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

FORM 10-Q

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

For the quarterly period ended September 30, 2021

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 001-38114

AVENUE THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**47-4113275**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

1140 Avenue of the Americas, Floor 9 New York, NY 10036
(Address of principal executive offices and zip code)

(781) 652-4500
(Registrant's telephone number, including area code)

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

Title of Class	Trading Symbol(s)	Exchange Name
Common Stock	ATXI	Nasdaq Capital Market

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the 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 definition 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 Exchange Act). Yes ☐ No ☒

Indicate the number of shares outstanding of each of the registrant's classes of common stock, as of the latest practicable date.

Class of Common Stock	Outstanding Shares as of November 12, 2021
Common Stock, $0.0001 par value	18,700,480

AVENUE THERAPEUTICS, INC.
Form 10-Q
For the Quarter Ended September 30, 2021

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SUMMARY RISK FACTORS

Our business is subject to risks of which you should be aware before making an investment decision. The risks described below are a summary of the principal risks associated with an investment in us and are not the only risks we face. You should carefully consider these risk factors, the risk factors described in Item 1A, and the other reports and documents that we have filed with the Securities and Exchange Commission ("SEC").

Risks Pertaining to the Influence of Fortress Biotech, Inc. ("Fortress")

- Fortress controls a voting majority of our capital stock pursuant to its ownership of a class of preferred stock, some of the features of which have been contractually suspended.

Risks Pertaining to Our Business and Influence

- If we fail to satisfy applicable listing standards, including compliance with the minimum market value of listed securities requirement, our common stock may be delisted from the NASDAQ Capital Market, which would impact the liquidity, and potentially the value, of your investment.
- We currently have no drug products for sale, and only one drug product candidate, Intravenous ("IV") Tramadol. We are dependent on the success of IV Tramadol and cannot guarantee that we will receive regulatory approval, or that IV Tramadol will be successfully commercialized.
- If serious adverse or unacceptable side effects are identified during the development of IV Tramadol or any future product candidates, we may need to abandon or limit our development of some of our product candidates.
- We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

Risks Pertaining to Our Finances

- There is substantial doubt about our ability to continue as a going concern, which may hinder our ability to obtain future financing.
- We have incurred significant losses since our inception. We expect to incur losses for the foreseeable future, and may never achieve or maintain profitability.
- We do not have any products that are approved for commercial sale and therefore do not expect to generate any revenues from product sales in the foreseeable future, if ever.
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish proprietary rights.

Risks Pertaining to Reliance on Third Parties

- We rely, and expect to continue to rely, on third parties to conduct our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials or complying with applicable regulatory requirements.
- We rely on clinical data and results obtained by third parties that could ultimately prove to be inaccurate or unreliable.

Risks Pertaining to Regulatory Approval Process

- We may not receive regulatory approval for IV Tramadol, or our approval may be significantly delayed due to scientific or regulatory reasons.
- We may encounter FDA deficiencies that delay our approval, or we may not obtain approval, if we do not sufficiently address the issues raised by FDA during our meetings with FDA, as described in Complete Response Letters ("CRLs"), or as part of our Formal Dispute Resolution Request.
- Even if we respond to FDA's requests for information and deficiencies, provide robust scientific justifications and supporting data, there is no guarantee that FDA will accept our responses, or change its own preliminary conclusions about our product candidate.

- Even if IV Tramadol receives regulatory approval, which may not occur, it and any other products we may market will remain subject to substantial ongoing regulatory scrutiny.
- We will need to obtain FDA approval of any proposed product brand names, and any failure or delay associated with such approval may adversely impact our business.
- If the Drug Enforcement Agency ("DEA") decides to reschedule Tramadol from a Schedule IV controlled substance to a more restrictive Schedule, IV Tramadol could lose its competitive advantage, and our related clinical development and regulatory approval could be delayed or prevented.

Risks Pertaining to the Commercialization of Product Candidates

- Current and future legislation and regulation may increase the difficulty and cost for us to obtain marketing approval of, and to commercialize, our product candidate and may affect the prices we are able to obtain.
- Public concern regarding the safety of opioid drug products such as IV Tramadol could delay or limit our ability to obtain regulatory approval, result in the inclusion of serious risk information in our labeling, negatively impact market performance, or require us to undertake other activities that may entail additional costs.
- We expect intense competition for IV Tramadol, and new products may emerge that provide different or better therapeutic alternatives for our targeted indications.
- If IV Tramadol does not achieve broad market acceptance, the revenues that we generate from its sales will be limited.

Risks Pertaining to Intellectual Property and Potential Disputes Thereof

- If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.
- If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in any litigation would harm our business.
- If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

AVENUE THERAPEUTICS, INC.
CONDENSED BALANCE SHEETS
($ in thousands, except share and per share amounts)

	September 30, 2021 (unaudited)	December 31, 2020
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 585	$ 3,132
Other receivables - related party	74	—
Prepaid expenses and other current assets	29	113
Total Assets	**$ 688**	**$ 3,245**
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current Liabilities:		
Accounts payable and accrued expenses	$ 672	$ 857
Accounts payable and accrued expenses - related party	176	29
Total current liabilities	848	886
Total Liabilities	848	886
Commitments and Contingencies		
Stockholders' Equity (Deficit)		
Preferred Stock ($0.0001 par value), 2,000,000 shares authorized		
Class A Preferred Stock, 250,000 shares issued and outstanding as of September 30, 2021 and December 31, 2020, respectively	—	—
Common Stock ($0.0001 par value), 50,000,000 shares authorized		
Common shares, 16,793,693 and 16,747,803 shares issued and outstanding as of September 30, 2021 and December 31, 2020, respectively	2	2
Additional paid-in capital	75,924	75,625
Accumulated deficit	(76,086)	(73,268)
Total Stockholders' Equity (Deficit)	(160)	2,359
Total Liabilities and Stockholders' Equity (Deficit)	**$ 688**	**$ 3,245**

The accompanying notes are an integral part of these unaudited condensed financial statements.

AVENUE THERAPEUTICS, INC.
CONDENSED STATEMENTS OF OPERATIONS
($ in thousands, except share and per share amounts)
(Unaudited)

	For the Three Months Ended		For the Nine Months Ended	
	September 30, 2021	September 30, 2020	September 30, 2021	September 30, 2020
Operating expenses:				
Research and development	$ 278	$ 466	$ 864	$ 2,382
General and administrative	594	571	1,960	1,832
Loss from operations	(872)	(1,037)	(2,824)	(4,214)
Interest income	(1)	(9)	(6)	(56)
Net Loss	**$ (871)**	**$ (1,028)**	**$ (2,818)**	**$ (4,158)**
Net loss per common share outstanding, basic and diluted	$ (0.05)	$ (0.06)	$ (0.17)	$ (0.25)
Weighted average number of common shares outstanding, basic and diluted	16,627,427	16,519,464	16,580,283	16,489,701

The accompanying notes are an integral part of these unaudited condensed financial statements.

