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

FORM 10-Q

(Mark one)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended March 31, 2021

☐ **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 of other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

1317 Carlton Avenue, Suite 200
Charlottesville, VA 22902
(Address of principal executive offices, including zip code)

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

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 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, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

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

The number of shares of common stock outstanding at May 7, 2021 was 101,903,979 shares.

DIFFUSION PHARMACEUTICALS INC.
FORM 10-Q
MARCH 31, 2021

INDEX

Note Regarding Company References and Other Defined Terms

Unless the context otherwise requires, in this Quarterly Report, (i) references to the "Company," "we," "our," or "us" refer to Diffusion Pharmaceuticals Inc. and its subsidiaries and (ii) references to "common stock" refer to the common stock, par value $0.001 per share, of the Company. We have also used several other defined terms in this Quarterly Report, many of which are explained or defined below:

Term	Definition
2015 Equity Plan	Diffusion Pharmaceuticals Inc. 2015 Equity Incentive Plan, as amended
2017 Tax Act	Tax Cuts and Jobs Act of 2017
401(k) Plan	Diffusion Pharmaceuticals Inc. 401(k) Defined Contribution Plan
Annual Report	our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 16, 2021
ASC	Accounting Standard Codification of the FASB
ASUs	Accounting Standards Updates of the FASB
COVID-19	Corona Virus Disease 2019, the novel coronavirus disease known as COVID-19, caused by SARS-CoV-2 infection
CRO	contract research organization
December 2019 Offering	our registered direct public offering and sale of 6,266,787 shares of common stock and concurrent private placement of warrants to purchase up to 6,266,787 shares of common stock completed in December 2019
DLCO	diffusion capacity of lung for carbon monoxide
Exchange Act	Securities Exchange Act of 1934, as amended
FASB	Financial Accounting Standards Board
February 2021 Offering	our public offering and sale of 33,658,538 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
January 2018 Offering	our public offering and sale of 1,131,375 shares of common stock and warrants to purchase up to 1,131,375 shares of common stock completed in January 2018
May 2019 Offering	our registered direct public offering and sale of 1,317,060 shares of common stock and concurrent private placement of warrants to purchase up to 1,317,060 shares of common stock completed in May 2019
May 2020 Investor Warrant Exercise	the exercise of the Prior Warrant in May 2020 pursuant to a warrant exercise agreement
May 2020 Offering	our registered direct public offering and sale of 11,428,572 shares of common stock completed in May 2020
Nasdaq	Nasdaq Stock Market, LLC
NOL	net operating loss
November 2019 Offering	our public offering and sale of 5,104,429 shares of common stock, pre-funded warrants to purchase up to 6,324,143 shares of common stock, and warrants to purchase up to 22,857,144 shares of common stock completed in November 2019
PaO2	partial pressure of blood oxygen
Planned Hypoxia-related Indication Trial(s)	one or more controlled, clinical outcome studies evaluating TSC in one or more appropriate hypoxia-related indications that we intend to initiate assuming success in one or more of the TSC Oxygenation Trials
Prior Warrant	a previously outstanding warrant to purchase up to 5,000,000 shares of common stock at an exercise price of $0.35 per share
Quarterly Report	this Quarterly Report on Form 10-Q
R&D	research and development
Regulation S-K	Regulation S-K promulgated under the Securities Act

SARS-CoV-2	severe acute respiratory syndrome coronavirus 2, the virus responsible for COVID-19
SEC	U.S. Securities and Exchange Commission
Securities Act	Securities Act of 1933, as amended
TCOM	transcutaneous oxygen measurement
TSC	trans sodium crocetinate
TSC COVID Trial	our Phase 1b clinical trial evaluating TSC in hospitalized COVID-19 patients, completed in February 2021
TSC DLCO Trial	our planned Phase 2a clinical trial evaluating the effects of TSC through the measure of DLCO through the lungs as a surrogate measure of oxygen transfer efficiency in patients with previously diagnosed interstitial lung disease who have a baseline DLCO test that is abnormal
TSC GBM Trial	our Phase 3 clinical trial evaluating TSC in a newly diagnosed inoperable GBM patient population initiated in December 2017
TSC Induced Hypoxia Trial	our planned Phase 1b clinical trial evaluating the effects of TSC on VO2 and PaO2 in normal healthy volunteers exposed to conditions that induce hypoxia
TSC Oxygenation Trials	collectively, the TSC TCOM Trial, the TSC Induced Hypoxia Trial, and the TSC DLCO Trial
TSC Stroke Trial	our Phase 2 clinical trial evaluating TSC in the treatment of acute ischemic or hemorrhagic stroke, initiated in October 2019
TSC TCOM Trial	our Phase 1b clinical trial evaluating the effects of TSC on peripheral tissue oxygenation in healthy normal volunteers using a TCOM device
U.S.	United States
VO2	maximal oxygen consumption

Note Regarding Forward-Looking Statements

This Quarterly 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 Quarterly 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 Quarterly Report. In addition, even if our results of operations, financial condition, liquidity, and prospects are consistent with the forward-looking statements contained in this Quarterly 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 Quarterly 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 concerning, among other things:

- the success and timing of our clinical and preclinical studies, including our ability to enroll subjects in our ongoing and planned clinical studies at anticipated rates;
- our ability to obtain and maintain regulatory approval of our product candidates and, if approved, our products, including the labeling under any approval we may obtain;
- our plans and ability to develop and commercialize our product candidates and the outcomes of our research and development activities;
- the accuracy of our estimates of the size and characteristics of the potential markets for our product candidates, the rate and degree of market acceptance of any of our product candidates that may be approved in the future, and our ability to serve those markets;
- the success of products that are or may become available which also target the potential markets for our product candidates;
- obtaining and maintaining intellectual property protection for our product candidates and our proprietary technology;
- our ability to operate our business without infringing the intellectual property rights of others and the potential for others to infringe upon our intellectual property rights;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the performance of third parties, including contract research organizations, manufacturers, suppliers, and outside consultants, to whom we outsource certain operational, staff and other functions;
- our ability to obtain additional financing in the future and continue as a going concern;
- our estimates regarding expenses, future revenues, capital requirements, and needs for additional financing;
- regulatory developments in the U.S., European Union, and other foreign jurisdictions;
- 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 U.S. Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act;
- any significant breakdown, infiltration, or interruption of our information technology systems and infrastructure;
- our ability to satisfy the continued listing requirements of the NASDAQ Capital Market or any other exchange on which our securities may trade in the future;
- uncertainties related to general economic, political, business, industry, and market conditions, including the ongoing COVID-19 pandemic; 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 Quarterly Report. Accordingly, we cannot assure you that the forward-looking statements contained or incorporated by reference in this Quarterly 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 risks 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 statements that we make in this Quarterly Report speak 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 Quarterly 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 Quarterly Report contains the following trademarks, trade names, and service marks of ours, "DIFFUSIO$_2$N." All other trade names, trademarks, and service marks appearing in this Quarterly 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 – FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

Diffusion Pharmaceuticals Inc.
Consolidated Balance Sheets
(unaudited)

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 46,634,977	$ 18,515,595
Prepaid expenses, deposits and other current assets	678,693	260,825
Total current assets	47,313,670	18,776,420
Property and equipment, net	124,751	149,198
Intangible asset	8,639,000	8,639,000
Right of use asset	120,110	149,162
Other assets	15,580	15,771
Total assets	$ 56,213,111	$ 27,729,551
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	952,909	545,844
Accrued expenses and other current liabilities	1,048,904	1,776,470
Current operating lease liability	111,291	113,469
Total current liabilities	2,113,104	2,435,783
Deferred income taxes	443,893	443,893
Noncurrent operating lease liability	8,819	35,693
Total liabilities	2,565,816	2,915,369
Commitments and Contingencies (Note 7)		
Stockholders' Equity:		
Common stock, $0.001 par value:		
Common stock, $0.001 par value: 1,000,000,000 shares authorized: 101,903,979 and 64,015,441 shares issued and outstanding at March 31, 2021 and December 31, 2020, respectively	101,904	64,016
Additional paid-in capital	164,098,694	130,659,550
Accumulated deficit	(110,553,303)	(105,909,384)
Total stockholders' equity	53,647,295	24,814,182
Total liabilities and stockholders' equity	$ 56,213,111	$ 27,729,551

See accompanying notes to unaudited interim consolidated financial statements.

Diffusion Pharmaceuticals Inc.
Consolidated Statements of Operations
(unaudited)

	Three Months Ended March 31,	
	2021	**2020**
Operating expenses:		
Research and development	$ 2,916,378	$ 1,534,467
General and administrative	1,743,510	1,393,808
Depreciation	24,447	27,020
Loss from operations	4,684,335	2,955,295
Other income:		
Interest income	(40,416)	(34,100)
Loss from operations before income tax benefit	(4,643,919)	(2,921,195)
Income tax benefit	—	(362,380)
Net loss	$ (4,643,919)	$ (2,558,815)
Per share information:		
Net loss per share of common stock, basic and diluted	$ (0.06)	$ (0.07)
Weighted average shares outstanding, basic and diluted	83,420,184	34,507,496

See accompanying notes to unaudited interim consolidated financial statements.

Diffusion Pharmaceuticals Inc.
Consolidated Statements of Changes in Stockholders' Equity
Three Months Ended March 31, 2020 and 2021
(unaudited)

	Stockholders' Equity				
	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount			
Balance at January 1, 2020	33,480,365	33,481	$ 111,824,859	$ (91,724,078)	20,134,262
Issuance of common stock upon exercise of warrants, net of issuance costs	1,124,071	1,124	133,674	—	134,798
Stock-based compensation expense	—	—	191,380	—	191,380
Net loss	—	—	—	(2,747,809)	(2,558,815)
Balance at March 31, 2020	34,604,436	$ 34,605	$ 112,149,913	$ (94,471,887)	$ 17,901,625

	Stockholders' Equity				
	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount			
Balance at January 1, 2021	64,015,441	64,016	$ 130,659,550	$ (105,909,384)	$ 24,814,182
Sale of common stock, net of issuance costs	33,658,538	33,658	31,060,644	—	31,094,302
Issuance of common stock upon exercise of warrants	4,230,000	4,230	2,197,220	—	2,201,450
Stock-based compensation expense	—	—	181,280	—	181,280
Net loss	—	—	—	(4,643,919)	(4,643,919)
Balance at March 31, 2021	101,903,979	$ 101,904	$ 164,098,694	$ (110,553,303)	$ 53,647,295

See accompanying notes to unaudited interim consolidated financial statements.

