) as specified in the Corporation's notice of meeting, if the stockholder's notice otherwise required by Section 2.2 of these Bylaws shall be delivered to the Secretary at the principal executive offices of the Corporation not earlier than the close of business on the one hundred twentieth (120th) day prior to such special meeting and not later than the close of business on the later of the ninetieth (90th) day prior to such meeting or the tenth (10th) day following the day on which public announcement is first made of the date of the special meeting and of the nominees proposed by the Board of Directors to be elected at such meeting. In no event shall the public announcement of an adjournment of a special meeting commence a new time period for the giving of a stockholder's notice as described above.

(d) Unless the Certificate of Incorporation provides otherwise, any special meeting of the stockholders may be cancelled by resolution duly adopted by a majority of the directors then in office upon public notice given prior to the date previously scheduled for such meeting of stockholders.

2.4 Notice of Meetings. Except as otherwise provided by law, notice, given in writing or by electronic transmission, of each meeting of stockholders shall be given not less than ten (10) nor more than sixty (60) days before the date of the meeting to each stockholder entitled to vote at such meeting as of the record date for determining the stockholders entitled to notice of the meeting. Such notice shall specify the place, date and hour of the meeting, the means of remote communication(s), if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such meeting (as authorized by the Board of Directors in its sole discretion pursuant to Section 211(a)(2) of the DGCL), the record date for determining the stockholders entitled to vote at the meeting if such date is different from the record date for determining stockholders entitled to notice of the meeting, and, in the case of a special meeting, the purpose or purposes of the meeting. Notice of any meeting of stockholders, if mailed, is given when deposited in the United States mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the records of the Corporation and otherwise is given when delivered. Notice of the time, place, and purpose of any meeting of stockholders may be waived in writing, signed by the person entitled to notice thereof, or by electronic transmission by such person, either before or after such meeting, and will be waived by any stockholder by his or her attendance thereat in person or by proxy, except when the stockholder attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Any stockholder so waiving notice of such meeting shall be bound by the proceedings of any such meeting in all respects as if due notice thereof had been given. Neither the business to be transacted at, nor the purpose of, any annual or special meeting of the stockholders need be specified in any written waiver of notice or any waiver by electronic transmission.

2.5 Determination of Stockholders of Record.

(a) In order that the Corporation may determine the stockholders entitled to notice of any meeting of stockholders or any adjournment thereof, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date shall not be more than sixty (60) nor less than ten (10) days before the date of such meeting. If the Board of Directors so fixes a date, such date shall also be the record date for determining the stockholders entitled to vote at such meeting unless the Board of Directors determines, at the time it fixes such record date, that a later date on or before the date of the meeting shall be the date for making such determination. If no record date is fixed by the Board of Directors, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day next preceding the day on which notice is given, or, if notice is waived, at the close of business on the day next preceding the day on which the meeting is held. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for determination of stockholders entitled to vote at the adjourned meeting, and in such case shall also fix as the record date for stockholders entitled to notice of such adjourned meeting the same or an earlier date as that fixed for determination of stockholders entitled to vote at the adjourned meeting.

(b) In order that the Corporation may determine the stockholders entitled to consent to corporate action in writing without a meeting, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which date shall not be more than ten (10) days after the date upon which the resolution fixing the record date is adopted by the Board of Directors. If no record date has been fixed by the Board of Directors, the record date for determining stockholders entitled to consent to corporate action in writing without a meeting, when no prior action by the Board of Directors is required by the DGCL, shall be the first date on which a signed written consent setting forth the action taken or proposed to be taken is delivered to the Corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the Corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to the Corporation's registered office shall be by hand or by certified or registered mail, return receipt requested. If no record date has been fixed by the Board of Directors and prior action by the Board of Directors is required by the DGCL, the record date for determining stockholders entitled to consent to corporate action in writing without a meeting shall be at the close of business on the day on which the Board of Directors adopts the resolution taking such prior action.

2.6 Quorum. At all meetings of the stockholders, except where otherwise provided by law, the Certificate of Incorporation or these Bylaws, the presence, in person or by proxy duly authorized, of the holders of 33.4% of the outstanding shares of stock entitled to vote shall constitute a quorum for the transaction of business. In the absence of a quorum, any meeting of stockholders may be adjourned, from time to time, either by the chairman of the meeting or by vote of the holders of a majority of the shares represented thereat, but no other business shall be transacted at such meeting. The stockholders present at a duly called or convened meeting, at which a quorum is present, may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum. Where a separate vote by a class or series or classes or series is required, except where otherwise provided by law or by the Certificate of Incorporation or these Bylaws, 33.4% the outstanding shares of such class or series or classes or series, present in person or represented by proxy duly authorized, shall constitute a quorum entitled to take action with respect to that vote on that matter.

2.7 Adjournment and Notice of Adjourned Meetings. Any meeting of stockholders, whether annual or special, may be adjourned from time to time either by the chairman of the meeting or by the vote of a majority of the shares present in person or represented by proxy at the meeting. When a meeting is adjourned to another time or place, notice need not be given of the adjourned meeting if the time and place thereof, and the means of remote communication(s), if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such adjourned meeting (as authorized by the Board of Directors in its sole discretion pursuant to Section 211(a)(2) of the DGCL), are announced at the meeting at which the adjournment is taken. At the adjourned meeting, the Corporation may transact any business which might have been transacted at the original meeting. If the adjournment is for more than thirty (30) days, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting. If after the adjournment a new record date for stockholders entitled to vote is fixed for the adjourned meeting, the Board of Directors shall fix a new record date for notice of such adjourned meeting, and shall give notice of the adjourned meeting to each stockholder of record entitled to vote at such adjourned meeting as of the record date fixed for notice of such adjourned meeting.

2.8 Voting. Except as otherwise provided by law or by the Certificate of Incorporation or these Bylaws, in all matters other than the election of directors, the affirmative vote of the majority of shares 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 these Bylaws, directors shall be elected by a plurality of the votes of the shares present in person or represented by proxy at the meeting and entitled to vote generally on the election of directors. Where a separate vote by a class or series or classes or series is required, except where otherwise provided by law or by the Certificate of Incorporation or these Bylaws, the affirmative vote of the majority (plurality, in the case of the election of directors) of shares of such class or series or classes or series present in person or represented by proxy at the meeting shall be the act of such class or series or classes or series.

2.9 Voting Rights. For the purpose of determining those stockholders entitled to vote at any meeting of the stockholders, except as otherwise provided by law, only persons in whose names shares stand on the stock records of the Corporation on the record date, as provided in Section 6.5 of these Bylaws, shall be entitled to vote at any meeting of stockholders. Every person entitled to vote shall have the right to do so either in person or by an agent or agents authorized by a proxy granted in accordance with the DGCL. An agent so appointed need not be a stockholder. No proxy shall be voted after three (3) years from its date of creation unless the proxy provides for a longer period.

2.10 Joint Owners of Stock. If shares or other securities having voting power stand of record in the names of two (2) or more persons, whether fiduciaries, members of a partnership, joint tenants, tenants in common, tenants by the entirety, or otherwise, or if two (2) or more persons have the same fiduciary relationship respecting the same shares, unless the Secretary is given written notice to the contrary and is furnished with a copy of the instrument or order appointing them or creating the relationship wherein it is so provided, their acts with respect to voting shall have the following effect: (a) if only one (1) votes, his or her act binds all; (b) if more than one (1) votes, the act of the majority so voting binds all; (c) if more than one (1) votes, but the vote is evenly split on any particular matter, each faction may vote the securities in question proportionally, or may apply to the Delaware Court of Chancery for relief as provided in Section 217(b) of the DGCL. If the instrument filed with the Secretary shows that any such tenancy is held in unequal interests, a majority or even-split for the purpose of clauses (b) and (c) shall be a majority or even-split in interest.

2.11 List of Stockholders. The officer who has charge of the stock ledger of the Corporation shall prepare and make, at least ten (10) days before every meeting of stockholders, a complete list of the stockholders entitled to vote at said meeting (provided, however, that if the record date for determining the stockholders entitled to vote is less than ten (10) days before the date of the meeting, the list shall reflect the stockholders entitled to vote as of the tenth (10) day before the meeting date), arranged in alphabetical order, showing the address of each stockholder and the number of shares registered in the name of each stockholder. Nothing contained in this Section 2.11 shall require the Corporation to include electronic mail addresses or other electronic contact information on such list. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting for a period of at least ten (10) days prior to the meeting, (a) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (b) during ordinary business hours, at the principal place of business of the Corporation. In the event the Corporation determines to make the list available on an electronic network, the Corporation may take reasonable steps to ensure that such information is available only to stockholders of the Corporation. If the meeting is to be held at a place, then a list of stockholders entitled to vote at the meeting shall be produced and kept at the time and place of the meeting during the whole time thereof and may be examined by any stockholder of the Corporation who is present. If the meeting is to be held solely by means of remote communication, then such list shall also be open to the examination of any stockholder of the Corporation during the whole time of the meeting on a reasonably accessible electronic network, and the information required to access such list shall be provided with the notice of the meeting.

2.12 Action Without Meeting.

(a) Any action to be taken at any annual or special meeting of stockholders may be taken without a meeting, without prior notice and without a vote, if a consent or consents in writing, setting forth the action to be so taken, shall be signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote thereon were present and voted and shall be delivered (by hand or by certified or registered mail, return receipt requested) to the Corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the Corporation having custody of the book in which proceedings of meetings of the stockholders are recorded.

(b) Every written consent shall bear the date of signature of each stockholder who signs the consent, and no written consent shall be effective to take the corporate action referred to therein unless, within sixty (60) days of the earliest dated consent delivered in the manner required by this Section 2.11, written consents signed by a sufficient number of holders to take action are delivered to the Corporation as aforesaid. Delivery made to the Corporation's registered office shall be by hand or by certified or registered mail, return receipt requested. Any person executing a consent may provide, whether through instruction to an agent or otherwise, that such a consent will be effective at a future time (including a time determined upon the happening of an event), no later than 60 days after such instruction is given or such provision is made, and, if evidence of such instruction or provision is provided to the Corporation, such later effective time shall serve as the date of signature. Unless otherwise provided, any such consent shall be revocable prior to its becoming effective.

(c) Any copy, facsimile or other reliable reproduction of a consent in writing may be substituted or used in lieu of the original writing for any and all purposes for which the original writing could be used, provided that such copy, facsimile or other reproduction shall be a complete reproduction of the entire original writing.