AVENUE THERAPEUTICS, INC.
CONDENSED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
($ in thousands, except share amounts)
(Unaudited)

Three months ended September 30, 2021

	Class A Preferred Shares		Common Shares		Additional paid-in capital	Accumulated deficit	Total Stockholders' equity (deficit)
	Shares	Amount	Shares	Amount			
Balance at June 30, 2021	**250,000**	**$ —**	**16,748,068**	**$ 2**	**$ 75,855**	**$ (75,215)**	**$ 642**
Share based compensation	—	—	45,000	—	69	—	69
Cashless exercise of warrants	—	—	625	—	—	—	—
Net loss	—	—	—	—	—	(871)	(871)
Balance at September 30, 2021	**250,000**	**$ —**	**16,793,693**	**$ 2**	**$ 75,924**	**$ (76,086)**	**$ (160)**

Nine months ended September 30, 2021

	Class A Preferred Shares		Common Shares		Additional paid-in capital	Accumulated deficit	Total Stockholders' equity (deficit)
	Shares	Amount	Shares	Amount			
Balance at December 31, 2020	**250,000**	**$ —**	**16,747,803**	**$ 2**	**$ 75,625**	**$ (73,268)**	**$ 2,359**
Share based compensation	—	—	45,000	—	299	—	299
Cashless exercise of warrants	—	—	890	—	—	—	—
Net loss	—	—	—	—	—	(2,818)	(2,818)
Balance at September 30, 2021	**250,000**	**$ —**	**16,793,693**	**$ 2**	**$ 75,924**	**$ (76,086)**	**$ (160)**

Three months ended September 30, 2020

	Class A Preferred Shares		Common Shares		Additional paid-in capital	Accumulated deficit	Total Stockholders' equity
	Shares	Amount	Shares	Amount			
Balance at June 30, 2020	**250,000**	**$ —**	**16,702,803**	**$ 2**	**$ 75,346**	**$ (71,247)**	**$ 4,101**
Share based compensation	—	—	45,000	—	161	—	161
Net loss	—	—	—	—	—	(1,028)	(1,028)
Balance at September 30, 2020	**250,000**	**$ —**	**16,747,803**	**$ 2**	**$ 75,507**	**$ (72,275)**	**$ 3,234**

Nine months ended September 30, 2020

	Class A Preferred Shares		Common Shares		Additional paid-in capital	Accumulated deficit	Total Stockholders' equity
	Shares	Amount	Shares	Amount			
Balance at December 31, 2019	**250,000**	**$ —**	**16,682,190**	**$ 2**	**$ 74,915**	**$ (68,117)**	**$ 6,800**
Share based compensation	—	—	65,000	—	592	—	592
Cashless exercise of warrants	—	—	613	—	—	—	—
Net loss	—	—	—	—	—	(4,158)	(4,158)
Balance at September 30, 2020	**250,000**	**$ —**	**16,747,803**	**$ 2**	**$ 75,507**	**$ (72,275)**	**$ 3,234**

The accompanying notes are an integral part of these unaudited condensed financial statements.

AVENUE THERAPEUTICS, INC.
CONDENSED STATEMENTS OF CASH FLOWS
(Unaudited)
($ in thousands)

	For the Nine Months Ended	
	September 30, 2021	**September 30, 2020**
Cash flows from operating activities:		
Net loss	$ (2,818)	$ (4,158)
Adjustments to reconcile net loss to net cash used in operating activities:		
Share based compensation	299	592
Changes in operating assets and liabilities:		
Other receivables - related party	(74)	—
Prepaid expenses and other current assets	84	143
Accounts payable and accrued expenses	(185)	(14)
Accounts payable and accrued expenses - related party	147	17
Net cash and cash equivalents used in operating activities	(2,547)	(3,420)
Cash flows from investing activities:		
Milestone payment for research and development licenses	—	(1,000)
Net cash and cash equivalents used in investing activities	—	(1,000)
Net change in cash and cash equivalents	(2,547)	(4,420)
Cash and cash equivalents, beginning of period	3,132	8,745
Cash and cash equivalents, end of period	**$ 585**	**$ 4,325**

The accompanying notes are an integral part of these unaudited condensed financial statements.

AVENUE THERAPEUTICS, INC.
NOTES TO UNAUDITED INTERIM CONDENSED FINANCIAL STATEMENTS

Note 1 - Organization, Plan of Business Operations

Avenue Therapeutics, Inc. (the "Company" or "Avenue") was incorporated in Delaware on February 9, 2015, as a wholly owned subsidiary of Fortress Biotech, Inc. ("Fortress"), to develop and market pharmaceutical products for the acute care setting in the United States. The Company is focused on developing its product candidate, an intravenous ("IV") formulation of tramadol HCI ("IV Tramadol"), for post-operative acute pain.

Stock Purchase and Merger Agreement

On November 12, 2018, the Company, InvaGen Pharmaceuticals Inc. ("InvaGen"), and Madison Pharmaceuticals, Inc. entered into a Stock Purchase and Merger Agreement ("SPMA"), pursuant to which the Company agreed to its sale in a two-stage transaction. In the first stage, InvaGen agreed to purchase, for $35 million, common shares representing 33.3% of the fully diluted capitalization of the Company. In the second stage, InvaGen would acquire the remaining issued and outstanding capital stock of the Company for approximately $180 million in a reverse subsidiary merger transaction (the "Merger Transaction"). The SPMA was approved by a majority of the Company's stockholders, including a majority of its non-affiliated stockholders, at its special shareholder meeting on February 6, 2019. On February 8, 2019, InvaGen acquired 5,833,333 shares of the Company's common stock at $6.00 per share (the "Stock Purchase Transaction") for net proceeds of $31.5 million after deducting commission fees and other offering costs, representing a 33.3% stake in the Company's capital stock on a fully diluted basis.

Consummation of the Merger Transaction was conditioned upon, among other things, U.S. Federal Drug Administration ("FDA") approval of IV Tramadol, its labeling and scheduling, and the absence of certain other restrictions in effect with respect to IV Tramadol. Pursuant to the SPMA, if FDA approval of IV Tramadol was not obtained on or before April 30, 2021, InvaGen would not be subject to the mandatory closing obligations set forth in the SPMA with respect to the Merger Transaction (but would instead retain an option to complete the Merger Transaction up until such time as the SPMA was terminated). Pursuant to the SPMA, the Company could choose to terminate the SPMA after October 31, 2021, if FDA approval of IV Tramadol had not occurred by such time. On November 1, 2021, the Company terminated the SPMA.

Even though the SPMA has been terminated, InvaGen retains certain rights pursuant to the Stockholders Agreement, entered into on November 12, 2018 between the Company, InvaGen and Fortress, and other agreements entered into in connection therewith on such date. These rights exist as long as InvaGen maintains at least 75% of the common shares acquired in the Stock Purchase Transaction and include among other things, the right to restrict the Company from certain equity issuances and changes to the Company's capital stock without obtaining InvaGen's prior written consent.