Diffusion Pharmaceuticals Inc.
Consolidated Statements of Cash Flows
(unaudited)

	Three Months Ended March 31,	
	2021	**2020**
Operating activities:		
Net loss	$ (4,643,919)	$ (2,558,815)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	24,447	27,020
Stock-based compensation expense	181,280	191,380
Change in deferred income taxes	—	(362,380)
Changes in operating assets and liabilities:		
Prepaid expenses, deposits and other assets	(417,677)	(346,030)
Accounts payable, accrued expenses and other liabilities	(320,501)	(455,489)
Net cash used in operating activities	(5,176,370)	(3,504,314)
Cash flows provided by financing activities:		
Proceeds from the sale of common stock, net of issuance costs	31,094,302	—
Proceeds received from the exercise of common stock warrants	2,201,450	393,425
Payment of financing costs that were previously classified in accounts payable	—	(238,232)
Net cash provided by financing activities	33,295,752	155,193
Net increase (decrease) in cash and cash equivalents	28,119,382	(3,349,121)
Cash and cash equivalents at beginning of period	18,515,595	14,177,349
Cash and cash equivalents at end of period	$ 46,634,977	$ 10,828,228
Supplemental disclosure of non-cash financing activities:		
Offering costs in accounts payable and accrued expenses	$ —	$ 258,627

See accompanying notes to unaudited interim consolidated financial statements.

1. Organization and Description of Business

Diffusion Pharmaceuticals Inc., a Delaware corporation, is an innovative biopharmaceutical company developing novel therapies that enhance the body's ability to deliver oxygen to the areas where it is needed most. The Company's lead product candidate, TSC, is being developed to enhance the diffusion of oxygen to tissues with low oxygen levels, also known as hypoxia, a serious complication of many of medicine's most intractable and difficult-to-treat conditions.

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

2. Liquidity

The Company has not generated any revenues from product sales and has funded operations primarily from the proceeds of public and private offerings of equity, convertible debt and convertible preferred stock. Substantial additional financing will be required by the Company to continue to fund its research and development activities. No assurance can be given that any such financing will be available when needed, or at all, or that the Company's research and development efforts will be successful.

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. The Company does not have any commitments to obtain additional funds and may be unable to obtain sufficient funding in the future on acceptable terms, if at all. If the Company cannot obtain the necessary funding, it will need to delay, scale back or eliminate some or all of its research and development programs or enter into collaborations with third parties to commercialize potential products or technologies that it might otherwise seek to develop or commercialize independently; consider other various strategic alternatives, including a merger or sale of the Company; or cease operations. If the Company engages in collaborations, it may receive lower consideration upon commercialization of such products than if it had not entered such arrangements or if it entered into such arrangements at later stages in the product development process.

Operations of the Company are subject to certain risks and uncertainties including various internal and external factors that will affect whether and when the Company's product candidates become approved drugs and how significant their market share will be, some of which are outside of the Company's control. The length of time and cost of developing and commercializing these product candidates and/or failure of them at any stage of the drug approval process will materially affect the Company's financial condition and future operations. The Company expects that its existing cash and cash equivalents as of March 31, 2021 will enable it to fund its operating expenses and capital expenditure requirements, including expected costs related to the planned TSC Oxygenation Trials and the Planned Hypoxia-related Indication Trials, through 2023.

3. Basis of Presentation and Summary of Significant Accounting Policies

The Summary of Significant Accounting Policies included in the Company's Annual Report for the year ended December 31, 2020 have not materially changed, except as set forth below.

Basis of Presentation

The accompanying unaudited interim consolidated financial statements of the Company have been prepared in accordance with GAAP for interim financial information as found in the ASC and ASUs of the FASB, and with the instructions to Form 10-Q and Article 10 of Regulation S-X promulgated by the SEC. In the opinion of management, the accompanying unaudited interim consolidated financial statements of the Company include all normal and recurring adjustments (which consist primarily of accruals, estimates and assumptions that impact the unaudited interim consolidated financial statements) considered necessary to present fairly the Company's financial position as of March 31, 2021, and its results of operations and cash flows for the three months ended March 31, 2021 and 2020. Operating results for the three months ended March 31, 2021 are not necessarily indicative of the results that may be expected for the year ending December 31, 2021. The unaudited interim consolidated financial statements presented herein do not contain the required disclosures under GAAP for annual financial statements. The accompanying unaudited interim consolidated financial statements should be read in conjunction with the annual audited financial statements and related notes as of and for the year ended December 31, 2020 filed with the SEC as part of the Company's Annual Report on Form 10-K on March 16, 2021.

Use of Estimate

The preparation of unaudited interim consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of assets and liabilities at the date the financial statements and reported amounts of expense during the reporting period. The COVID-19 pandemic had no material impact on the Company's estimates and assumptions used in the preparation of the unaudited interim consolidated financial statements for the quarterly period ended March 31, 2021. However, the full extent to which the ongoing COVID-19 pandemic will directly or indirectly impact the Company's business, results of operations and financial condition, including sales, expenses, reserves and allowances, clinical studies, research and development costs and employee-related amounts, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19, governmental and business responses to the pandemic, further actions taken to contain or treat COVID-19, the ongoing economic impact on local, regional, national and international markets, and the speed of the anticipated economic recovery. Due to the uncertainty of factors surrounding these estimates or judgments, actual results may materially vary from estimates. Estimates and assumptions are periodically reviewed, and the effects of revisions are reflected in the unaudited interim consolidated financial statements in the period they are determined. The Company's future assessment of the magnitude and duration of COVID-19, as well as other factors, could result in material impacts to the consolidated financial statements in future reporting periods.