(d) Prompt notice of the taking of the corporate action without a meeting by less than unanimous written consent shall, to the extent required by applicable law, be given to those stockholders who have not consented in writing, and who, if the action had been taken at a meeting, would have been entitled to notice of the meeting if the record date for notice of such meeting had been the date that written consents signed by a sufficient number of holders to take the action were delivered to the Corporation.

2.13 Organization.

(a) At every meeting of stockholders, (i) the Chairman of the Board of Directors or, if a Chairman of the Board of Directors has not been appointed or is absent, (ii) the Vice Chairman of the Board of Directors, if any, or, if the Vice Chairman of the Board of Directors is absent or there is no Vice Chairman of the Board of Directors, (iii) the Chief Executive Officer or, if the Chief Executive Officer is absent, (iv) such person as the Chairman of the Board of Directors shall appoint or, if such Chairman has not been appointed, (v) any officer of the Corporation chosen by the Board of Directors, shall act as chairman of the meeting. The Secretary, or in the absence of the Secretary an Assistant Secretary, shall act as secretary of the meeting, but in the absence of the Secretary and any Assistant Secretary the chairman of the meeting may appoint any person to act as secretary of the meeting.

(b) The Board of Directors, in advance of any meeting of stockholders, may, and shall if required by law, appoint one (1) or more inspector(s), who may include individual(s) who serve the Corporation in other capacities, including without limitation as officers, employees or agents, to act at the meeting of stockholders and make a written report thereof. The Board of Directors may designate one (1) or more persons as alternate inspector(s) to replace any inspector who fails to act. If no inspector or alternate has been appointed or is able to act at a meeting of stockholders, the chairman of the meeting shall appoint one (1) or more inspector(s) to act at the meeting. Each inspector, before discharging his or her duties, shall take and sign an oath to faithfully execute the duties of inspector with strict impartiality and according to the best of his or her ability. The inspector(s) or alternate(s) shall have the duties prescribed pursuant to Section 231 of the DGCL or other applicable law.

(c) The Board of Directors of the Corporation shall be entitled to make such rules or regulations for the conduct of meetings of the stockholders as it shall deem necessary, appropriate or convenient. Subject to such rules and regulations of the Board of Directors, if any, the chairman of the meeting shall have the right and authority to prescribe such rules, regulations and procedures and to do all such acts as, in the judgment of such chairman, are necessary, appropriate or convenient for the proper conduct of the meeting, including, without limitation, establishing an agenda or order of business for the meeting, rules and procedures for maintaining order at the meeting and the safety of those present, limitations on participation in such meeting to stockholders of record of the Corporation and their duly authorized and constituted proxies and such other persons as the chairman shall permit, restrictions on entry to the meeting after the time fixed for the commencement thereof, limitations on the time allotted to questions or comments by participants and regulation of the opening and closing of the polls for balloting on matters which are to be voted on by ballot. The date and time of the opening and closing of the polls for each matter upon which the stockholders will vote at the meeting shall be announced at the meeting. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of the stockholders shall not be required to be held in accordance with rules of parliamentary procedure.

2.14 Postponement and Cancellation of Meeting. Any previously scheduled annual or special meeting of stockholders may be postponed, and any previously scheduled annual or special meeting of stockholders may be cancelled, by resolution of the Board of Directors upon public notice given prior to the time previously scheduled for such meeting.

ARTICLE III
DIRECTORS

3.1 General Powers. The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors, except as may be otherwise provided in the DGCL or in the Certificate of Incorporation. The Board of Directors may adopt such rules and procedures, not inconsistent with the Certificate of Incorporation, these Bylaws or applicable law, as it may deem proper for the conduct of its meetings and the management of the Corporation, except as may be otherwise provided by the DGCL or by the Certificate of Incorporation.

3.2 Number, Term of Office and Qualifications. The Board of Directors shall consist of one or more members, the number thereof to be determined from time to time by resolution of the Board of Directors. Each director shall hold office until a successor is duly elected and qualified or until the director's earlier death, resignation, disqualification or removal. Directors shall be natural persons, but need not be stockholders of the Corporation unless otherwise required by the Certificate of Incorporation.

3.3 Vacancies. Unless otherwise provided in the Certificate of Incorporation and subject to the rights of the holders of any series of preferred stock then outstanding, any vacancies on the Board of Directors resulting from death, resignation, disqualification, removal or other causes and any newly created directorships resulting from any increase in the number of directors shall, unless the Board of Directors determines by resolution that any such vacancies or newly created directorships shall be filled by stockholders, be filled only by the affirmative vote of a majority of the directors then in office, even if less than a quorum of the Board of Directors. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the director for which the vacancy was created or occurred and until such director's successor shall have been elected and qualified.

3.4 Resignation. Any director may resign at any time by delivering his or her notice in writing or by electronic transmission to theSecretary, such resignation to specify whether it will be effective at a particular time, upon receipt by the Secretary or at the pleasure of the Board of Directors. If no such specification is made, it shall be deemed effective at the pleasure of the Board of Directors. Verbal resignation shall not be deemed effective until confirmed by the director in writing or by electronic transmission to the Secretary. When one or more directors shall resign from the Board of Directors effective at a future date, a majority of the directors then in office, including those who have so resigned, shall have the power to fill such vacancy or vacancies, the vote thereon to take effect when such resignation or resignations shall become effective, and each director so chosen shall hold office for the unexpired portion of the term of the director whose place shall be vacated and until his or her successor shall have been duly elected and qualified.

3.5 Removal. Subject to the Certificate of Incorporation, any director or the entire Board of Directors may be removed, with or without cause, by the affirmative vote of the holders of a majority of the voting power of all of then outstanding shares of capital stock of the Corporation then entitled to vote in the election of directors, voting together as a single class. No reduction of the authorized number of directors shall have the effect of removing any director prior to the expiration of such director's term of office.

3.6 Meetings.

(a) Unless otherwise restricted by the Certificate of Incorporation, regular meetings of the Board of Directors may be held at any time or date and at any place within or without the State of Delaware which has been designated by the Board of Directors and publicized among all directors, either orally or in writing, by telephone, including a voice-messaging system or other system designed to record and communicate messages, facsimile, telegraph or telex, or by electronic mail or other electronic means. No further notice shall be required for regular meetings of the Board of Directors.

(b) Unless otherwise restricted by the Certificate of Incorporation, special meetings of the Board of Directors may be held at any time and place within or without the State of Delaware whenever called by the Chairman of the Board of Directors, the Chief Executive Officer, or a majority of the directors then in office.

(c) Any member of the Board of Directors, or of any committee thereof, may participate in a meeting by means of conference telephone or other communications equipment pursuant to which all persons participating in the meeting can hear each other, and participation in a meeting by such means shall constitute presence in person at such meeting.

(d) Notice of the time and place of all special meetings of the Board of Directors shall be given to each director (i) by giving notice to such director in person or by telephone, including a voice messaging system or other system designed to record and communicate messages, during normal business hours, at least twenty-four (24) hours before the meeting, (ii) by sending a telegram or delivering notice by facsimile transmission, by electronic mail or by hand, to such director at his or her last known business or home address, during normal business hours, at least twenty-four (24) hours before the meeting, or (iii) by mailing notice, via first class United States mail, to such director at his or her last known business or home address at least three (3) days in advance of the meeting. Notice of any meeting may be waived in writing, or by electronic transmission, at any time before or after the meeting and will be waived by any director by attendance thereat, except when the director attends the meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Notice of a special meeting of the Board of Directors need not specify the purpose of the meeting.

(e) The transaction of all business at any meeting of the Board of Directors, or any committee thereof, however called or noticed, or wherever held, shall be as valid as though had at a meeting duly held after regular call and notice, if a quorum be present and if, either before or after the meeting, each of the directors not present who did not receive notice shall sign a written waiver of notice or shall waive notice by electronic transmission. All such waivers shall be filed with the corporate records or made a part of the minutes of the meeting. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the Board of Directors need be specified in any written waiver of notice or any waiver by electronic transmission.

3.7 Quorum and Voting.

(a) Unless the Certificate of Incorporation requires a greater number, a quorum of the Board of Directors shall consist of a majority of the directors then in office. At any meeting whether a quorum be present or otherwise, a majority of the directors present may adjourn from time to time until the time fixed for the next regular meeting of the Board of Directors, without notice other than by announcement at the meeting.

(b) At each meeting of the Board of Directors at which a quorum is present, all questions and business shall be determined by the affirmative vote of a majority of the directors present at the meeting, unless a different vote be required by law, the Certificate of Incorporation or these Bylaws.

3.8 Action Without Meeting. Unless otherwise restricted by the Certificate of Incorporation or these Bylaws, any action required or permitted to be taken at any meeting of the Board of Directors, or of any committee thereof, may be taken without a meeting, if all members of the Board of Directors or committee, as the case may be, consent thereto in writing or by electronic transmission, and such writing or writings or transmission or transmissions are filed with the minutes of proceedings of the Board of Directors or committee. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form. Any person (whether or not then a director) may provide, whether through instruction to an agent or otherwise, that a consent to action will be effective at a future time (including a time determined upon the happening of an event), no later than 60 days after such instruction is given or such provision is made and such consent shall be deemed to have been given at such effective time so long as such person is then a director and did not revoke the consent prior to such time. Any such consent shall be revocable prior to its becoming effective.

3.9 Fees and Compensation. Directors shall be entitled to such compensation for their services as may be approved by the Board of Directors, or any committee thereof, including, if so approved by resolution of the Board of Directors or such committee, a fixed sum and expenses of attendance, if any, for attendance at each regular or special meeting of the Board of Directors and at any meeting of a committee of the Board of Directors. Nothing herein contained shall be construed to preclude any director from serving the Corporation in any other capacity as an officer, agent, employee, or otherwise and receiving compensation therefor.

3.10 Committees.

(a) The Board of Directors may, from time to time, appoint such committees as may be permitted by law. Such committees appointed by the Board of Directors shall consist of one (1) or more members of the Board of Directors and shall have such powers and perform such duties as may be prescribed by the resolution or resolutions creating such committees, but no committee shall have the power or authority in reference to (i) approving or adopting, or recommending to the stockholders, any action or matter expressly required by the DGCL to be submitted to stockholders for approval, or (ii) adopting, amending or repealing any provision of these Bylaws.