Over the past year, the Company has communicated with InvaGen relating to InvaGen's assertions that Material Adverse Effects (as defined in the SPMA) have occurred due to the impact of the COVID-19 pandemic on potential commercialization and projected sales of IV Tramadol. Additionally, in connection with the resubmission of the Company's New Drug Application ("NDA") in February 2021, InvaGen communicated to the Company that it believes the proposed label for IV Tramadol would also constitute a Material Adverse Effect (as defined in the SPMA) on the purported basis that the proposed label under certain circumstances would make the product commercially unviable. Even though the SPMA has been terminated, it is still possible for InvaGen to pursue monetary claims against the Company and/or Fortress based on the foregoing or other potential causes of action.

Liquidity and Capital Resources

Going Concern

The Company is not yet generating revenue, has incurred substantial operating losses since its inception and expects to continue to incur significant operating losses for the foreseeable future as it executes on its product development plan and may never become profitable. As of September 30, 2021, the Company had an accumulated deficit of $76.1 million.

On October 12, 2020, the Company announced that it had received a Complete Response Letter ("the First CRL") from the FDA regarding the Company's NDA for IV Tramadol. The First CRL cited deficiencies related to the terminal sterilization validation and stated that IV Tramadol, intended to treat patients in acute pain who require an opioid, is not safe for the intended patient population. On February 12, 2021, the Company resubmitted its NDA to the FDA for IV Tramadol. The NDA resubmission followed the receipt of official minutes from a Type A meeting with the FDA. The resubmission included revised language relating to the proposed product label and a report relating to terminal sterilization validation. On June 14, 2021, the Company announced that it had received a second Complete Response Letter (the "Second CRL") from the FDA regarding the Company's NDA for IV Tramadol. The Second CRL stated that the delayed and unpredictable onset of analgesia with IV Tramadol does not support its benefit as a monotherapy to treat patients in acute pain and that there is insufficient information to support that IV Tramadol in combination with other analgesics is safe and effective for the intended patient population. In particular, the Second CRL stated that, while the primary endpoint was met in two efficacy studies, meaningful pain relief was delayed (accounting for the use of rescue medication, e.g., ibuprofen), and some patients never achieved pain relief. The Company continues to pursue regulatory approval for IV Tramadol and had a Type A meeting with the FDA in July 2021. The FDA did not deviate from any of the positions the FDA previously took in the First CRL and the Second CRL. The Company submitted a formal dispute resolution request ("FDRR") with the Office of Neuroscience of the FDA on July 27, 2021. On August 26, 2021, the Company received an Appeal Denied Letter from the Office of Neuroscience of the FDA in response to the FDRR submitted on July 27, 2021. On August 31, 2021, the Company submitted a FDRR with the Office of New Drugs ("OND") of the FDA. On October 21, 2021, the Company received a written response from the OND of the FDA stating that the OND needs additional input from an Advisory Committee in order to reach a decision on the FDRR. There can be no assurance that any such FDRR will be successful. The Company's ability to potentially commercialize IV Tramadol, and the timing of any potential commercialization, are dependent on the FDA's review of the FDRR for IV Tramadol, whether or not the FDA ultimately approves IV Tramadol which would follow shortly after a potentially successful outcome from the FDRR review, and potentially on whether or not the Company procures additional capital.

As of September 30, 2021, the Company had cash and cash equivalents of $0.6 million. The Company believes that its cash and cash equivalents are only sufficient to fund its operating expenses into the fourth quarter of 2021. The Company will need to secure additional funds through equity or debt offerings, or other potential sources. Furthermore, under the SPMA, any equity funding must be approved by InvaGen. The Company cannot be certain that additional funding will be available to it on acceptable terms, or at all. These factors individually and collectively raise substantial doubt about the Company's ability to continue as a going concern within one year from the date of this report. The unaudited interim condensed financial statements do not contain any adjustments that might result from the resolution of any of the above uncertainty.

In light of the foregoing, it may be necessary at some point for the Company to seek protection under Chapter 11 of the United States Bankruptcy Code, which could have a material adverse impact on the Company's business, financial condition, operations and could place its shareholders at significant risk of losing all of their investment. In any such Chapter 11 proceeding, the Company may seek to restructure its obligations or commence an orderly wind-down of its operations and sale of its assets, in either event, holders of equity interests could receive or retain little or no recovery. The Company also notes that the process of exploring refinancing or restructuring alternatives, including those under Chapter 11, may be disruptive to its business and operations.

Note 2 — Significant Accounting Policies

Basis of Presentation

The accompanying unaudited interim condensed financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America ("U.S. GAAP") for interim financial information and the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by U.S. GAAP for complete financial statements. In the opinion of management, the unaudited interim condensed financial statements reflect all adjustments, which include only normal recurring adjustments necessary for the fair statement of the balances and results for the periods presented. Certain information and footnote disclosures normally included in the Company's annual financial statements prepared in accordance with U.S. GAAP have been condensed or omitted. These unaudited interim condensed financial statement results are not necessarily indicative of results to be expected for the full fiscal year or any future period.

Therefore, these unaudited interim condensed financial statements should be read in conjunction with the Company's audited financial statements and notes thereto for the year ended December 31, 2020, which were included in the Company's Form 10-K, and filed with the U.S. Securities and Exchange Commission ("SEC") on March 31, 2021. The results of operations for any interim periods are not necessarily indicative of the results that may be expected for the entire fiscal year or any other interim period.

The Company has no subsidiaries.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management 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 unaudited condensed financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from those estimates.

Summary of Significant Accounting Policies

The Company's significant accounting policies are described in Note 2 in its audited financial statements for the year ended December 31, 2020 included in the Company's Form 10-K. With the exception of those noted below, there have been no material changes to the Company's significant accounting policies.

Net Loss Per Share

Loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding, excluding unvested restricted stock and stock options and preferred shares, during the period. Since dividends are declared paid and set aside among the holders of shares of common stock and Class A common stock pro-rata on an as-if-converted basis, the two-class method of computing net loss per share is not required.

The following table sets forth the potential common shares that could potentially dilute basic income per share in the future that were not included in the computation of diluted net loss per share because to do so would have been anti-dilutive for the periods presented:

	For the Three and Nine Months Ended	
	September 30, 2021	September 30, 2020
Unvested restricted stock units/awards	1,014,256	1,139,910
Preferred shares	250,000	250,000
Total potential dilutive effect	1,264,256	1,389,910

Recently Adopted Accounting Standards

In December 2019, the Financial Accounting Standards Board ("FASB") issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes,* ("ASU 2019-12") which is intended to simplify various aspects related to accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. This guidance is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020, with early adoption permitted. The Company adopted ASU 2019-12 on January 1, 2021 and its adoption did not have a material impact on the Company's unaudited interim condensed financial statements and related disclosures.