Fair Value of Financial Instruments

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

Intangible Asset

The Company's DFN-529 (formerly RES-529) intangible asset is assessed for impairment annually on October 1 of the Company's fiscal year or more frequently if impairment indicators exist. There was no impairment to the Company's DFN-529 intangible asset recognized during the three months ended March 31, 2021 and 2020.

Net Loss Per Common Share

Basic net loss per share is computed by dividing net loss attributable to common stockholders 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 convertible debt, convertible preferred stock, 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 as of March 31, 2021 and 2020 have been excluded from the computation of diluted weighted average shares outstanding, as they would be anti-dilutive:

	March 31,	
	2021	2020
Common stock warrants	6,553,039	21,261,070
Stock options	3,116,819	1,182,629
Unvested restricted stock awards	153,000	98,100
	9,822,858	22,541,799

Recently Adopted Accounting Pronouncements

In December 2019, the FASB issued ASU No. 2019-12, Income Taxes (Topic 740): *Simplifying the Accounting for Income Taxes*. This guidance applies to all entities and aims to reduce the complexity of tax accounting standards while enhancing reporting disclosures. This guidance is effective for fiscal years beginning after December 15, 2020 and interim periods therein. 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.

4. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	March 31, 2021	December 31, 2020
Accrued payroll and payroll related expenses	$ 510,002	$ 653,899
Accrued professional fees	77,258	31,809
Accrued clinical studies expenses	406,439	1,055,398
Other accrued expenses	55,205	35,364
Total	$ 1,048,904	$ 1,776,470

5. Stockholders' Equity and Common Stock Warrants

February 2021 Common Stock Offering

In February 2021, the Company completed the February 2021 Offering in which it offered and sold 33,658,538 shares of its common stock in an underwritten public offering for a purchase price to the public of $1.025 per share, inclusive of shares offered and sold pursuant to the underwriter's fully-exercised 30-day option to purchase additional shares. The February 2021 Offering resulted in aggregate net proceeds to the Company of $31.1 million, after deducting underwriting commissions, discounts, expenses and other offering costs. In addition, at the closings of the February 2021 Offering, the Company issued to designees of the underwriter of the transaction warrants to purchase up to an aggregate of 1,682,927 shares of common stock. The underwriter warrants have an exercise price of $1.28125 per share and a term of five years from the date of issuance.

Common Stock Warrants

As of March 31, 2021, the Company had the following warrants to acquire shares of its common stock outstanding:

	Outstanding	Range of exercise price per share	Expiration dates
Common stock warrants issued in 2017 related to Series A convertible preferred stock offering	903,870	$33.30	March 2022
Common stock warrants issued in 2018 related to January 2018 Offering	1,181,421	$12.00 - $15.00	January 2023
Common stock warrants issued related to the May 2019 Offering	1,382,913	$5.00 - $6.11875	May and December 2024
Common stock warrants issued related to the November 2019 Offering	267,140	$0.35	May 2021 and November 2024
Common stock warrants issued related to the December 2019 Offering	313,339	$0.4335 - $0.6981	December 2024 and June 2025
Common stock warrants issued related to the May 2020 Offering	571,429	$1.31	March 2025
Common stock warrants issued related to the May 2020 Investor Warrant Exercise	250,000	$0.5938	November 2025
Common stock warrants issued related to the February 2021 Offering	1,682,927	$1.28	February 2026
	6,553,039		

During the three months ended March 31, 2021, no warrants expired, and warrants were exercised by multiple holders to purchase a total of 4,230,000 shares of the Company's common stock for aggregate proceeds of approximately $2.2 million.

6. 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, 2,560,618 shares were added to the reserve as of January 1, 2021, 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 March 31, 2021, there were 1,229,005 available for future issuance under the 2015 Equity Plan.

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

	Three Months Ended March 31,	
	2021	2020
Research and development	$ 33,000	$ 96,530
General and administrative	148,280	94,850
Total stock-based compensation expense	$ 181,280	$ 191,380

The following table summarizes the activity related to all stock option grants for the three months ended March 31, 2021:

	Number of Options	Weighted average exercise price per share	Weighted average remaining contractual life (in years)	Aggregate intrinsic value
Balance at January 1, 2021	2,240,204	$ 8.28		
Granted	876,615	1.11		
Outstanding at March 31, 2021	3,116,819	$ 6.26	9.01	$ 475,258
Exercisable at March 31, 2021	1,363,373	$ 13.10	8.25	$ 331,618
Vested and expected to vest at March 31, 2021	3,116,819	$ 6.26	9.01	$ 475,258

The weighted average grant date fair value of stock option awards granted was $1.06 during the three months ended March 31, 2021. The total fair value of options vested during the three months ended March 31, 2021 and 2020 was $0.2 million and $0.2 million, respectively. No options were exercised during any of the periods presented. At March 31, 2021, there was $1.4 million of unrecognized compensation expense that will be recognized over a weighted-average period of 2.29 years. During the three months ended March 31, 2021, the Company granted 385,267 performance-based stock options with an exercise price of $1.11 per share, subject to vesting based on the satisfaction of specified performance criteria. Compensation expense for the performance-based awards is recorded over the estimated service period for each milestone when the performance conditions are deemed probable of achievement. The Company recorded stock-based compensation expense of approximately $27,000 during the three months ended March 31, 2021, for service-based awards and performance conditions deemed probable of achievement and/or achieved. For performance-based awards containing performance conditions which were not deemed probable of achievement at March 31, 2021, no stock compensation expense was recognized.