(b) The Board of Directors, subject to any requirements of any outstanding series of preferred stock and the provisions of subsections (a) and (b) of this Section 3.10, may at any time increase or decrease the number of members of a committee or terminate the existence of a committee. The membership of a committee member shall terminate on the date of his or her death or voluntary resignation from the committee or from the Board of Directors. The Board of Directors may at any time for any reason remove any individual committee member and the Board of Directors may fill any committee vacancy created by death, resignation, removal or increase in the number of members of the committee. The Board of Directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee, and, in addition, in the absence or disqualification of any member of a committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not he, she or they constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of any such absent or disqualified member.

(c) Unless the Board of Directors shall otherwise provide, regular meetings of any committee appointed pursuant to this Section 3.10 shall be held at such times and places as are determined by the Board of Directors, or by any such committee, and when notice thereof has been given to each member of such committee, no further notice of such regular meetings need be given thereafter. Special meetings of any such committee may be held at any place which has been determined from time to time by such committee, and may be called by any director who is a member of such committee, upon notice to the members of such committee of the time and place of such special meeting given in the manner provided for the giving of notice to members of the Board of Directors of the time and place of special meetings of the Board of Directors. Notice of any special meeting of any committee may be waived in writing at any time before or after the meeting and will be waived by any director by attendance thereat, except when the director attends such special meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Unless otherwise provided by the Board of Directors in the resolutions authorizing the creation of the committee, a majority of the members of any such committee shall constitute a quorum for the transaction of business, and the act of a majority of those present at any meeting at which a quorum is present shall be the act of such committee.

3.11 Organization. At every meeting of the directors, the Chairman of the Board of Directors, or, if a Chairman of the Board of Directors has not been appointed or is absent, the Vice Chairman of the Board of Directors, or if a Vice Chairman of the Board of Directors has not been appointed or is absent, the Chief Executive Officer (if a director), or if the Chief Executive Officer is absent, or, in the absence of any such person, a chairman of the meeting chosen by a majority of the directors present, shall preside over the meeting. The Secretary, or in the absence of the Secretary an Assistant Secretary, shall act as secretary of the meeting, but in the absence of the Secretary and any Assistant Secretary the chairman of the meeting may appoint any person to act as secretary of the meeting.

ARTICLE IV
OFFICERS

4.1 Positions; Election and Qualification. The officers of the Corporation shall be elected annually by the Board of Directors and shall include a President or Chief Executive Officer ("Chief Executive Officer"), a Chief Financial Officer, a Treasurer and a Secretary. The Board of Directors, in its discretion, may also elect a Chairman (who must be a director), one or more Vice Chairmen (who must be directors) and one or more Vice Presidents, Assistant Treasurers, Assistant Secretaries and other officers. The Board of Directors may assign such additional titles to one or more of the officers as it shall deem appropriate. Any two or more offices may be held by the same person. No officer need be a stockholder.

4.2 Term. Each officer of the Corporation shall hold office at the pleasure of the Board of Directors and until such officer's successor is elected and qualified or until such officer's earlier death, resignation or removal, subject to the rights, if any, of an officer under contract of employment. If the office of any officer becomes vacant for any reason, the vacancy may be filled by the Board of Directors. The election or appointment of an officer shall not of itself create contract rights

4.3 Duties.

(a) The Chairman of the Board of Directors shall, if present, preside at meetings of the Board of Directors and stockholders and exercise and perform such other powers and duties as may from time to time be assigned to him or her by the Board of Directors or as may be prescribed by these Bylaws.

(b) Subject to such supervisory powers, if any, as the Board of Directors may give to the Chairman of the Board of Directors, the Chief Executive Officer shall, subject to the control of the Board of Directors, have general supervision, direction and control of the business and affairs of the Corporation and shall report directly to the Board of Directors. All other officers, officials, employees and agents shall report directly or indirectly to the Chief Executive Officer. The Chief Executive Officer shall see that all orders and resolutions of the Board of Directors are carried into effect.

(c) In the absence or disability of the Chief Executive Officer, the Vice President(s), if any, in order of their rank as fixed by the Board of Directors or, if not ranked, a Vice President designated by the Board of Directors, shall perform all the duties of the Chief Executive Officer and, when so acting, shall have all the powers of, and be subject to all the restrictions upon, the Chief Executive Officer. The Vice President(s) shall have such other powers and perform such other duties as form time to time may be prescribed for them respectively by the Board of Directors, these Bylaws, the Chairman of the Board of Directors, the Chief Executive Officer. The Board of Directors may designate one or more Executive Vice Presidents or Senior Vice Presidents or may otherwise specify the order of seniority of the Vice Presidents.

(d) The Chief Financial Officer shall keep and maintain, or cause to be kept and maintained, adequate and correct books and records of accounts of the properties and business transactions of the Corporation, including accounts of its assets, liabilities, receipts, disbursements, gains, losses, capital and retained earnings. The Chief Financial Officer shall deposit all money and other valuables in the name and to the credit of the Corporation with such depositaries as may be designated by the Board of Directors or Chief Executive Officer. The Chief Financial Officer shall disburse the funds of the Corporation as may be ordered by the Board of Directors, shall render to the Board of Directors and Chief Executive Officer, whenever they request, an account of all of his or her transactions as Chief Financial Officer and of the financial condition of the Corporation, and shall have such other powers and perform such other duties as may be prescribed by the Board of Directors or these Bylaws. In lieu of any contrary resolution duly adopted by the Board of Directors, the Chief Financial Officer shall also be the Treasurer of the Corporation.

(e) The Secretary shall keep or cause to be kept, at the principal executive office of the Corporation, or such other place as the Board of Directors may direct, a book of minutes of all meetings and actions of directors, committees of directors, and stockholders. The minutes shall show the time and place of each meeting, whether regular or special (and, if special, how authorized and the notice given), the names of those present at directors' meetings or committee meetings, the number of shares present or represented at stockholders' meetings, and the proceedings thereof.

The Secretary shall keep, or cause to be kept, at the principal executive office of the Corporation or at the office of the Corporation's transfer agent or registrar, as determined by resolution of the Board of Directors, a share register, or a duplicate share register, showing the names of all stockholders and their addresses, the number and classes of shares held by each, the number and date of certificates evidencing such shares, and the number and date of cancellation of every certificate surrendered for cancellation.

The Secretary shall give, or cause to be given, notice of all meetings of the stockholders, the Board of Directors and any committee(s) of the Board of Directors, required to be given by law or by these Bylaws. The Secretary shall keep the seal of the Corporation, if one be adopted, in safe custody and shall have such other powers and perform such other duties as may be prescribed by the Board of Directors or by these Bylaws.

(f) The Vice Chairman of the Board, if any, shall, in the absence of the Chairman of the Board, or in the event of his or her inability or refusal to act, perform the duties and exercise the powers of the Chairman of the Board and shall perform such other duties and have such other powers as the Board of Directors may from time to time prescribe.

(g) The Assistant Secretary(ies), if any, in the order determined by the Board of Directors (or if there be no such determination, then in the order of their election) shall, in the absence of the Secretary or in the event of his or her inability or refusal to act, perform the duties and exercise the powers of the Secretary and shall perform such other duties and have such other powers as the Board of Directors may from time to time prescribe.

(h) The Assistant Treasurer(s), if any, in the order determined by the Board of Directors (or if there be no such determination, then in the order of their election), shall, in the absence of the Chief Financial Officer or in the event of his or her inability or refusal to act, perform the duties and exercise the powers of the Chief Financial Officer and shall perform such other duties and have such other powers as the Board of Directors may from time to time prescribe.

4.4 Delegation of Authority. The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

4.5 Resignations. Any officer may resign at any time by giving notice in writing or by electronic transmission to the Chairman of the Board, or to the Chief Executive Officer or to the Secretary. Verbal resignation shall not be deemed effective until confirmed by the officer in writing or by electronic transmission to the Chairman of the Board, Chief Executive Officer or Secretary. Any such resignation shall be effective when received by the person or persons to whom such notice is given, unless a later time is specified therein, in which event the resignation shall become effective at such later time. Unless otherwise specified in such notice, the acceptance of any such resignation shall not be necessary to make it effective. Any resignation shall be without prejudice to the rights, if any, of the Corporation under any contract with the resigning officer.

4.6 Removal. Subject to the rights, if any, of an officer under contract of employment, any officer may be removed from office at any time, either with or without cause, by the affirmative vote of a majority of the directors in office at the time, or by the unanimous written consent of the directors in office at the time, or by any committee or superior officers upon whom such power of removal may have been conferred by the Board of Directors.

ARTICLE V
EXECUTION OF CORPORATE INSTRUMENTS AND VOTING OF SECURITIES OWNED BY THE CORPORATION

5.1 Execution of Corporate Instruments. The Board of Directors may, in its discretion, determine the method and designate the signatory officer or officers, or other person or persons, to execute on behalf of the Corporation any corporate instrument or document, or to sign on behalf of the Corporation the corporate name without limitation, or to enter into contracts on behalf of the Corporation, except where otherwise provided by law or these Bylaws, and such execution or signature shall be binding upon the Corporation.

All checks and drafts drawn on banks or other depositaries on funds to the credit of the Corporation or in special accounts of the Corporation shall be signed by such person or persons as the Board of Directors shall authorize so to do.

Unless authorized or ratified by the Board of Directors or within the agency power of an officer, no officer, agent or employee shall have any power or authority to bind the Corporation by any contract or engagement or to pledge its credit or to render it liable for any purpose or for any amount.

5.2 Voting of Securities Owned by the Corporation. All stock and other securities of other Corporations owned or held by the Corporation for itself, or for other parties in any capacity, shall be voted, and all proxies with respect thereto shall be executed, by the person authorized so to do by resolution of the Board of Directors, or, in the absence of such authorization, by the Chairman of the Board of Directors, the Chief Executive Officer or any Vice President.

ARTICLE VI
SHARES OF STOCK

6.1 Form and Execution of Certificates. Shares of stock of the Corporation shall be represented by certificates, or shall be uncertificated. Certificates for the shares of stock of the Corporation, if any, shall be in such form as is consistent with the Certificate of Incorporation and applicable law. Every holder of stock represented by certificate shall be entitled to have a certificate signed by or in the name of the Corporation by the Chairman of the Board of Directors, or the Chief Executive Officer or any Vice President and by the Treasurer or Assistant Treasurer or the Secretary or Assistant Secretary, certifying the number of shares owned by him or her in the Corporation. Any or all of the signatures on the certificate may be facsimiles. In case any officer, transfer agent, or registrar who has signed or whose facsimile signature has been placed upon a certificate shall have ceased to be such officer, transfer agent, or registrar before such certificate is issued, it may be issued with the same effect as if he or she were such officer, transfer agent, or registrar at the date of issue.