Coronavirus Aid, Relief and Economic Security Act ("CARES Act")

In response to the COVID-19 pandemic, the Coronavirus Aid, Relief and Economic Security Act ("CARES Act") was signed into law on March 27, 2020. On December 27, 2020, the President of the United States signed the Consolidated Appropriations Act, 2021 ("Consolidated Appropriations Act") into law. The Consolidated Appropriations Act is intended to enhance and expand certain provisions of the CARES Act, allows for the deductions of expenses related to the Payroll Protection Program funds received by companies, and provides an update to meals and entertainment expensing for 2021. The Company does not anticipate the Consolidated Appropriations Act to have a material impact to the Company's income tax provision (benefit) for 2021.

Note 3 — Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consisted of the following (in thousands):

	As of September 30, 2021	As of December 31, 2020
Accounts payable	$ 202	$ 143
Accrued employee compensation	302	23
Accrued contracted services and other	168	691
Accounts payable and accrued expenses	$ 672	$ 857

Note 4 — Related Party Transactions

Effective June 1, 2021, the Company, InvaGen, Fortress and Journey Medical Corporation ("Journey"), a consolidated entity under Fortress, entered into a secondment agreement for a certain Avenue employee to be seconded to Journey. During the secondment, Journey will have the authority to supervise the Avenue employee and will reimburse the Company for the employee's salary and salary-related costs. The term of this agreement lasts until the approval of IV tramadol by the FDA or until the employee's services are needed again by the Company. The amounts reimbursable to Avenue are $74,000 and $98,000 for the three and nine months ended September 30, 2021, respectively. The amount due to the Company as of September 30, 2021 that is related to this secondment agreement is $74,000 and is included in "Other receivables - related party" on the Company's condensed balance sheets.

Effective June 24, 2021, Fortress and certain of the Company's key employees entered into retention agreements (the "Fortress Retention Agreements") pursuant to which retention bonuses are payable only if the Merger Transaction (as defined in the SPMA) occurs and the applicable employee remains employed by the Company immediately prior to the closing of the Merger Transaction. These Fortress Retention Agreements are effective until the earlier of the consummation of the Merger Transaction or the termination of the SPMA. Amounts potentially payable to these key employees are $2.9 million as of September 30, 2021. On October 7, 2021, an agreement with a fourth key employee was signed with the same terms and conditions as set forth in the Fortress Retention Agreements. The amount potentially payable to this employee is $0.3 million. As the SPMA was terminated on November 1, 2021, there are no amounts payable under the Fortress Retention Agreements.

Note 5 — Stockholders' Equity

Equity Incentive Plan

The Company has in effect the 2015 Incentive Plan ("2015 Incentive Plan"). The 2015 Incentive Plan was adopted in December 2015 by our stockholders. Under the 2015 Incentive Plan, the compensation committee of the Company's board of directors is authorized to grant stock-based awards to directors, officers, employees and consultants. The plan authorizes grants to issue up to 2,000,000 shares of authorized but unissued common stock and expires 10 years from adoption and limits the term of each option to no more than10 years from the date of grant.

Restricted Stock Units and Restricted Stock Awards

The following table summarizes restricted stock unit and award activity for the nine months ended September 30, 2021:

	Number of Units and Awards	Weighted Average Grant Date Fair Value
Unvested balance at December 31, 2020	1,139,910	$ 5.96
Granted	—	$ —
Vested	(125,654)	$ 4.97
Unvested balance at September 30, 2021	1,014,256	$ 6.09

For the three months ended September 30, 2021 and 2020, stock-based compensation expenses associated with the amortization of restricted stock units and restricted stock awards for employees and non-employees were approximately $69,000 and $0.2 million, respectively. For the nine months ended September 30, 2021 and 2020, stock-based compensation expenses associated with the amortization of restricted stock units and restricted stock awards for employees and non-employees were approximately $0.3 million and $0.6 million, respectively.

At September 30, 2021, the Company had unrecognized stock-based compensation expense related to restricted stock units and restricted stock awards of $0.1 million, which is expected to be recognized over the remaining weighted-average vesting period of 0.9 years. This amount does not include, as of September 30, 2021, 487,586 shares of restricted stock outstanding which are performance-based and vest upon achievement of certain corporate milestones. The expense is recognized over the vesting period of the award. Stock-based compensation for milestone awards will be measured and recorded if and when it is probable that the milestone will be achieved.

Stock Warrants

The following table summarizes the warrant activity for the nine months ended September 30, 2021:

	Warrants	Weighted Average Exercise Price	Aggregate Intrinsic Value (in thousands)
Outstanding, December 31, 2020	15,841	$ 0.6315	$ 84
Exercised	(890)	$ 0.0001	—
Outstanding, September 30, 2021	14,951	$ 0.6691	$ 19

Note 6 — Subsequent Events

On November 12, 2021, the Company, pursuant to an underwritten public offering, sold 1,946,787 shares of its common stock at a price of $1.34 per share for gross proceeds of approximately $2.6 million before deducting underwriting discounts and commissions and other estimated expenses. In addition, the Company granted the underwriters a 45-day option to purchase additional shares of common stock, representing up to 15% of the number of the shares, solely to cover over-allotments, if any, which would increase the total gross proceeds of the offering to approximately $3.0 million, if the over-allotment option is exercised in full.

Item 2. Financial Information.

Management's Discussion and Analysis of the Results of Operations

Forward-Looking Statements

Statements in the following discussion and throughout this report that are not historical in nature are "forward-looking statements." You can identify forward-looking statements by the use of words such as "expect," "anticipate," "estimate," "may," "will," "should," "intend," "believe," and similar expressions. Although we believe the expectations reflected in these forward-looking statements are reasonable, such statements are inherently subject to risk and we can give no assurances that our expectations will prove to be correct. Actual results could differ from those described in this report because of numerous factors, many of which are beyond our control. These factors include, without limitation, those described under Item 1A "Risk Factors." We undertake no obligation to update these forward-looking statements to reflect events or circumstances after the date of this report or to reflect actual outcomes.

The following discussion and analysis of our financial condition and results of operations should be read together with our unaudited financial statements and the notes to those financial statements appearing elsewhere in this Quarterly Report on Form 10-Q and the audited financial statements and notes thereto and management's discussion and analysis of financial condition and results of operations for the year ended December 31, 2020 included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 31, 2021. This discussion contains forward-looking statements that involve significant risks and uncertainties. As a result of many factors, such as those set forth in Item 1.A. "Risk Factors" of this Quarterly Report on Form 10-Q and any updates to those risk factors contained in our subsequent periodic and current reports filed with the Securities and Exchange Commission, our actual results may differ materially from those anticipated in these forward-looking statements.