Options granted were valued using the Black-Scholes-Merton derivative investment instrument pricing model and assumptions used to value the options granted during the three months ended March 31, 2021 were as follows:

Expected term (in years)	10
Risk-free interest rate	1.4%
Expected volatility	124.6%
Dividend yield	—

Restricted Stock Unit Awards

During the year ended December 31, 2020, the Company granted 153,000 restricted stock units to various members of the board of directors of the Company. The shares begin to vest 18 months after the grant date, none of which have vested as of March 31, 2021. The Company recognized approximately $5,000 in expense related to these awards during the three months ended March 31, 2021. At March 31, 2021, there was approximately $77,000 of unrecognized compensation cost that will be recognized over a weighted average period of 2.19 years.

7. Commitments and Contingencies

Office Space Lease Commitment

The Company has a non-cancelable operating lease for office and laboratory space in Charlottesville, Virginia, which began in April 2017 and, as of March 31, 2021, has a remaining lease term of approximately 1.1 years. The discount rate used to account for the Company's operating lease is the Company's estimated incremental borrowing rate of 10.0%. The original term of the lease ends in the second quarter of 2022 and the Company has an option to extend for another 5 years. This option to extend was not recognized as part of the Company's measurement of the right-of-use asset and operating lease liability as of March 31, 2021.

Rent expense related to the Company's operating lease was approximately $31,000 and $30,000 for the three months ended March 31, 2021 and 2020, respectively. Future minimum rental payments under the Company's non-cancelable operating lease at was as follows as of March 31, 2021:

	Rental Commitments
2021 (remaining)	89,232
2022	39,735
Total	128,967
Less: imputed interest	(8,857)
Current and noncurrent operating lease liability	$ 120,110

Research and Development Arrangements

In the course of normal business operations, the Company enters into agreements with universities and 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 its 401(k) Plan, which covers all employees who qualify under the terms of the plan. Eligible employees may elect to contribute to the 401(k) Plan up to 90.00% of their compensation, limited by the IRS-imposed maximum. The Company provides a safe harbor match with a maximum amount of 4.0% of the participant's compensation. The Company made matching contributions under the 401(k) Plan of approximately $16,000 and $17,000 for the three months ended March 31, 2021 and 2020, 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 hearing for the petition and motion 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 for November 2020. In August 2020, due to the ongoing COVID-19 pandemic and related restrictions on gatherings in the State of California, the arbitration hearing was postponed to August 16, 2021. The Company believes this matter is without merit and intends to defend the arbitration vigorously. However, at this stage, the Company is unable to predict its outcome and the 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 financial position.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion of our financial condition and results of operations together with the unaudited interim consolidated financial statements and the notes thereto included elsewhere in this report and other financial information included in this report. The following discussion may contain predictions, estimates and other forward-looking statements that involve a number of risks and uncertainties, including those discussed under "*Part I — Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations—Special Note Regarding Forward-Looking Statements*" in this report and under "*Part I — Item 1A. Risk Factors*" in our annual report on Form 10-K for the fiscal year ended December 31, 2020. These risks could cause our actual results to differ materially from any future performance suggested below.

Diffusion Pharmaceuticals: Enhancing Oxygen, Fueling Life

We are an innovative biopharmaceutical company developing novel therapies that enhance the body's ability to deliver oxygen to the areas where it is needed most. Our lead product candidate, TSC, is being developed to enhance the diffusion of oxygen to tissues with low oxygen levels, also known as hypoxia, a serious complication of many of medicine's most intractable and difficult-to-treat conditions. In addition to TSC, our product candidate DFN-529, a novel, allosteric PI3K/Akt/mTOR pathway inhibitor, is in early-stage development.

Highlights from the First Quarter of 2021

- ***Completion of Dosing in TSC TCOM Trial*** – In March 2021, we completed enrollment and dosing of all 30 participants in the first of our three Oxygenation Trials, the TSC TCOM Trial, a Phase 1 trial utilizing a transcutaneous oxygen monitoring device to evaluate the pharmacodynamic effects of TSC on peripheral tissue oxygenation. We anticipate collection and analysis of topline data from the TSC TCOM Trial will be completed and announced by the end of the second quarter of 2021.

- ***Completion of TSC COVID Trial*** - In February 2021, we completed dosing of the twenty-fourth and final patient in our TSC COVID Trial evaluating TSC in hospitalized COVID-19 patients and announced that the primary endpoint was met, with no dose-limiting toxicities or serious adverse events observed among any patients in the study, including those who received the highest dose of 1.5 mg/kg every 6 hours. Evaluation of secondary endpoint data from this safety and tolerability trial remains ongoing and we anticipate topline data from these secondary endpoint analyses will be completed and announced before the end of May 2021.

- ***February 2021 Equity Offering*** – In February 2021, we completed the February 2021 Offering, an underwritten, public offering of approximately 33.7 million shares of our common stock for a purchase price to the public of $1.025 per share, resulting in aggregate net proceeds to the Company of $31.1 million, after deducting underwriting commissions, discounts, expenses and other offering costs. As a result, combined with our other cash and cash equivalents as of March 31, 2021, we expect that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditures (including our planned clinical trials) through 2023.

TSC Development Update

In November 2020, we announced plans to modify the TSC development program with the intent of accomplishing two principal strategic objectives: 1) Optimize the clinical dose and dosing frequency for TSC; and 2) Evaluate TSC in clinical models designed to establish proof of concept for improvement in oxygenation. Given the totality of available data, including clinical data from the more than 200 subjects included in our TSC clinical studies to-date, we have initiated a plan to execute three, short-term TSC Oxygenation Trials during 2021, to be conducted in the U.S. and funded with cash-on-hand, to explore the relationship between TSC dose and change in oxygenation.