6.2 Transfers of Stock. Transfers of record of shares of stock of the Corporation shall be made only upon its books by the holders thereof, in person or by attorney duly authorized, and, in the case of stock represented by certificate, upon the surrender of a properly endorsed certificate or certificates for a like number of shares. To the extent designated by the Chief Executive Officer or any Vice President or the Treasurer of the Corporation, the Corporation may recognize the transfer of fractional uncertificated shares, but shall not otherwise be required to recognize the transfer of fractional shares. The Corporation shall have power to enter into and perform any agreement with any number of stockholders of any one or more classes of stock of the Corporation to restrict the transfer of shares of stock of the Corporation of any one or more classes owned by such stockholders in any manner not prohibited by the DGCL.

6.3 Transfer Agents and Registrars. The Board of Directors may appoint, or authorize any officer or officers to appoint, one or more transfer agents and one or more registrars.

6.4 Lost, Stolen or Destroyed Certificates. A new certificate or certificates or uncertificated shares shall be issued in place of any certificate or certificates theretofore issued by the Corporation alleged to have been lost, stolen or destroyed, upon the making of an affidavit of that fact by the person claiming the certificate of stock to be lost, stolen or destroyed. The Corporation may require, as a condition precedent to the issuance of a new certificate or certificates or uncertificated shares, the owner of such lost, stolen or destroyed certificate or certificates, or the owner's legal representative, to agree to indemnify the Corporation in such manner as it shall require or to give the Corporation a surety bond in such form and amount as it may direct as indemnity against any claim that may be made against the Corporation with respect to the certificate alleged to have been lost, stolen or destroyed.

6.5 Fixing Record Dates.

(a) In order that the Corporation may determine the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date shall not be more than sixty (60) nor less than ten (10) days before the date of such meeting. If the Board of Directors so fixes a date, such date shall also be the record date for determining the stockholders entitled to vote at such meeting unless the Board of Directors determines, at the time it fixes such record date, that a later date on or before the date of the meeting shall be the date for making such determination. If no record date is fixed by the Board of Directors, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day next preceding the day on which notice is given, or, if notice is waived, at the close of business on the day next preceding the day on which the meeting is held. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for the determination of stockholders entitled to vote at the adjourned meeting and in such case shall also fix as the record date for stockholders entitled to notice of such adjourned meeting the same or an earlier date as that fixed for the determination of stockholders entitled to vote therewith at the adjourned meeting.

(b) In order that the Corporation may determine the stockholders entitled to consent to corporate action in writing without a meeting, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date shall not be more than ten (10) days after the date upon which the resolution fixing the record date is adopted by the Board of Directors. If no record date has been fixed by the Board of Directors, the record date for determining stockholders entitled to consent to corporate action in writing without a meeting: (i) when no prior action by the Board of Directors is required by law, the record date for such purpose shall be the first date on which a signed written consent setting forth the action taken or proposed to be taken is delivered to the Corporation by delivery (by hand, or by certified or registered mail, return receipt requested) to its registered office in the State of Delaware, its principal place of business, or an officer or agent of the Corporation having custody of the book in which proceedings of meetings of the stockholders are recorded and (ii) if prior action by the Board of Directors is required by law, the record date for such purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution taking such prior action.

(c) In order that the Corporation may determine the stockholders entitled to receive payment of any dividend or other distribution or allotment of any rights or the stockholders entitled to exercise any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted, and which record date shall be not more than 60 days prior to such action. If no record date is fixed, the record date for determining stockholders for any such purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating thereto.

6.6 Registered Stockholders. The Corporation shall be entitled to recognize the exclusive right of a person registered on its books as the owner of shares to receive dividends, and to vote as such owner, and shall not be bound to recognize any equitable or other claim to or interest in such share or shares on the part of any other person whether or not it shall have express or other notice thereof, except as otherwise provided by applicable law.

ARTICLE VII
OTHER SECURITIES OF THE CORPORATION

7.1 Execution of Other Securities. All bonds, debentures and other corporate securities of the Corporation, other than stock certificates (covered in Section 6.1), may be signed by the Chairman of the Board of Directors, the Chief Executive Officer, the President or any Vice President, or such other person as may be authorized by the Board of Directors, and the corporate seal, if any, may be impressed thereon or a facsimile of such seal imprinted thereon and attested by the signature of the Secretary or an Assistant Secretary, or the Chief Financial Officer or Treasurer or an Assistant Treasurer; provided, however, that where any such bond, debenture or other corporate security shall be authenticated by the manual signature, or where permissible facsimile signature, of a trustee under an indenture pursuant to which such bond, debenture or other corporate security shall be issued, the signatures of the persons signing and, if applicable, attesting the corporate seal on such bond, debenture or other corporate security may be the imprinted facsimile of the signatures of such persons. Interest coupons appertaining to any such bond, debenture or other corporate security, authenticated by a trustee as aforesaid, shall be signed by the Treasurer or an Assistant Treasurer of the Corporation or such other person as may be authorized by the Board of Directors, or bear imprinted thereon the facsimile signature of such person. In case any officer who shall have signed or attested any bond, debenture or other corporate security, or whose facsimile signature shall appear thereon or on any such interest coupon, shall have ceased to be such officer before the bond, debenture or other corporate security so signed or attested shall have been delivered, such bond, debenture or other corporate security nevertheless may be adopted by the Corporation and issued and delivered as though the person who signed the same or whose facsimile signature shall have been used thereon had not ceased to be such officer of the Corporation.

ARTICLE VIII
DIVIDENDS

8.1 Declaration of Dividends. Dividends upon the capital stock of the Corporation, subject to the provisions of the Certificate of Incorporation and applicable law, if any, may be declared by the Board of Directors pursuant to law at any regular or special meeting. Dividends may be paid in cash, in property, or in shares of the capital stock, subject to the provisions of the Certificate of Incorporation and applicable law.

8.2 Dividend Reserve. Before payment of any dividend, there may be set aside out of any funds of the Corporation available for dividends such sum or sums as the Board of Directors from time to time, in their absolute discretion, think proper as a reserve or reserves to meet contingencies, or for equalizing dividends, or for repairing or maintaining any property of the Corporation, or for such other purpose as the Board of Directors shall think conducive to the interests of the Corporation, and the Board of Directors may modify or abolish any such reserve in the manner in which it was created.

ARTICLE IX
GENERAL PROVISIONS

9.1 Fiscal Year. The fiscal year of the Corporation shall be fixed from time to time by resolution of the Board of Directors.

9.2 Corporate Seal. The Corporation may, but need not, have a corporate seal. In the event the Corporation has a seal, the seal need not be affixed for any contract, resolution or other document executed by or on behalf of the Corporation to be valid and duly authorized.

9.3 Notices.

(a) Written notice to stockholders of stockholder meetings shall be given as provided in Section 2.4 herein. Without limiting the manner by which notice may otherwise be given effectively to stockholders under any agreement or contract with such stockholder, and except as otherwise required by law, written notice to stockholders for purposes other than stockholder meetings may be sent by United States mail or nationally recognized overnight courier, or by facsimile, telegraph or telex or by electronic mail or other electronic means.

(b) Notice to directors of special meetings shall be given as provided in Section 3.7(d) herein. Subject to the preceding sentence and except as expressly stated otherwise herein, notice may otherwise be given by the methods stated in subsection (a) above.

(c) An affidavit of mailing, executed by a duly authorized and competent employee of the Corporation or its transfer agent appointed with respect to the class of stock affected, or other agent, specifying the name and address or the names and addresses of the stockholder or stockholders, or director or directors, to whom any such notice or notices was or were given, and the time and method of giving the same, shall in the absence of fraud, be prima facie evidence of the facts therein contained.

(d) It shall not be necessary that the same method of giving notice be employed in respect of all recipients of notice, but one permissible method may be employed in respect of any one or more recipients, and any other permissible method or methods may be employed in respect of any other or others.

(e) Whenever notice is required to be given, under any provision of the DGCL, the Certificate of Incorporation or these Bylaws, to any person with whom communication is unlawful, the giving of such notice to such person shall not be required and there shall be no duty to apply to any governmental authority or agency for a license or permit to give such notice to such person. Any action or meeting which shall be taken or held without notice to any such person with whom communication is unlawful shall have the same force and effect as if such notice had been duly given. In the event the action taken by the Corporation is such as to require the filing of a certificate under any provision of the DGCL, the certificate shall state, if such is the fact and if notice is required, that notice was given to all persons entitled to receive notice except such persons with whom communication is unlawful.

(f) Whenever notice is required to be given, under any provision of the DGCL, the Certificate of Incorporation or these Bylaws, to any stockholder to whom (i) notice of two (2) consecutive annual meetings, or (ii) all, and at least two (2), payments (if sent by first-class mail) of dividends or interest on securities during a twelve (12) month period, have been mailed addressed to such person at such person's address as shown on the records of the Corporation and have been returned undeliverable, the giving of such notice to such person shall not be required. Any actions or meeting which shall be taken or held without notice to such person shall have the same force and effect as if such notice had been duly given. If any such person shall deliver to the Corporation a written notice setting forth such person's then current address, the requirement that notice be given to such person shall be reinstated. In the event that the action taken by the Corporation is such as to require the filing of a certificate under any provision of the DGCL, the certificate need not state that the Corporation did not give notice to persons not required to be given notice pursuant to Section 230(b) of the DGCL. The exception in clause (i) above to the requirement that notice be given shall not be applicable to any notice returned as undeliverable if the notice was given by electronic transmission.

(g) Except as otherwise prohibited under the DGCL, any notice given under the provisions of the DGCL, the Certificate of Incorporation or these Bylaws shall be effective if given by a single written notice to stockholders who share an address if consented to by the stockholders at that address to whom such notice is given. Such consent shall be deemed to have been given if such stockholder fails to object in writing to the Corporation within sixty (60) days of having been given notice by the Corporation of its intention to send the single notice. Any consent shall be revocable by the stockholder by written notice to the Corporation.