Overview

We are a specialty pharmaceutical company that seeks to develop and commercialize our product principally for use in the acute/intensive care hospital setting. Our current product candidate is intravenous (IV) Tramadol, for the treatment of post-operative acute pain. Under the terms of certain agreements described herein, we have an exclusive license to develop and commercialize IV Tramadol in the United States. In 2016, we completed a pharmacokinetic study for IV Tramadol in healthy volunteers as well as an end of phase 2 meeting with the U.S. Food and Drug Administration (FDA). In the third quarter of 2017, we initiated a Phase 3 development program of IV Tramadol for the management of post-operative pain. In December 2019, we submitted a New Drug Application (NDA) for IV Tramadol and received a Complete Response Letter (the First CRL) from the FDA in October 2020. In February 2021, we resubmitted the NDA for IV Tramadol. The FDA assigned a Prescription Drug User Fee Act (PDUFA) goal date of April 12, 2021 for the resubmitted NDA for IV Tramadol. On June 14, 2021, we announced that we had received a second Complete Response Letter (the Second CRL) from the FDA regarding our NDA for IV tramadol. We continue to pursue regulatory approval for IV Tramadol and had a Type A meeting with the FDA in July 2021. We submitted a formal dispute resolution request (FDRR) with the Office of Neuroscience of the FDA on July 27, 2021. On August 26, 2021, we received an Appeal Denied Letter from the Office of Neuroscience of the FDA in response to the FDRR submitted on July 27, 2021. On August 31, 2021, we submitted a FDRR with the Office of New Drugs (OND) of the FDA. On October 21, 2021, we received a written response from the OND of the FDA stating that the OND needs additional input from an Advisory Committee in order to reach a decision on the FDRR. To date, we have not received approval for the sale of our product candidate in any market and, therefore, have not generated any sales revenue from our product candidate.

Recent Developments

On November 12, 2018, we, InvaGen Pharmaceuticals Inc. (InvaGen), and Madison Pharmaceuticals, Inc. entered into a Stock Purchase and Merger Agreement (SPMA), pursuant to which we agreed to our sale in a two-stage transaction. In the first stage, InvaGen agreed to purchase, for $35 million, common shares representing 33.3% of the fully diluted capitalization of our stock. In the second stage, InvaGen would acquire the remaining issued and outstanding of our capital stock for approximately $180 million in a reverse subsidiary merger transaction (the Merger Transaction). The SPMA was approved by a majority of our stockholders, including a majority of our non-affiliated stockholders, at our special shareholder meeting on February 6, 2019. On February 8, 2019, InvaGen acquired 5,833,333 shares of our common stock at $6.00 per share (the Stock Purchase Transaction) for net proceeds of $31.5 million after deducting commission fees and other offering costs, representing a 33.3% stake in our capital stock on a fully diluted basis. On November 1, 2021, we terminated the SPMA.

On November 12, 2021, through an underwritten public offering, we sold 1,946,787 shares of our common stock at a price of $1.34 per share for gross proceeds of approximately $2.6 million before deducting underwriting discounts and commissions and other estimated expenses. In addition, we granted the underwriters a 45-day option to purchase additional shares of common stock, representing up to 15% of the number of the shares, solely to cover over-allotments, if any, which would increase the total gross proceeds of the offering to approximately $3.0 million, if the over-allotment option is exercised in full.

Background

On June 26, 2017, we completed an initial public offering (IPO) of our common stock, resulting in net proceeds of approximately $34.2 million after deducting underwriting discounts, and other offering costs.

We used the proceeds from our IPO to initiate our first Phase 3 trial of IV Tramadol in patients with moderate-to-severe pain following bunionectomy, which had its first patient dosed in September 2017. In May 2018, we announced the study met its primary endpoint and all key secondary endpoints.

In December 2018, we initiated the second Phase 3 trial in patients with moderate-to-severe pain following abdominoplasty upon successful completion of the bunionectomy study. In June 2019, we announced the study met its primary endpoint and all key secondary endpoints.

In December 2017, we initiated an open-label safety study, which was completed during the second quarter of 2019. The results showed that IV Tramadol is well-tolerated with a side effect profile consistent with known pharmacology.

In December 2019, we submitted an NDA pursuant to Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act. In February 2020, the FDA accepted our NDA submission and set a PDUFA goal date of October 10, 2020. On October 12, 2020, we announced that we had received the First CRL from the FDA regarding our NDA. In November 2020, we had a Type A Meeting with the FDA to discuss issues raised in the First CRL. On February 12, 2021, we resubmitted the NDA to the FDA for IV Tramadol. The NDA resubmission followed the receipt of official minutes from a Type A meeting with the FDA, which was conducted following receipt of the First CRL. The NDA resubmission included revised language relating to the proposed product label and a report relating to terminal sterilization validation. The FDA assigned a PDUFA goal date of April 12, 2021 for the resubmitted NDA for IV Tramadol. On June 14, 2021, we announced that we had received the Second CRL from the FDA regarding our NDA for IV Tramadol. We continue to pursue regulatory approval for IV Tramadol and in connection therewith, had a Type A meeting with the FDA in July 2021. We submitted a FDRR with the Office of Neuroscience of the FDA on July 27, 2021. On August 26, 2021, we received an Appeal Denied Letter from the Office of Neuroscience of the FDA in response to the FDRR submitted on July 27, 2021. On August 31, 2021, we submitted a FDRR with the OND of the FDA. On October 21, 2021, we received a written response from the OND of the FDA stating that the OND needs additional input from an Advisory Committee in order to reach a decision on the FDRR.

On November 12, 2018, we, InvaGen, and Madison Pharmaceuticals, Inc. entered into the SPMA, in which we agreed to our sale in a two-stage transaction. In the first stage, InvaGen agreed to purchase, for $35 million, common shares representing 33.3% of our fully diluted capital stock. In the second stage, InvaGen would acquire our remaining issued and outstanding capital stock for approximately $180 million pursuant to the Merger Transaction. The SPMA was approved by a majority of our stockholders, including a majority of our non-affiliated stockholders, at our special shareholder meeting on February 6, 2019. On February 8, 2019, InvaGen acquired 5,833,333 shares of our common stock at $6.00 per share (the Stock Purchase Transaction) for net proceeds of $31.5 million after deducting commission fees and other offering costs, representing a 33.3% stake in our capital stock on a fully diluted basis.

Consummation of the Merger Transaction was conditioned upon, among other things, FDA approval of IV Tramadol, its labeling and scheduling, and the absence of certain other restrictions in effect with respect to IV Tramadol. Pursuant to the SPMA, if FDA approval of IV Tramadol was not obtained on or before April 30, 2021, InvaGen would not be subject to the mandatory closing obligations set forth in the SPMA with respect to the Merger Transaction (but would instead retain an option to complete the Merger Transaction up until such time as the SPMA was terminated). Pursuant to the SPMA, we could choose to terminate the SPMA after October 31, 2021, if FDA approval of IV Tramadol had not occurred by such time. On November 1, 2021, we terminated the SPMA.