TSC TCOM Trial: TSC's Effects on Peripheral Tissue Oxygenation

The first of the three Oxygenation Trials was the TSC TCOM Trial, for which the treatment of study participants was both commenced and completed dosing in March 2021. The transcutaneous oxygen monitoring, device directly measures the release of oxygen from the blood vessels through the skin and is commonly used to predict the likelihood of wound healing, the potential for success with hyperbaric therapy, and to map the appropriate location for limb amputation. The study was a double-blind, randomized, placebo-controlled study in healthy volunteers breathing 100% oxygen designed to test single, ascending doses of TSC in an attempt to establish the dose-response relationship between TSC and enhanced oxygen delivery. Thirty healthy volunteers were enrolled and randomized into one of six subgroups with each subject receiving supplemental oxygen and a single intravenous dose of placebo or one of five different doses of TSC ranging from 0.5 mg/kg to 2.5 mg/kg in a before/after design. The study was designed and statistically powered to evaluate the pharmacodynamic effects of TSC on peripheral tissue oxygenation. We anticipate data collection and analyses from the TSC TCOM Trial will be completed and topline data will be announced by the end of the second quarter of 2021. Dosing data from the TSC TCOM Trial will also be used to guide dose selection for the TSC Induced Hypoxia Trial and TSC DLCO Trial.

TSC Induced Hypoxia Trial: TSC's Effects Under Induced Hypoxic Conditions

The second TSC Oxygenation Trial is our planned TSC Induced Hypoxia Trial, which will evaluate the effects of TSC on maximal oxygen consumption, or VO2, and partial pressure of blood oxygen, or PaO2, in normal healthy volunteers subjected to incremental levels of physical exertion while exposed to hypoxic and hypobaric conditions. The TSC Induced Hypoxia Trial is expected to be a double-blind, randomized, placebo-controlled study, and primary endpoints in the study will be change from baseline in VO2 and PaO2 after receiving a single intravenous dose of TSC. The study will be statistically powered to evaluate the difference in effect of TSC versus placebo on oxygen availability and consumption. We anticipate this study will be initiated and completed in the second half of 2021, with topline results available within two months of study completion.

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

The third TSC Oxygenation Trial is our planned TSC DLCO Trial, which will evaluate the effects of TSC on the diffusion of carbon monoxide through the lungs, also known as DLCO, in patients with previously diagnosed interstitial lung disease who have a baseline DLCO test result that is abnormal. DLCO testing is commonly performed as part of standard pulmonary function testing and aids in the diagnosis or dyspnea, also known as shortness of breath, as well as to track improvement or progression over time on prescribed treatments. DLCO provides a surrogate measure of oxygen transfer efficiency, or uptake, from the alveoli of the lungs, through the plasma, and onto hemoglobin within red blood cells. The TSC DLCO Trial is expected to be a double-blind, randomized, placebo-controlled study which will test varied doses of TSC in an attempt to establish the exposure-response relationship between TSC and oxygen transfer efficiency. The study will be statistically powered to evaluate the difference in effect of TSC versus placebo on improvement in DLCO. We anticipate this study will be initiated and completed in the second half of 2021, with topline results available within two months of study completion.

We believe positive data from any one or more of the three Oxygenation Trials would provide evidence of a definitive effect of TSC on oxygenation. If such positive data are obtained from one or more of the Oxygenation Trials, we expect to announce in the fourth quarter of 2021 the identity of up to two hypoxia-related indications in which TSC would be studied as part of our clinical development strategy aimed at supporting regulatory approval and commercialization of TSC. The plan would be to initiate the identified clinical studies in the first quarter of 2022.

Financial Summary

As of March 31, 2021, we had cash and cash equivalents of $46.6 million. We have incurred operating losses since inception, have not generated any product sales revenue and have not achieved profitable operations. We incurred a net loss of $4.6 million for the three months ended March 31, 2021. Our accumulated deficit as of March 31, 2021 was $110.6 million, and we expect to continue to incur substantial losses in future periods. We also anticipate that our operating expenses will increase substantially as we continue to advance the development of TSC, including any costs related to:

- our ongoing and planned clinical trials, including the ongoing and planned TSC Oxygenation Trials and our Planned Hypoxia-related Indication Trials;
- any additional studies we may undertake, including other preclinical and clinical studies to support the filing of any new drug application with the U.S. Food and Drug Administration;
- 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; and
- investments in operational, financial, and management information systems.

We intend to use our existing cash and cash equivalents for working capital and to fund the research and development of TSC, including the TSC TCOM Trial, the TSC VO2 Trial, and the TSC DLCO Trial. We expect that our cash and cash equivalents as of March 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements, including expected costs related to the planned TSC Oxygenation Trials and our Planned Hypoxia-related Indication Trials through 2023.

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. As we advance our product candidates, we expect the amount of R&D costs will continue to increase for the foreseeable future. R&D costs are charged to expense as incurred.

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 is interest earned from our cash and cash equivalents.

Income Tax Benefit

Prior to 2021, we recognized income tax benefit to utilize indefinite deferred tax liabilities as a source of income against indefinite lived portions of our deferred tax assets. As of December 31, 2020, we recognized the full income tax benefit allowed by the 2017 Tax Act to utilize indefinite deferred tax liabilities as a source of income against indefinite lived portions of our deferred tax assets. 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. These limitations may, in certain cases, limit the amount of income tax benefit that can be utilized annually to offset taxable income or tax liabilities in future periods. 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 complete 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 year ended December 31, 2020 or during the three months ended March 31, 2021 give rise to any further limitations.