(h) Without limiting the manner by which notice otherwise may be given effectively to stockholders, any notice to stockholders given by the Corporation under any provision of the DGCL, the Certificate of Incorporation or these Bylaws shall be effective if given by a form of electronic transmission previously consented to by the stockholder to whom the notice is given. Any such consent shall be revocable by the stockholder by written notice to the Corporation. Any such consent shall be deemed revoked if (i) the Corporation is unable to deliver by electronic transmission two (2) consecutive notices given by the Corporation in accordance with such consent, and (ii) such inability becomes known to the Secretary or an Assistant Secretary of the Corporation, the transfer agent or other person responsible for the giving of notice; provided, however, the inadvertent failure to treat such inability as a revocation shall not invalidate any meeting or other action.

Notice given pursuant to the above paragraph shall be deemed given (i) if by facsimile telecommunication, when directed to a number at which the stockholder has consented to receive notice, (ii) if by electronic mail, when directed to an electronic mail address at which the stockholder has consented to receive notice, (iii) if by a posting on an electronic network together with a separate notice to the stockholder of such specific posting, upon the later of (A) such posting and (B) the giving of such separate notice, and (iv) if by any other form of electronic transmission, when directed to the stockholder. An affidavit of the Secretary or Assistant Secretary, the transfer agent or other agent of the Corporation that the notice has been given by a form of electronic transmission shall in the absence of fraud, be prima facie evidence of the facts stated therein.

For purposes of these Bylaws, "electronic transmission" means any form of communication, not directly involving the physical transmission of paper, that creates a record that may be retained, retrieved and reviewed by a recipient thereof, and that may be directly reproduced in paper form by such a recipient through an automated process. This Section 9.3 shall not apply to Section 164 (failure to pay for stock; remedies), Section 296 (adjudication of claims; appeal), Section 311 (revocation of voluntary dissolution), Section 312 (renewal, revival, extension and restoration of certificate of incorporation) or Section 324 (attachment of shares of stock) of the DGCL.

9.4 Construction. Unless the context requires otherwise, the general provisions, rules of construction and definitions in the DGCL shall govern the construction of these Bylaws. The singular number includes the plural, and the plural number includes the singular. All pronouns used in these Bylaws shall be deemed to refer to the masculine, feminine and/or neuter, as the identity of the person or persons so designated may require.

9.5 Conflict With Applicable Law or Certificate of Incorporation. These Bylaws are adopted subject to any applicable law and the Certificate of Incorporation. Whenever these Bylaws may conflict with any applicable law or the Certificate of Incorporation, such conflict shall be resolved in favor of such law or the Certificate of Incorporation.

ARTICLE X
INDEMNIFICATION AND ADVANCEMENT OF EXPENSES

10.1 Right to Indemnification. The Corporation shall indemnify and hold harmless, to the fullest extent permitted by applicable law as it presently exists or may hereafter be amended, any person (an "Indemnitee") who was or is made or is threatened to be made a party or is otherwise involved in any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (a "Proceeding"), by reason of the fact that he or she, or a person for whom he or she is the legal representative, is or was a director, officer, employee or agent of the Corporation or, is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation or of a partnership, joint venture, trust or other enterprise, including service with respect to employee benefit plans (any such entity, an "Other Entity"), against all liability and loss suffered (including, but not limited to expenses (including but not limited to, attorneys' fees and expenses), judgments, fines and amounts paid in settlement actually and reasonably incurred by such Indemnitee in connection with any such Proceeding) provided, that the Indemnitee acted in good faith and in a manner such Indemnitee reasonably believed to be in or not opposed to the best interests of the Corporation and, with respect to any Proceeding that is criminal in nature, had no reasonable cause to believe that his or her conduct was unlawful. The termination of any Proceeding by judgment, order, settlement, conviction or upon a plea of nolo contendere or its equivalent, does not, of itself, create a presumption that the Indemnitee did not act in good faith and in a manner in which he or she reasonably believed to be in or not opposed to the best interests of the Corporation, or that, with respect to any criminal proceeding he or she had reasonable cause to believe that his or her conduct was unlawful. The Corporation shall not indemnify an Indemnitee for any claim, issue or matter as to which the Indemnitee has been adjudged by a court of competent jurisdiction, after exhaustion of all appeals therefrom, to be liable to the Corporation or for any amounts paid in settlement to the Corporation, unless and only to the extent that the court in which the Proceeding was brought or other court of competent jurisdiction determines upon application that in view of all the circumstances of the case, the Indemnitee is fairly and reasonably entitled to indemnity for such amounts as the court deems proper.

10.2 Advancement of Expenses. The Corporation shall to the fullest extent not prohibited by applicable law pay the expenses (including attorneys' fees) incurred by an Indemnitee in defending any Proceeding in advance of its final disposition, provided, however, that, to the extent required by law, such payment of expenses in advance of the final disposition of the Proceeding shall be made only upon receipt of an undertaking by the Indemnitee to repay all amounts advanced if it should be ultimately determined that the Indemnitee is not entitled to be indemnified under this Article X or otherwise.

10.3 Former Directors, Officers, Employees and Agents. Indemnification pursuant to this Article X shall continue as to an Indemnitee who has ceased to be a director, officer, employee or agent of the Corporation or member, manager or managing member of a predecessor limited liability company or affiliate of such limited liability company or a director, officer, employee, agent, partner, member, manager or fiduciary of, or to serve in any other capacity for, another corporation or any partnership, joint venture, limited liability company, trust, or other enterprise and shall inure to the benefit of his or her heirs, executors and administrators.

10.4 Claims. If a claim for indemnification (following the final disposition of the Proceeding with respect to which indemnification is sought, including any settlement of such Proceeding) or advancement of expenses under this Article X is not paid in full within sixty (60) days after a written claim therefor by the Indemnitee has been received by the Corporation, the Indemnitee may file suit to recover the unpaid amount of such claim and, if successful in whole or in part, shall be entitled to be paid the expense of prosecuting such claim to the fullest extent permitted by applicable law. In any such action the Corporation shall have the burden of proving that the Indemnitee is not entitled to the requested indemnification or advancement of expenses under this Article X and applicable law.

10.5 Non-Exclusivity of Rights. The rights conferred on any Indemnitee by this Article X shall not be exclusive of any other rights which such Indemnitee may have or hereafter acquire under any statute, the Certificate of Incorporation, these Bylaws, or any agreement, vote of stockholders or disinterested directors or otherwise.

10.6 Insurance. The Corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation or of a partnership, joint venture, trust or other enterprise, including service with respect to employee benefit plans, against any liability asserted against such person and incurred by such person in any such capacity, or arising out of such person's status as such, whether or not the Corporation would have the power to indemnify such person against such liability under this Article X, the DGCL or otherwise.

10.7 Amendment or Repeal. Any right to indemnification or to advancement of expenses of any Indemnitee arising hereunder shall not be eliminated or impaired by an amendment to or repeal of this Article X after the occurrence of the act or omission that is the subject of the Proceeding for which indemnification or advancement of expenses is sought.

10.8 Saving Clause. If this Article X or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Corporation shall nevertheless indemnify each director, officer, employee and agent to the fullest extent not prohibited by any applicable portion of this Article X that shall not have been invalidated, or by any other applicable law. If this Article X shall be invalid due to the application of the indemnification provisions of another jurisdiction, then the Corporation shall indemnify each director, officer, employee and agent to the fullest extent under any other applicable law.

ARTICLE XI
EXCLUSIVE JURISDICTION FOR CERTAIN ACTIONS

11.1 Exclusive Jurisdiction for Certain Actions. Unless the Corporation consents 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 behalf of the Corporation, (ii) any action asserting a claim for breach of a fiduciary duty owed by any director, officer, employee or agent of the Corporation to the Corporation or the Corporation's stockholders, (iii) any action asserting a claim arising pursuant to any provision of the DGCL, the Certificate of Incorporation or the Bylaws of the Corporation 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.

ARTICLE XII
AMENDMENTS

12.1 Amendments. The Board of Directors is expressly empowered to adopt, amend or repeal these Bylaws or adopt new Bylaws of the Corporation. Any adoption, amendment or repeal of these Bylaws or adoption of new Bylaws of the Corporation by the Board of Directors shall require the approval of a majority of the directors then in office. Notwithstanding the foregoing, the stockholders of the Corporation shall also have power to adopt, amend or repeal the Bylaws of the Corporation; provided, however, that, in addition to any vote of the holders of any class or series of stock of the Corporation required by law or by the Certificate of Incorporation, the affirmative vote of the holders of at least sixty-six and two-thirds percent (66-2/3%) of the voting power of all of the then-outstanding shares of the capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required to adopt, amend or repeal any provision of the Bylaws of the Corporation.

Adopted as of June 18, 2015.

Amended: January 8, 2016; March 18, 2022.

Exhibit 10.14

Diffusion Pharmaceuticals Inc.

February 22, 2023

Re: Separation from Employment and General Release

Dear Chris,

This letter agreement and general release (this "***Agreement***") sets forth the terms of your separation from employment with Diffusion Pharmaceuticals Inc. (together with its subsidiaries, "***Diffusion***" or the "***Company***") effective March 1, 2023 (the "***Separation Date***"). References in this Agreement to "you" and "your" refer to Dr. Christopher D. Galloway, M.D.

1. **Separation from Employment**. Your employment as the Company's Medical Officer, as well as your employment and all other positions you currently hold or held with the Company or any of its affiliates (including, without limitation, as a director, employee, officer or manager) terminate on the Separation Date. All benefits and perquisites of employment are ceased as of the Separation Date, except that you will receive, to the extent not already paid to you, the Accrued Benefits (as defined in your employment agreement with the Company, dated as of October 19, 2020 (as amended and/or restated from time to time, the "***Employment Agreement***")). All payments due to you from the Company or any of its affiliates from and after the date of this Agreement will be determined under the applicable provisions of this Agreement. You and the Company agree that you are not entitled to any further compensation or benefits from the Company or any of its affiliates other than (i) the Accrued Benefits, (ii) if applicable, the Separation Benefits (as defined below), and (iii) without duplication of any Accrued Benefits or Separation Benefits, the following:

    a. You will retain any vested balance in your Diffusion 401(k) account;

    b. You will be entitled to retain all Diffusion purchased computer and electronic equipment in your possession, provided that you must allow the Company the ability to remove/disconnect your access to Diffusion's systems and technology infrastructure; and

    c. Diffusion will not oppose any application for unemployment compensation you may make, if any.