Even though the SPMA has been terminated, InvaGen retains certain rights pursuant to the Stockholders Agreement, entered into on November 12, 2018 between us, InvaGen and Fortress, and other agreements entered into in connection therewith on such date. These rights exist as long as InvaGen maintains at least 75% of the common shares acquired in the Stock Purchase Transaction and include among other things, the right to restrict us from certain equity issuances and changes to our capital stock without obtaining InvaGen's prior written consent.

Over the past year, we have communicated with InvaGen relating to InvaGen's assertions that Material Adverse Effects (as defined in the SPMA) have occurred due to the impact of the COVID-19 pandemic on potential commercialization and projected sales of IV Tramadol. Additionally, in connection with the resubmission of our NDA in February 2021, InvaGen communicated to us that it believes the proposed label for IV Tramadol would also constitute a Material Adverse Effect (as defined in the SPMA) on the purported basis that the proposed label under certain circumstances would make the product commercially unviable. Even though the SPMA has been terminated, it is still possible for InvaGen to pursue monetary claims against us and/or Fortress based on the foregoing or other potential causes of action.

Our net loss for the nine months ended September 30, 2021 and 2020 was approximately $2.8 million and $4.2 million, respectively. As of September 30, 2021, we had an accumulated deficit of approximately $76.1 million. Substantially all our net losses resulted from costs incurred in connection with our research and development program of IV Tramadol and from general and administrative costs associated with our operations.

We expect to continue to incur research and development costs and increased general and administration related costs and incur operating losses for at least the next several years as we develop and seek regulatory approval for IV Tramadol in the U.S.

We need to obtain additional capital through the sale of debt or equity financings or other arrangements to fund our operations, research and development activity or regulatory approval activity; however, there can be no assurance that we will be able to raise needed capital under acceptable terms, if at all. The sale of additional equity may dilute existing stockholders and newly issued shares may contain senior rights and preferences compared to currently outstanding shares of common stock. Issued debt securities may contain covenants and limit our ability to pay dividends or make other distributions to stockholders. If we are unable to obtain such additional financing, future operations would need to be scaled back or discontinued.

We are a majority controlled subsidiary of Fortress.

Avenue Therapeutics, Inc. was incorporated in Delaware on February 9, 2015. Our executive offices are located at 1140 Avenue of the Americas, Floor 9, New York, NY 10036. Our telephone number is (781) 652-4500, and our email address is info@avenuetx.com.

Impact of COVID-19

On March 11, 2020, the World Health Organization declared the outbreak of a novel coronavirus (COVID-19) as a global pandemic, which continues to spread throughout the United States and around the world. Through the filing date of this Form 10-Q, we have not experienced a significant impact on our business resulting from government restrictions on the movement of people, goods, and services. Management believes any disruption, when and if experienced would be temporary, however, there is uncertainty around when any disruption might occur, the duration and the potential impact.

Critical Accounting Policies and Use of Estimates

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States (GAAP). The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are described in more detail in the notes to our unaudited interim condensed financial statements.

Results of Operations

General

At September 30, 2021, we had an accumulated deficit of $76.1 million, primarily as a result of expenditures for licenses acquired, for research and development and for general and administrative purposes. While we may in the future generate revenue from a variety of sources, including license fees, milestone payments, research and development payments in connection with strategic partnerships and/or product sales, our product candidate is still in development and may never be successfully developed or commercialized. Accordingly, we expect to continue to incur substantial losses from operations for the foreseeable future, and there can be no assurance that we will ever generate significant revenues.

Comparison of the Three Months Ended September 30, 2021 and 2020

	For The Three Months Ended		Change	
($ in thousands)	September 30, 2021	September 30, 2020	$	%
Operating expenses:				
Research and development	$ 278	$ 466	$ (188)	(40)%
General and administrative	594	571	23	4 %
Loss from operations	(872)	(1,037)	165	(16)%
Interest income	(1)	(9)	(8)	(89)%
Net Loss	**$ (871)**	**$ (1,028)**	**$ 157**	(15)%

Research and Development Expenses

Research and development expenses primarily consist of personnel related expenses, including salaries, benefits, travel, and other related expenses, stock-based compensation, payments made to third parties for license and milestone costs related to in-licensed products and technology, payments made to third party contract research organizations for preclinical and clinical studies, investigative sites for clinical trials, consultants, the cost of acquiring and manufacturing clinical trial materials, costs associated with pre-commercialization validation manufacturing, costs associated with regulatory filings, laboratory costs and other supplies.

For the three months ended September 30, 2021 and 2020, research and development expenses were $0.3 million and $0.5 million, respectively. The decrease of $0.2 million is primarily associated with NDA review related costs.

We expect our research and development activities to continue as we attempt to gain regulatory approval for our existing product candidate, reflecting costs associated with the following:

- employee-related expenses;
- license fees and milestone payments related to in-licensed product and technology;
- expenses incurred under agreements with contract research organizations, investigative sites and consultants that conduct our clinical trials;
- the cost of acquiring and manufacturing clinical trial materials; and
- costs associated with non-clinical activities, and regulatory approvals.

General and Administrative Expenses

General and administrative expenses consist principally of professional fees for legal and consulting services, market research, personnel-related costs, public reporting company related costs and other general operating expenses not otherwise included in research and development expenses. We expect our general and administrative costs to continue as we seek potential regulatory approval and potential commercialization of our product candidate.

For the three months ended September 30, 2021 and 2020, general and administrative expenses were $0.6 million. We incurred increased legal costs of $0.1 million related to our FDRR while this was offset with a decrease of $0.1 million in professional fees.

Interest Income

Interest income was $1,000 and $9,000 for the three months ended September 30, 2021 and 2020, respectively. The decrease in interest income was due to the reduction in cash and cash equivalents.

Comparison of the Nine Months Ended September 30, 2021 and 2020

	For The Nine Months Ended		Change	
($ in thousands)	September 30, 2021	September 30, 2020	$	%
Operating expenses:				
Research and development	$ 864	$ 2,382	$ (1,518)	(64)%
General and administrative	1,960	1,832	128	7 %
Loss from operations	(2,824)	(4,214)	1,390	(33)%
Interest income	(6)	(56)	(50)	(89)%
Net Loss	**$ (2,818)**	**$ (4,158)**	**$ 1,340**	(32)%

Research and Development Expenses

For the nine months ended September 30, 2021 and 2020, research and development expenses were $0.9 million and $2.4 million, respectively. The decrease of $1.5 million is primarily due to decreases of $1.0 million for NDA related and advisory committee preparation costs, $0.3 million in commercial validation manufacturing activities, $0.1 million in personnel costs and $0.1 million in stock compensation costs.

General and Administrative Expenses

For the nine months ended September 30, 2021 and 2020, general and administrative expenses were $1.9 million and $1.8 million, respectively. General and administrative expenses increased by $0.1 million primarily due to an increase of $0.4 million in legal costs partially offset by decreases of $0.2 million in stock compensation costs and $0.1 million in professional fees.