Results of Operations for Three Months Ended March 31, 2021 Compared to Three Months Ended March 31, 2020

The following table sets forth our results of operations for the three months ended March 31, 2021, and 2020.

	Three Months Ended March 31,		
	2021	**2020**	**Change**
Operating expenses:			
Research and development	$ 2,916,378	$ 1,534,467	$ 1,381,911
General and administrative	1,743,510	1,393,808	349,702
Depreciation	24,447	27,020	(2,573)
Loss from operations	4,684,335	2,955,295	1,729,040
Other income:			
Interest income	(40,416)	(34,100)	(6,316)
Loss from operations before income tax benefit	(4,643,919)	(2,921,195)	(1,722,724)
Income tax benefit	—	(362,380)	362,380
Net loss	$ (4,643,919)	$ (2,558,815)	$ (2,085,104)

We recognized $2.9 million in research and development expenses during the three months ended March 31, 2021 compared to $1.5 million during the three months ended March 31, 2020. A significant portion of this increase was attributable to the $0.7 million of costs incurred related to our TSC COVID Trial, which was initiated in September 2020, and $0.6 million of costs incurred related to our TSC TCOM trial, which was initiated in March 2021. Manufacturing costs also increased by $0.5 million to support these trials. Additionally, salaries and wages increased by $0.2 million. These increases were slightly offset by decreases of $0.5 million and $0.1 million related to the wind-down of our TSC Stroke Trial and our TSC GBM Trial, respectively.

General and administrative expenses increased by $0.3 million during the three months ended March 31, 2021 compared to the three months ended March 31, 2020, mainly due to an increase in salaries and wages, stock-based compensation and professional fees, including additional amounts related to increased headcount and costs associated with the separation of former executives that will not recur in future years.

The increase in interest income for the three months ended March 31, 2021 compared to the three months ended March 31, 2020 is primarily attributable to having a larger cash and cash equivalents balance earning more interest during the three months ended March 31, 2021 compared to the three months ended March 31, 2020.

During the three months ended March 31, 2020, we recognized income tax benefit of $0.4 million during the three months ended March 31, 2020, to reflect the utilization of indefinite deferred tax liabilities as a source of income against indefinite lived portions of the our deferred tax assets. Prior to 2021, we recognized the full income tax benefit allowed by the 2017 Tax Act to utilize indefinite deferred tax liabilities as a source of income against indefinite lived portions of our deferred tax assets. No additional benefit was recognized during the three months ended March 31, 2021 as the benefit was fully realized in prior periods.

Liquidity and Capital Resources

Working Capital

To date, we have funded our operations primarily through the sale and issuance of preferred stock, common stock and convertible promissory notes. As of March 31, 2021, we had $46.6 million in cash and cash equivalents, working capital of $45.2 million and an accumulated deficit of $110.6 million. We expect to continue to incur net losses for the foreseeable future. We intend to use our existing cash and cash equivalents to fund our working capital and research and development of our product candidates.

Cash Flows

The following table sets forth our cash flows for the three months ended March 31, 2021 and 2020:

	Three Months Ended March 31,	
Net cash (used in) provided by:	**2021**	**2020**
Operating activities	$ (5,176,370)	$ (3,504,314)
Financing activities	33,295,752	155,193
Net increase (decrease) in cash and cash equivalents	$ 28,119,382	$ (3,349,121)

Operating Activities

Net cash used in operating activities of $5.2 million during the three months ended March 31, 2021 was primarily attributable to our net loss of $4.6 million and our net change in operating assets and liabilities of $0.7 million. This amount was offset by $0.2 million in stock-based compensation expense and depreciation expense. The net change in our operating assets and liabilities is primarily attributable to a decrease in our accrued expenses and other current liabilities due to the timing of our payments to our vendors and employees as well as an increase in our prepaid expenses, deposits and other current assets.

Net cash used in operating activities of $3.5 million during the three months ended March 31, 2020 was primarily attributable to our net loss of $2.6 million, our net change in operating assets and liabilities of $0.8 million and our change in deferred income taxes of $0.4 million. This amount was offset by $0.2 million in stock-based compensation expense and depreciation expense. The net change in our operating assets and liabilities is primarily attributable to a decrease in our accounts payable and accrued expenses due to the timing of our payments to our vendors and employees as well as an increase in our prepaid expenses, deposits and other current assets.

Financing Activities

Net cash provided by financing activities was $33.3 million during the three months ended March 31, 2021, which was attributable to net proceeds of $31.1 million received from the sale of our common stock and $2.2 million in proceeds received from the exercise of common stock warrants.

Net cash provided by financing activities was $0.2 million during the three months ended March 31, 2020, which was attributable to the $0.4 million in proceeds received from the exercise of common stock warrants, offset by approximately $0.2 million in payments for offering costs.

Capital Requirements

We expect to continue to incur substantial expenses and generate significant operating losses as we continue to pursue our business strategy of developing TSC. Our operations have consumed substantial amounts of cash since inception and we expect to continue to spend substantial amounts of cash to advance the clinical development of TSC, DFN-529, and our other product candidates. As of the date of this Annual Report, most our cash resources for clinical development are dedicated to our ongoing and planned TSC Oxygenation Trials and our Planned Hypoxia-related Indication Trials. While we believe we have adequate cash resources to continue operations through 2023, we anticipate that we will need additional funding in order to complete development of TSC which, if available, could be obtained through additional capital raising transactions, entry into strategic partnerships or collaborations, or alternative financing arrangements.