    For the avoidance of doubt, the Accrued Benefits to be paid in accordance with the Employment Agreement include the following amounts:

    - a lump-sum cash payment (less applicable taxes and other withholdings) in respect of the cash portion of your base salary earned but unpaid through the Separation Date, paid in accordance with the Company's normal payroll policies;

    - a lump-sum cash payment of $47,801.21 (less applicable taxes and other withholdings and amounts in respect of any days utilized after the date of this letter and prior to the Separation Date) in respect of accrued but unused vacation in accordance with the Company's policies and applicable law; and

- any unreimbursed business expenses incurred by you prior to the Separation Date that are otherwise reimbursable in accordance with the Company's expense reimbursement policies.

2. **Separation Benefits**. Subject to your execution and non-revocation of this Agreement and your compliance with the terms of this Agreement and the terms of the Employment Agreement that survive the Separation Date as described below in Section 5(a), the Company will pay or provide you with the following payments and benefits, less applicable taxes and withholdings (collectively, such payments and benefits, the "***Separation Benefits***"):

    a. An amount equal to $293,906, representing nine months of your current base salary, to be paid as a lump-sum on the first Company payroll date after the Effective Date (as defined below);

    b. An amount equal to $25,767, representing your target annual bonus for the 2023 calendar year multiplied by a fraction (A) the numerator of which is 60 (i.e., the number of days during calendar year 2023 on which you served as the Company's 365, and (B) the denominator of which is 365, to be paid in cash as a lump-sum on the first Company payroll date after the Effective Date (as defined below);

    c. In lieu of the COBRA Benefit (as defined in your Employment Agreement), an amount equal to $35,534, representing potential future premium payments for continued coverage in Diffusion's group health plans pursuant to Virginia Code §38.2-3541 (the "***Virginia Mini-COBRA Law***"), to be paid in cash as a lump-sum on the first Company payroll date after the Effective Date (as defined below);

    d. You will retain all options to purchase shares of Diffusion common stock granted to you under Diffusion's equity incentive plans that have vested as of the Separation Date, which, in accordance with the terms of your previously granted option award agreements, will remain exercisable for a period of three (3) months after the Separation Date.

3. **Virginia Mini-COBRA Law**. If timely elected, you and your eligible dependents may be eligible for continuation or conversion coverage under Diffusion's group health plans pursuant to the Virginia Mini-COBRA Law. **IF YOU WISH TO CONTINUE COVERAGE UNDER THE VIRGINIA MINI-COBRA LAW, IT IS ESSENTIAL THAT YOU PROPERLY AND TIMELY ELECT SUCH COVERAGE IN ACCORDANCE WITH THE INSTRUCTIONS THAT WILL BE PROVIDED BY DIFFUSION'S THIRD-PARTY ADMINISTRATOR FOLLOWING THE SEPARATION DATE. DIFFUSION CANNOT MAKE THIS ELECTION FOR YOU.**

4. **Complete General Release of Claims**.

a. In consideration of the Separation Benefits, and other good and valuable consideration to which you would not otherwise be entitled, you (on behalf of yourself, and your heirs, executors, and assigns) hereby irrevocably release and discharge the Company and its past, present and future subsidiaries, divisions, affiliates and parents; each of their respective current and former officers, directors, shareholders, employees, attorneys, agents, benefit plans, and/or owners, in their individual and official capacities; and any other person or entity claimed to be jointly or severally liable with the Company or any of the aforementioned persons or entities (the "***Released Parties***") from any and all claims and/or causes of action, known or unknown, contingent or noncontingent, accrued or unaccrued, which you may have or could claim to have against any of the Released Parties up to and including the date you sign this Agreement. The general release in this paragraph includes, but is not limited to: (i) all claims arising from or during your employment or service, or as a result of the termination of your employment or service, in any case, with any of the Released Parties; (ii) all claims arising under the Employment Agreement; (iii) all claims arising under any Plan or any of the Options; (iv) any other claims for unpaid or withheld wages, severance, paid time off or vacation pay, benefits, bonuses and/or other compensation of any kind, including claims arising under any Diffusion equity incentive plan or equity-based awards granted to you thereunder; (v) any other claims of retaliation or wrongful discharge, or of discrimination and/or harassment based on sex, race, religion, color, creed, disability, handicap, citizenship, national origin, age or any other factor prohibited by federal, state or local law, including, without limitation, such as Title VII of the Civil Rights Act, the Age Discrimination in Employment Act, the Older Workers Benefit Protection Act, and/or the Americans with Disabilities Act; (vi) any claims under the Corporate and Criminal Fraud Accountability Act of 2002 (also known as the Sarbanes Oxley Act), the Employee Retirement Income Security Act, or the Family and Medical Leave Act; (vii) any claims under Title 40 of the Virginia Code, the Virginia Equal Pay Act, the Virginia Human Rights Act, the Virginia Labor and Employment Code, the Virginians with Disabilities Act, the Virginia whistleblower statute (Va. Code Ann § 40.1-27.3), the Virginia wage payment law (Va. Code Ann § 40.1-29 et seq.); (viii) any claims under the Delaware Discrimination in Employment Act, the Delaware Persons with Disabilities Employment Protections Act, the Delaware Whistleblowers' Protection Act, the Delaware jury duty leave law (Del. Code Ann. tit. 10, § 4515), the Delaware polygraph testing statute (Del. Code Ann. tit. 19, § 704), the Delaware telephone, electronic mail, and Internet monitoring statute (Del. Code Ann. tit. 19, § 705), the Delaware social media statute (Del. Code Ann. tit. 19, § 709A), the Delaware compensation history statute (Del. Code Ann. tit. 19, § 709B); (ix) all claims arising under any similar federal, state, or local statute, rule, regulation or ordinance, or under the common law, of any other jurisdiction; (x) all claims for attorneys' fees, costs, or expenses; and (xi) any other statutory or common law claims, now existing or hereinafter recognized, including, but not limited to, breach of contract, quasi-contract, detrimental reliance, libel, slander, fraud, wrongful discharge, promissory estoppel, equitable estoppel, misrepresentation, or intentional infliction of emotional distress.

b. The release in Section 4(a) (the "***Release***") applies fully to protect the past, present, and future directors, officers, employees, stockholders, attorneys, and other agents of Diffusion, as well as its affiliates, the directors, officers, employees, attorneys, and other agents of such affiliates, and any benefit plans of Diffusion and/or its affiliates. Further, the Release applies fully to release the rights of your heirs, agents, successors, assigns, and spouse (if any) concerning the matters described therein. It is the intention of you and the Company that the language relating to the description of released claims in this Agreement shall be given the broadest possible interpretation permitted by law. It is understood that nothing in this Agreement is to be construed as an admission on behalf of any of the Released Parties of any wrongdoing (with any such wrongdoing being expressly denied).

c. Notwithstanding the foregoing, the Release shall not apply to, and you are not releasing, any claims (i) in respect of any of your rights under this Agreement (including, without limitation, to the Separation Benefits); (ii) relating to your right to receive workers' compensation benefits; (iii) relating to your right to continue your group health benefits in accordance with the Virginia Mini-COBRA Law; (iv) relating to any express right you have to indemnification for acts performed or omissions while an officer, employee, director or manager of the Company or any of its subsidiaries, as provided under the organizational documents of the Company or such subsidiary, under any applicable insurance policy or otherwise; and (v) that cannot be waived as a matter of law. Furthermore, for the avoidance of doubt, nothing in the Release or otherwise in this Agreement shall restrict your rights to (x) make disclosures specifically required under applicable law or (y) provide truthful statements or testimony before, or otherwise assist in any investigation or proceeding brought by, any self-regulatory organization, state or federal regulatory authority, administrative agency, of Diffusion's internal compliance department regarding your employment with Diffusion, unlawful employment practices, or any other possible violations of applicable laws, rules, or regulations.

5. **Covenant Not to Sue**.

a. You agree and covenant not to institute or join any lawsuit (either individually, with others, or as part of a class), in any forum, pleading, raising, or asserting any claim(s) barred or released by this Agreement.

b. Notwithstanding Section 5(a), you understand that nothing in this Agreement precludes you from filing a charge with, cooperating with, communicating with, or providing information to, the U.S. Equal Employment Opportunity Commission, U.S. Securities and Exchange Commission, or other government agency, or in connection with any proceedings by any such agency. You agree, however, that you will not seek or accept any relief obtained on your behalf by any government agency, private party, class, or otherwise with respect to any claims released in this Agreement, provided that this Agreement does not limit your right to receive an award for information provided to any government agency.

6. **Continuing Obligations**.

a. Surviving Provisions of the Employment Agreement. The Employment Agreement is terminated effective as of the Separation Date, but you acknowledge and agree that you remain bound by (i) Section 2.1, (ii) Sections 4.3 through 4.17, (iii) Article 5, and (iv) any corresponding definitions in Article 1, in each case, of the Employment Agreement in accordance with their terms, each of which remain in effect notwithstanding the termination of the Employment Agreement.

b. Return of Property. Subject to Section 1(b) above, you represent that you have returned (and have not retained) in good working condition any and all property, equipment, documents, and other information, confidential or otherwise, of the Company or any of its affiliates that was in your possession, custody, or control.

c. Material Non-Public Information. You acknowledge that the Company is a reporting company under the Securities Exchange Act of 1934, as amended, and its equity securities are currently traded on the NASDAQ Capital Market. You hereby acknowledge and agree that you shall not (i) trade in the securities of the Company while in possession of material, non-public information regarding the Company or (ii) communicate any such information to any other person under circumstances in which it is reasonably foreseeable that such person is likely to purchase or sell such securities.

d. Confidential Information. You will continue to protect and will not disclose to any person or other third-party any of Diffusion's confidential or proprietary information of which you are aware.

e. Supplemental Separation Agreement and Release. If you sign this Agreement prior to the Separation Date, you agree (i) you will continue to diligently and conscientiously devote the your business time, attention, energy, skill, and best efforts to the business and affairs of Diffusion through the Separation Date, (ii) to sign a Supplemental Separation Agreement and General Release which will restate the terms of the Release through and including the Separation Date and (iii) that Diffusion's obligations with respect to the Separation Payment will not apply until and unless you sign such Supplemental Separation Agreement and General Release.