Interest Income

Interest income was $6,000 and $56,000 for the nine months ended September 30, 2021 and 2020, respectively. The decrease in interest income was due to the reduction in cash and cash equivalents and short-term investments and falling interest rates.

Liquidity and Capital Resources

We have incurred substantial operating losses since our inception and expect to continue to incur significant operating losses for the foreseeable future and may never become profitable. As of September 30, 2021, we had an accumulated deficit of $76.1 million. We have used the funds from our IPO and from the InvaGen share purchase to finance our operations and will continue to use the funds primarily for general corporate purposes, which may include financing our growth and developing our product candidate.

We believe that our cash and cash equivalents are only sufficient to fund our operating expenses into the fourth quarter of 2021. We need to secure additional funds through equity or debt offerings, or other potential sources. Furthermore, under the Stockholder's Agreement, any equity funding must be approved by InvaGen. We cannot be certain that additional funding will be available on acceptable terms, or at all. These factors individually and collectively raise substantial doubt about our ability to continue as a going concern.

In addition to the foregoing, based on current assessments, we do not expect any material impact on our regulatory timeline and our liquidity due to the worldwide spread of the COVID-19 virus. However, we are continuing to assess the effect on our operations by monitoring the spread of COVID-19 and the actions implemented to combat the virus throughout the world.

Recently Adopted and Issued Accounting Pronouncements

See Note 2.

Cash Flows for the Nine Months Ended September 30, 2021 and 2020

	For The Nine Months Ended September 30,	
($ in thousands)	**2021**	**2020**
Total cash and cash equivalents used in:		
Operating activities	$ (2,547)	$ (3,420)
Investing activities	—	(1,000)
Net decrease in cash and cash equivalents	$ (2,547)	$ (4,420)

Operating Activities

Net cash and cash equivalents used in operating activities was $2.5 million for the nine months ended September 30, 2021, primarily comprised of our $2.8 million net loss partially offset by $0.3 million in share based compensation.

Net cash used in operating activities was $3.4 million for the nine months ended September 30, 2020, primarily comprised of our $4.2 million net loss partially offset by increases in operating assets and liabilities of $0.2 million and $0.6 million in share based compensation.

Investing Activities

Net cash and cash equivalents used in investing activities for the nine months ended September 30, 2021 and 2020 was $0 and $1.0 million, respectively. Net cash used in the nine months ended September 30, 2020 was the milestone payment due to our licensor pursuant to our NDA submission.

Contractual Obligations and Commitments

There have been no material changes to our contractual obligations and commitments outside the ordinary course of business from those disclosed under the heading “Management’s Discussion and Analysis of Financial Condition and Results of Operations- Contractual Obligations and Commitments” in our Annual Report on Form 10-K for the year ended December 31, 2020.

Off-Balance Sheet Arrangements

We are not party to any off-balance sheet transactions. We have no guarantees or obligations other than those which arise out of normal business operations.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

N/A.

Item 4. Controls and Procedures

Disclosure Controls and Procedures

We maintain “disclosure controls and procedures,” as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), that are designed to ensure that information required to be disclosed by us in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in Securities and Exchange Commission rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and our Principal Financial Officer, to allow timely decisions regarding required disclosure.

The design of any disclosure controls and procedures also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions.

With respect to the quarter ended September 30, 2021, under the supervision and with the participation of our management, we conducted an evaluation of the effectiveness of the design and operations of our disclosure controls and procedures. Based upon this evaluation, the Company's Chief Executive Officer and Principal Financial Officer have concluded that the Company's disclosure controls and procedures are effective.

Management does not expect that our internal control over financial reporting will prevent or detect all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control systems 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 a cost-effective control system, no evaluation of internal control over financial reporting can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud, if any, have been or will be detected.

Changes in Internal Control over Financial Reporting:

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the fiscal quarter ended September 30, 2021 which have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Part II. Other Information

Item 1. Legal Proceedings.

We are not involved in any litigation that we believe could have a material adverse effect on our financial position or results of operations.

Item 1A. Risk Factors

The following information sets forth risk factors that could cause our actual results to differ materially from those contained in the forward-looking statements we have made in this Form 10-Q and those we may make from time to time. You should carefully consider the risks described below, in addition to the other information contained in this Form 10-Q, before making an investment decision. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.

Risks Pertaining to Our Stockholders Agreement with InvaGen Pharmaceuticals

While the SPMA has been terminated, InvaGen retains certain rights pursuant to the Stockholders Agreement between us and InvaGen. These rights exist as long as InvaGen maintains at least 75% of the common shares acquired in the first stage closing. The following are some of the actions that shall not be taken without the prior written consent of InvaGen:

- increase in authorized shares of our stock;
- any agreement or transaction that would adversely treat the holders of our common shares as compared to the holders of our Class A Preferred Shares;
- issuance of any shares of our capital stock or any securities convertible into, or other rights to acquire, shares of our capital stock (including options, warrants or bonds), except for issuances to our officers for services performed;
- any transfer or license of any asset for less than fair market value, as determined by a recognized independent valuation firm agreed upon by us and InvaGen; or
- entry into any transaction or agreement with any affiliate of ours (including Fortress or its Affiliates).

Risks Pertaining to the Influence of Fortress

Fortress controls a voting majority of our common stock.

Pursuant to the terms of the Class A Preferred Stock held by Fortress, Fortress will be entitled to cast, for each share of Class A Preferred Stock held by Fortress, the number of votes that is equal to 1.1 times a fraction, the numerator of which is the sum of (A) the aggregate number of shares of outstanding common stock and (B) the whole shares of common stock into which the shares of outstanding the Class A Preferred Stock are convertible and the denominator of which is the aggregate number of shares of outstanding Class A Preferred Stock, or the Class A Preferred Stock Ratio. Thus, Fortress will at all times have voting control of us. Further, for a period of ten years from the date of the first issuance of shares of Class A Preferred Stock, the holders of record of the shares of Class A Preferred Stock (or other capital stock or securities issued upon conversion of or in exchange for the Class A Preferred Stock), exclusively and as a separate class, shall be entitled to appoint or elect the majority of our directors.

At such time (if ever) as InvaGen no longer holds at least 75% of the Avenue shares it received in its initial 2019 equity subscription, Fortress would have the right to receive a significant grant of shares of our common stock annually, which would result in the dilution of your holdings of common stock upon each grant, which could reduce their value.