As of March 31, 2021, we did not have any credit facilities in place under which we could borrow funds or any other sources of committed capital. 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 to meet our needs or be on terms acceptable to us. This risk may increase if economic and market conditions deteriorate. If we are unable to obtain additional financing when needed, we may need to terminate, significantly modify, or delay the development of TSC or our product candidates, or we may need to obtain funds through collaborations or otherwise on terms that may require us to relinquish rights to our technologies or product candidates that we might otherwise seek to develop or commercialize independently. 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, 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.

Critical Accounting Policies

The Critical Accounting Policies included in our Form 10-K for the year ended December 31, 2020, filed with the SEC pursuant to Section 13 or 15(d) under the Securities Act on March 16, 2021 have not changed.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As a "smaller reporting company" as defined by Item 10 of Regulation S-K promulgated by the SEC under the U.S. Securities Act of 1933, as amended, we are not required to provide the information required by this Item 3.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) promulgated under the Exchange Act) that are designed to provide reasonable assurance that information required to be disclosed by us in the reports 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 and that such information is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. In designing and evaluating our disclosure controls and procedures, we recognize that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and we are required to apply our judgment in evaluating the cost-benefit relationship of possible internal controls. Our management evaluated, with the participation of our principal executive officer and principal financial officer, the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered in this report. Based on that evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of the end of such period to provide reasonable assurance that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding disclosure.

Change in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as such term is defined in Rule 13a-15(f) promulgated under the Exchange Act) that occurred during the period ended March 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

.

PART II – OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

For this item, please refer to *Note 7, Commitments and Contingencies* in the notes accompanying the unaudited interim consolidated financial statements included in Part I, Item 1 of this Quarterly Report, which is incorporated herein by reference.

ITEM 1A. RISK FACTORS

As of the date of this Quarterly Report, there have been no material changes to our risk factors previously disclosed in our Annual Report other than as set forth below.

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

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

There is no assurance that we will continue to meet the minimum closing price requirement and other listing requirements. For example, on May 6, 2021, we received a written notice from the staff of the Nasdaq Listing Qualifications Department indicating that we were not in compliance with Nasdaq Listing Rule 5550(a)(2) because the bid price for our common stock had closed below $1.00 per share for the previous 30 consecutive business days. In accordance with Nasdaq Listing Rule 5810(c)(3)(A), we have 180 calendar days from the date of such notice, or until November 2, 2021, to regain compliance with the minimum bid price requirement. To regain compliance, the bid price for our common stock must close at $1.00 per share or more for a minimum of 10 consecutive business days. Nasdaq's written notice has no effect on the listing or trading of our common stock at this time, and we are currently evaluating our alternatives to resolve this listing deficiency. If necessary to regain compliance with Nasdaq listing standards, we intend, subject to approval of our board of directors and stockholders, to implement a reverse stock split. However, there can be no assurance that the reverse stock split will be approved or will result in a sustained higher stock price that will allow us to meet the Nasdaq stock price listing requirements, and there is no guarantee we will continue to satisfy the other Nasdaq Capital Market continued listing standards.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Unregistered Sales of Equity Securities

None.

Issuer Purchases of Equity Securities

None.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

None.

ITEM 6. EXHIBITS

See attached Exhibit Index.

DIFFUSION PHARMACEUTICALS INC.

QUARTERLY REPORT ON FORM 10-Q
EXHIBIT INDEX

Exhibit No.	Description	Method of Filing
4.1	Form of 2021 Common Stock Offering Underwriter's Warrant	Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on February 18, 2021
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 Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	Furnished herewith
32.2	Certification of principal financial officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	Furnished herewith
101	The following materials from Diffusion's quarterly report on Form 10-Q for the quarter ended March 31, 2021, formatted in XBRL (Extensible Business Reporting Language): (i) the Unaudited Consolidated Balance Sheets, (ii) the Unaudited Consolidated Statements of Operations, (iii) the Unaudited Consolidated Statement of Changes in Stockholders' Equity, (iv) the Unaudited Consolidated Statements of Cash Flows, and (v) Notes to Unaudited Consolidated Financial Statements	Filed herewith

SIGNATURES

Pursuant to the requirements 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.

Date: May 7, 2021

DIFFUSION PHARMACEUTICALS INC.

By: /s/ Robert J. Cobuzzi, Jr., Ph.D.
Robert J. Cobuzzi, Jr., Ph.D.

President and Chief Executive Officer
(Principal Executive Officer)

By: /s/ William Hornung
William Hornung
Chief Financial Officer
(Principal Financial and Accounting Officer)

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 quarterly report on Form 10-Q 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: May 7, 2021

/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 quarterly report on Form 10-Q 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: May 7, 2021

/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 Quarterly Report on Form 10-Q of Diffusion Pharmaceuticals Inc. (the "Company") for the quarter ended March 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Robert J. Cobuzzi, Jr., Ph.D, President and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my 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
May 7, 2021

Exhibit 32.2

CERTIFICATION OF PRINCIPAL FINANCIAL 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 Quarterly Report on Form 10-Q of Diffusion Pharmaceuticals Inc. (the "Company") for the quarter ended March 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, William K. Hornung, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my 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/ William K. Hornung
William K. Hornung
Chief Financial Officer (Principal Financial and Accounting Officer)
May 7 , 2021