7. **Miscellaneous**.

a. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Virginia, irrespective of conflicts of law principles, and you and the Company hereby agree that all disputes arising under or relating to this Agreement, your employment or other service with the Company or any of its affiliates or the termination thereof, in each case, shall be resolved in accordance with Sections 5.2 and 5.3 of the Employment Agreement (including, without limitation, the **WAIVER OF JURY TRIAL** provision set forth therein).

b. This Agreement is solely for the purpose of resolving and concluding amicably all possible matters between you and Diffusion and nothing in this Agreement shall be construed as an admission or concession of liability or wrongdoing by you or by Diffusion.

c. This Agreement embodies the complete understanding and agreement between you and Diffusion, and, except to the extent explicitly set forth herein with respect to the Employment Agreement, supersedes any and all prior agreements, oral or written, express or implied, except that this Agreement does not supersede or affect any prior agreement between you and Diffusion concerning Diffusion's confidential information.

d. This Agreement may not be modified, supplemented, or terminated without the express written consent of both you and Diffusion, making specific reference to this Agreement. Should any provision of this Agreement be declared illegal or unenforceable by any court of competent jurisdiction and cannot be modified to be enforceable, such provision shall immediately become null and void, leaving the remainder of this Agreement in full force and effect.

e. The Company, but not you, may assign its rights and obligations under this Agreement, and such rights and obligations inure to the benefit of, and are binding upon, the Company ' s successors and assigns. You and the Company intend that the terms of this Agreement be considered severable, such that if any provision of this Agreement is adjudged to be invalid for whatever reason, such invalidity will not affect any other provision of this Agreement, and such other provisions will remain in full force and effect. The principle of construction that all ambiguities are to be construed against the drafter will not be employed in the interpretation of this Agreement. Rather, it is agreed that this Agreement should not be construed for or against any party. The captions of this Agreement are not part of the provisions hereof and shall have no force or effect. This Agreement may be executed in counterparts and delivered by facsimile transmission or electronic transmission in "portable document format," each of which shall be an original and which taken together shall constitute one and the same document.

8. **Acknowledgements**. You acknowledge, represent, covenant, and agree that:

- you have read carefully the terms of this Agreement, including the Release;
- you have had an opportunity to and have been encouraged to review this Agreement, including the Release, with an attorney;
- you understand the meaning and effect of the terms of this Agreement, including the Release;
- you were given as much time as you needed – and in no event less than twenty-one (21) days – to determine whether you wished to enter into this Agreement, including the Release;
- your entry into and execution of this Agreement, including the Release, is your own free and voluntary act without compulsion of any kind; and
- no promise or inducement to enter into this Agreement not expressed herein has been made to you.

9. **Effective Date**. You may revoke this Agreement for a period of seven (7) days following the day you sign it. If you choose to revoke this Agreement following execution, you must do so in writing, the writing must be received by Diffusion via e-mail to the Company's General Counsel, and it must be received by Diffusion within that seven (7) day period. Accordingly, this Agreement shall not become effective or enforceable until 12:00 a.m. on the eighth (8th) day following your signature hereof (the "***Effective Date***").

[*Remainder of Page Intentionally Left Blank*]

By signing this Agreement, you acknowledge that you have carefully reviewed this Agreement, that you have had an opportunity to consult with counsel of your choice, that you have entered into this Agreement freely and voluntarily and without reliance on any promises not expressly contained herein, that you have been afforded an adequate time to review carefully the terms of this Agreement, and that this Agreement will not be deemed void or avoidable by claims of duress, deception, mistake of fact or otherwise.

Sincerely,

DIFFUSION PHARMACEUTICALS INC.

/s/ Robert J. Cobuzzi
Robert J. Cobuzzi, Jr., Ph.D.
Chief Executive Officer

I have reviewed the Agreement as set forth above, I understand the Agreement, and, intending to be legally bound by my signature below, knowingly, and voluntarily accept all its terms and conditions.

/s/ Christopher D. Galloway
Name: Christopher D. Galloway, M.D.

March 1, 2023
Date

Exhibit 10.15

Diffusion Pharmaceuticals Inc.

February 16, 2023

Re: Separation from Employment and General Release

Dear Raven,

This letter agreement and general release (this "***Agreement***") sets forth the terms of your separation from employment with Diffusion Pharmaceuticals Inc. (together with its subsidiaries, "***Diffusion***" or the "***Company***") effective March 1, 2023 (the "***Separation Date***"). References in this Agreement to "you" and "your" refer to Ms. Raven Jaeger, M.S.

1. **Separation from Employment**. Your employment as the Company's Regulatory Officer, as well as your employment and all other positions you currently hold or held with the Company or any of its affiliates (including, without limitation, as a director, employee, officer or manager) terminate on the Separation Date. All benefits and perquisites of employment are ceased as of the Separation Date, except that you will receive, to the extent not already paid to you, the Accrued Benefits (as defined in your employment agreement with the Company, dated as of May 18, 2022 (as amended and/or restated from time to time, the "***Employment Agreement***")). All payments due to you from the Company or any of its affiliates from and after the date of this Agreement will be determined under the applicable provisions of this Agreement. You and the Company agree that you are not entitled to any further compensation or benefits from the Company or any of its affiliates other than (i) the Accrued Benefits, (ii) if applicable, the Separation Benefits (as defined below), and (iii) without duplication of any Accrued Benefits or Separation Benefits, the following:

    a. You will retain any vested balance in your Diffusion 401(k) account;

    b. You will be entitled to retain all Diffusion purchased computer and electronic equipment in your possession, provided that you must allow the Company the ability to remove/disconnect your access to Diffusion's systems and technology infrastructure; and

    c. Diffusion will not oppose any application for unemployment compensation you may make, if any

2. **Separation Benefits**. Subject to your execution and non-revocation of this Agreement and your compliance with the terms of this Agreement and the terms of the Employment Agreement that survive the Separation Date as described below in Section 5(a), the Company will pay or provide you with the following payments and benefits, less applicable taxes and withholdings (collectively, such payments and benefits, the "***Separation Benefits***"):

    a. An amount equal to $300,000, representing nine months of your current base salary, to be paid as a lump-sum on the first Company payroll date after the Effective Date (as defined below);

b. An amount equal to $23,014, representing your target annual bonus for the 2023 calendar year multiplied by a fraction (A) the numerator of which is 60 (i.e., the number of days during calendar year 2023 on which you served as the Company's 365, and (B) the denominator of which is 365, to be paid in cash as a lump-sum on the first Company payroll date after the Effective Date (as defined below);

c. In lieu of the COBRA Benefit (as defined in your Employment Agreement), an amount equal to $68,989, representing potential future premium payments for continued coverage in Diffusion's group health plans pursuant to Virginia Code §38.2-3541 (the "***Virginia Mini-COBRA Law***"), to be paid in cash as a lump-sum on the first Company payroll date after the Effective Date (as defined below);

d. You will retain all options to purchase shares of Diffusion common stock granted to you under Diffusion's equity incentive plans that have vested as of the Separation Date, which, in accordance with the terms of your previously granted option award agreements, will remain exercisable for a period of three (3) months after the Separation Date.

3. **Virginia Mini-COBRA Law**. If timely elected, you and your eligible dependents may be eligible for continuation or conversion coverage under Diffusion's group health plans pursuant to the Virginia Mini-COBRA Law. **IF YOU WISH TO CONTINUE COVERAGE UNDER THE VIRGINIA MINI-COBRA LAW, IT IS ESSENTIAL THAT YOU PROPERLY AND TIMELY ELECT SUCH COVERAGE IN ACCORDANCE WITH THE INSTRUCTIONS THAT WILL BE PROVIDED BY DIFFUSION'S THIRD-PARTY ADMINISTRATOR FOLLOWING THE SEPARATION DATE. DIFFUSION CANNOT MAKE THIS ELECTION FOR YOU.**

4. **Complete General Release of Claims**.

a. In consideration of the Separation Benefits, and other good and valuable consideration to which you would not otherwise be entitled, you (on behalf of yourself, and your heirs, executors, and assigns) hereby irrevocably release and discharge the Company and its past, present and future subsidiaries, divisions, affiliates and parents; each of their respective current and former officers, directors, shareholders, employees, attorneys, agents, benefit plans, and/or owners, in their individual and official capacities; and any other person or entity claimed to be jointly or severally liable with the Company or any of the aforementioned persons or entities (the "***Released Parties***") from any and all claims and/or causes of action, known or unknown, contingent or noncontingent, accrued or unaccrued, which you may have or could claim to have against any of the Released Parties up to and including the date you sign this Agreement. The general release in this paragraph includes, but is not limited to: (i) all claims arising from or during your employment or service, or as a result of the termination of your employment or service, in any case, with any of the Released Parties; (ii) all claims arising under the Employment Agreement; (iii) all claims arising under any Plan or any of the Options; (iv) any other claims for unpaid or withheld wages, severance, paid time off or vacation pay, benefits, bonuses and/or other compensation of any kind, including claims arising under any Diffusion equity incentive plan or equity-based awards granted to you thereunder; (v) any other claims of retaliation or wrongful discharge, or of discrimination and/or harassment based on sex, race, religion, color, creed, disability, handicap, citizenship, national origin, age or any other factor prohibited by federal, state or local law, including, without limitation, such as Title VII of the Civil Rights Act, the Age Discrimination in Employment Act, the Older Workers Benefit Protection Act, and/or the Americans with Disabilities Act; (vi) any claims under the Corporate and Criminal Fraud Accountability Act of 2002 (also known as the Sarbanes Oxley Act), the Employee Retirement Income Security Act, or the Family and Medical Leave Act; (vii) any claims under Title 40 of the Virginia Code, the Virginia Equal Pay Act, the Virginia Human Rights Act, the Virginia Labor and Employment Code, the Virginians with Disabilities Act, the Virginia whistleblower statute (Va. Code Ann § 40.1-27.3), the Virginia wage payment law (Va. Code Ann § 40.1-29 et seq.); (viii) any claims under the Delaware Discrimination in Employment Act, the Delaware Persons with Disabilities Employment Protections Act, the Delaware Whistleblowers' Protection Act, the Delaware jury duty leave law (Del. Code Ann. tit. 10, § 4515), the Delaware polygraph testing statute (Del. Code Ann. tit. 19, § 704), the Delaware telephone, electronic mail, and Internet monitoring statute (Del. Code Ann. tit. 19, § 705), the Delaware social media statute (Del. Code Ann. tit. 19, § 709A), the Delaware compensation history statute (Del. Code Ann. tit. 19, § 709B); (ix) all claims arising under any similar federal, state, or local statute, rule, regulation or ordinance, or under the common law, of any other jurisdiction; (x) all claims for attorneys' fees, costs, or expenses; and (xi) any other statutory or common law claims, now existing or hereinafter recognized, including, but not limited to, breach of contract, quasi-contract, detrimental reliance, libel, slander, fraud, wrongful discharge, promissory estoppel, equitable estoppel, misrepresentation, or intentional infliction of emotional distress.

b. The release in Section 4(a) (the "***Release***") applies fully to protect the past, present, and future directors, officers, employees, stockholders, attorneys, and other agents of Diffusion, as well as its affiliates, the directors, officers, employees, attorneys, and other agents of such affiliates, and any benefit plans of Diffusion and/or its affiliates. Further, the Release applies fully to release the rights of your heirs, agents, successors, assigns, and spouse (if any) concerning the matters described therein. It is the intention of you and the Company that the language relating to the description of released claims in this Agreement shall be given the broadest possible interpretation permitted by law. It is understood that nothing in this Agreement is to be construed as an admission on behalf of any of the Released Parties of any wrongdoing (with any such wrongdoing being expressly denied).

c. Notwithstanding the foregoing, the Release shall not apply to, and you are not releasing, any claims (i) in respect of any of your rights under this Agreement (including, without limitation, to the Separation Benefits); (ii) relating to your right to receive workers' compensation benefits; (iii) relating to your right to continue your group health benefits in accordance with the Virginia Mini-COBRA Law; (iv) relating to any express right you have to indemnification for acts performed or omissions while an officer, employee, director or manager of the Company or any of its subsidiaries, as provided under the organizational documents of the Company or such subsidiary, under any applicable insurance policy or otherwise; and (v) that cannot be waived as a matter of law. Furthermore, for the avoidance of doubt, nothing in the Release or otherwise in this Agreement shall restrict your rights to (x) make disclosures specifically required under applicable law or (y) provide truthful statements or testimony before, or otherwise assist in any investigation or proceeding brought by, any self-regulatory organization, state or federal regulatory authority, administrative agency, of Diffusion's internal compliance department regarding your employment with Diffusion, unlawful employment practices, or any other possible violations of applicable laws, rules, or regulations.

5. **Covenant Not to Sue**.

   a. You agree and covenant not to institute or join any lawsuit (either individually, with others, or as part of a class), in any forum, pleading, raising, or asserting any claim(s) barred or released by this Agreement.

   b. Notwithstanding Section 5(a), you understand that nothing in this Agreement precludes you from filing a charge with, cooperating with, communicating with, or providing information to, the U.S. Equal Employment Opportunity Commission, U.S. Securities and Exchange Commission, or other government agency, or in connection with any proceedings by any such agency. You agree, however, that you will not seek or accept any relief obtained on your behalf by any government agency, private party, class, or otherwise with respect to any claims released in this Agreement, provided that this Agreement does not limit your right to receive an award for information provided to any government agency.

6. **Continuing Obligations**.

   a. Surviving Provisions of the Employment Agreement. The Employment Agreement is terminated effective as of the Separation Date, but you acknowledge and agree that you remain bound by (i) Section 2.1, (ii) Sections 4.3 through 4.17, (iii) Article 5, and (iv) any corresponding definitions in Article 1, in each case, of the Employment Agreement in accordance with their terms, each of which remain in effect notwithstanding the termination of the Employment Agreement.

   b. Return of Property. Subject to Section 1(b) above, you represent that you have returned (and have not retained) in good working condition any and all property, equipment, documents, and other information, confidential or otherwise, of the Company or any of its affiliates that was in your possession, custody, or control.

   c. Material Non-Public Information. You acknowledge that the Company is a reporting company under the Securities Exchange Act of 1934, as amended, and its equity securities are currently traded on the NASDAQ Capital Market. You hereby acknowledge and agree that you shall not (i) trade in the securities of the Company while in possession of material, non-public information regarding the Company or (ii) communicate any such information to any other person under circumstances in which it is reasonably foreseeable that such person is likely to purchase or sell such securities.

   d. Confidential Information. You will continue to protect and will not disclose to any person or other third-party any of Diffusion's confidential or proprietary information of which you are aware.

e. Supplemental Separation Agreement and Release. If you sign this Agreement prior to the Separation Date, you agree (i) you will continue to diligently and conscientiously devote the your business time, attention, energy, skill, and best efforts to the business and affairs of Diffusion through the Separation Date, (ii) to sign a Supplemental Separation Agreement and General Release which will restate the terms of the Release through and including the Separation Date and (iii) that Diffusion's obligations with respect to the Separation Payment will not apply until and unless you sign such Supplemental Separation Agreement and General Release.

7. **Miscellaneous**.

a. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Virginia, irrespective of conflicts of law principles, and you and the Company hereby agree that all disputes arising under or relating to this Agreement, your employment or other service with the Company or any of its affiliates or the termination thereof, in each case, shall be resolved in accordance with Sections 5.2 and 5.3 of the Employment Agreement (including, without limitation, the **WAIVER OF JURY TRIAL** provision set forth therein).

b. This Agreement is solely for the purpose of resolving and concluding amicably all possible matters between you and Diffusion and nothing in this Agreement shall be construed as an admission or concession of liability or wrongdoing by you or by Diffusion.

c. This Agreement embodies the complete understanding and agreement between you and Diffusion, and, except to the extent explicitly set forth herein with respect to the Employment Agreement, supersedes any and all prior agreements, oral or written, express or implied, except that this Agreement does not supersede or affect any prior agreement between you and Diffusion concerning Diffusion's confidential information.

d. This Agreement may not be modified, supplemented, or terminated without the express written consent of both you and Diffusion, making specific reference to this Agreement. Should any provision of this Agreement be declared illegal or unenforceable by any court of competent jurisdiction and cannot be modified to be enforceable, such provision shall immediately become null and void, leaving the remainder of this Agreement in full force and effect.

e. The Company, but not you, may assign its rights and obligations under this Agreement, and such rights and obligations inure to the benefit of, and are binding upon, the Company ' s successors and assigns. You and the Company intend that the terms of this Agreement be considered severable, such that if any provision of this Agreement is adjudged to be invalid for whatever reason, such invalidity will not affect any other provision of this Agreement, and such other provisions will remain in full force and effect. The principle of construction that all ambiguities are to be construed against the drafter will not be employed in the interpretation of this Agreement. Rather, it is agreed that this Agreement should not be construed for or against any party. The captions of this Agreement are not part of the provisions hereof and shall have no force or effect. This Agreement may be executed in counterparts and delivered by facsimile transmission or electronic transmission in "portable document format," each of which shall be an original and which taken together shall constitute one and the same document.

8. **Acknowledgements**. You acknowledge, represent, covenant, and agree that:

- you have read carefully the terms of this Agreement, including the Release;
- you have had an opportunity to and have been encouraged to review this Agreement, including the Release, with an attorney;
- you understand the meaning and effect of the terms of this Agreement, including the Release;
- you were given as much time as you needed – and in no event less than twenty-one (21) days – to determine whether you wished to enter into this Agreement, including the Release;
- your entry into and execution of this Agreement, including the Release, is your own free and voluntary act without compulsion of any kind; and
- no promise or inducement to enter into this Agreement not expressed herein has been made to you.

9. **Effective Date**. You may revoke this Agreement for a period of seven (7) days following the day you sign it. If you choose to revoke this Agreement following execution, you must do so in writing, the writing must be received by Diffusion via e-mail to the Company's General Counsel, and it must be received by Diffusion within that seven (7) day period. Accordingly, this Agreement shall not become effective or enforceable until 12:00 a.m. on the eighth (8th) day following your signature hereof (the "***Effective Date***").

[*Remainder of Page Intentionally Left Blank*]

By signing this Agreement, you acknowledge that you have carefully reviewed this Agreement, that you have had an opportunity to consult with counsel of your choice, that you have entered into this Agreement freely and voluntarily and without reliance on any promises not expressly contained herein, that you have been afforded an adequate time to review carefully the terms of this Agreement, and that this Agreement will not be deemed void or avoidable by claims of duress, deception, mistake of fact or otherwise.

Sincerely,

DIFFUSION PHARMACEUTICALS INC.

/s/ Robert J. Cobuzzi
Robert J. Cobuzzi, Jr., Ph.D.
Chief Executive Officer

I have reviewed the Agreement as set forth above, I understand the Agreement, and, intending to be legally bound by my signature below, knowingly, and voluntarily accept all its terms and conditions.

/s/ Raven Jaeger
Name: Raven Jaeger, M.S.

March 1, 2023
Date

Exhibit 21.1

SIGNIFICANT SUBSIDIARIES OF THE REGISTRANT

Name of Subsidiary	State or Other Jurisdiction of Incorporation or Organization	Direct or Indirect Ownership Interest by Company
Canterbury Laboratories, LLC	DE	100%
Hygeia Therapeutics, Inc.	DE	100%
Diffusion Pharmaceuticals LLC	VA	100%

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statements (Nos. 333-206408, 333-206409, 333-218060, 333-2267182, 333-233381, 333-238233, 333-258760 and 333-266827) on Form S-8, (Nos. 333-222203, 333-233686, 333-234234, 333-235670, and 333-238818) on Form S-1, and (Nos. 333-218062, 333-222879, 333-231541, and 333-249057) on Form S-3 of our report dated March 24, 2023, with respect to the consolidated financial statements of Diffusion Pharmaceuticals Inc.

/s/ KPMG LLP

McLean, Virginia
March 24, 2023

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO SECTION 302 OF THE SARBANES OXLEY ACT OF 2002 AND SEC RULE 13a-14(a)

I, Robert J. Cobuzzi, Jr., Ph.D., certify that:

1. I have reviewed this annual report on Form 10-K of Diffusion Pharmaceuticals Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 24, 2023

/s/ Robert J. Cobuzzi, Jr., Ph.D.
Robert J. Cobuzzi, Jr., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO SECTION 302 OF THE SARBANES OXLEY ACT OF 2002 AND SEC RULE 13a-14(a)

I, William K. Hornung, certify that:

1. I have reviewed this annual report on Form 10-K of Diffusion Pharmaceuticals Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 24, 2023

/s/ William K. Hornung
William K. Hornung
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Diffusion Pharmaceuticals Inc. (the "Company") for the period ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), we, Robert J. Cobuzzi, Jr., Ph.D. and William K. Hornung, President and Chief Executive Officer and Chief Financial Officer, respectively, of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to our knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Robert J. Cobuzzi, Jr., Ph.D
Robert J. Cobuzzi, Jr., Ph.D
President and Chief Executive Officer
March 24, 2023

/s/ William K. Hornung
William K. Hornung
Chief Financial Officer (Principal Financial and Accounting Officer)
March 24, 2023