Under the terms of the Amended and Restated Founders Agreement, which became effective September 13, 2016, Fortress is entitled to receive a grant of shares of our common stock equal to 2.5% of the gross amount of any equity or debt financing. Additionally, the holders of Class A Preferred Stock, as a class, are to receive an annual dividend, payable in shares of common stock in an amount equal to 2.5% of our fully-diluted outstanding capital stock as of the business day immediately prior to the date such dividend is payable. Fortress currently owns all outstanding shares of Class A Preferred Stock. At our Annual Meeting of the Stockholder's held on June 13, 2018, the Company's shareholders approved an amendment to the Company's Third Amended and Restated Certificate of Incorporation, amending the Class A Preferred dividend payment date from February 17 to January 1 of each year. Fortress' right to receive this dividend was contractually waived in connection with the Waiver and Termination Agreement signed on November 12, 2018 between Avenue, Fortress and InvaGen, but Fortress' right to receive such dividend will be revived at such time (if ever) as InvaGen no longer holds at least 75% of the Avenue shares it received in its initial 2019 equity subscription. These potential future share issuances to Fortress and any other holder of Class A Preferred Stock will dilute your holdings in our common stock and, if our value has not grown proportionately over the prior year, would result in a reduction in the value of your shares. The Amended and Restated Founders Agreement has a term of 15 years and renews automatically for subsequent one-year periods unless terminated by Fortress or upon a Change in Control (as defined in the Amended and Restated Founders Agreement).

We might have received better terms from unaffiliated third parties than the terms we receive in our agreements with Fortress.

The agreements we entered into with Fortress in connection with the separation include the Management Services Agreement, or the MSA, and the Founders Agreement. While we believe the terms of these agreements are reasonable, they might not reflect terms that would have resulted from arm's-length negotiations between unaffiliated third parties. The terms of the agreements relate to, among other things, payment of a royalty on product sales and the provision of employment and transition services. We might have received better terms from third parties because, among other things, third parties might have competed with each other to win our business. Effective November 12, 2018, the MSA fee and certain payment obligations pursuant to the Founders Agreement were waived under the Waiver and Termination Agreement signed between Avenue, Fortress and InvaGen.

The ownership by our executive officers and some of our directors of equity securities of Fortress and/or rights to acquire equity securities of Fortress might create, or appear to create, conflicts of interest.

Because of their current or former positions with Fortress, some of our executive officers and directors own shares of Fortress common stock and/or options to purchase shares of Fortress common stock. Their individual holdings of common stock and/or options to purchase common stock of Fortress may be significant compared to their total assets. Ownership by our directors and officers, after our separation, of common stock and/or options to purchase common stock of Fortress create or might appear to create conflicts of interest when these directors and officers are faced with decisions that could have different implications for Fortress than for us. For instance, and by way of example, if there were to be a dispute between Fortress and us regarding the calculation of the royalty fee due to Fortress under the terms of the Founders Agreement, then certain of our officers and directors may have and will appear to have a conflict of interest with regard to the outcome of such dispute.

Risks Pertaining to Our Business and Industry

We currently have no drug products for sale, and only one drug product candidate, IV Tramadol. We are dependent on the success of IV Tramadol and cannot guarantee that this product candidate will receive regulatory approval or be successfully commercialized.

Our business success depends on our ability to obtain regulatory approval to successfully commercialize, market and sell our only product candidate, IV Tramadol, and any significant delays in obtaining approval to commercialize, market and sell IV Tramadol will have a substantial adverse impact on our business and financial condition.

If the application for IV Tramadol is approved, our ability to generate revenues from IV Tramadol will depend on our ability to:

- establish and maintain agreements with our contract manufacturers, wholesalers, distributors and group purchasing organizations on commercially reasonable terms;

- obtain sufficient quantities of IV Tramadol from qualified third-party manufacturers that manufacture in accordance with Current Good Manufacturing Practices (CGMP) requirements, as required to meet commercial demand at launch and thereafter;
- hire, train, deploy and support our sales force;
- create market demand for IV Tramadol through our own marketing and sales activities, and any other arrangements to promote this product candidate we may later establish;
- conduct such marketing and sales activities in a manner that is compliant with federal and state laws, including restrictions on off-label promotion and anti-kickback requirements;
- obtain and maintain government and private payer reimbursement for our product; and
- maintain patent protection and regulatory exclusivity for IV Tramadol.

We may not receive regulatory approval for IV Tramadol or future product candidates, or its or their approvals may be delayed, which would have a material adverse effect on our business and financial condition.

IV Tramadol and other future product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to premarket approval and comprehensive regulation by the FDA, DEA and other regulatory agencies in the United States. Failure to obtain marketing approval for IV Tramadol or any future product candidates will prevent us from commercializing our product candidates. We have not received approval to market IV Tramadol from regulatory authorities in any jurisdiction. We have only limited experience in conducting preclinical and clinical studies and filing and supporting the applications necessary to gain marketing approvals and expect to rely on third party contract research organizations as well as consultants and vendors to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities.

Our product candidate IV Tramadol or any future product candidates must meet FDA's standards for safety and efficacy, but may be determined not to be effective, to be only moderately effective, to not be safe for use in its intended population, or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

On October 12, 2020, we announced that we had received a Complete Response Letter ("CRL") from the FDA regarding our New Drug Application ("NDA") for IV Tramadol. The CRL cited deficiencies related to the terminal sterilization validation and stated that IV Tramadol, intended to treat patients in acute pain who require an opioid, is not safe for the intended patient population.

On February 12, 2021, we resubmitted our NDA to the FDA for IV Tramadol. The NDA resubmission followed the receipt of official minutes from a Type A meeting with the FDA. The resubmission included revised language relating to the proposed product label and a report relating to terminal sterilization validation. On June 14, 2021, we announced that we had received a second Complete Response Letter (the "Second CRL") from the FDA regarding the Company's NDA for IV Tramadol. The Second CRL stated that the delayed and unpredictable onset of analgesia with IV Tramadol does not support its benefit as a monotherapy to treat patients in acute pain and that there is insufficient information to support that IV tramadol in combination with other analgesics is safe and effective for the intended patient population. We continues to pursue regulatory approval for IV Tramadol and had a Type A meeting with the FDA in July 2021. The FDA did not deviate from any of the positions the FDA previously took in the First CRL and the Second CRL.. We submitted a formal dispute resolution request ("FDRR") with the Office of Neuroscience of the FDA on July 27, 2021. On August 26, 2021, we received an Appeal Denied Letter from the Office of Neuroscience of the FDA in response to the FDRR submitted on July 27, 2021. On August 31, 2021, we submitted a FDRR with the Office of New Drugs ("OND") of the FDA. On October 21, 2021, we received a written response from the OND of the FDA stating that the OND needs additional input from an Advisory Committee in order to reach a decision on the FDRR.. Our ability to potentially commercialize IV Tramadol, and the timing of any potential commercialization, are dependent on the FDA's review of the FDRR for IV Tramadol, whether or not the FDA ultimately approves IV Tramadol, and potentially on whether or not we procure additional capital.

If our product candidate or any future product candidate receives marketing approval, the approved label indication and accompanying label information may be required to contain information limiting the approved use of our drug, which could limit sales of the product. In addition, our third-party supplier may be subject to an inspection by the FDA that identifies deficiencies in its manufacturing facilities and concludes they are not operating in compliance with CGMP requirements, which in turn, may force us to identify, qualify and rely upon additional suppliers.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if approval is granted at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in the regulatory review process for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical studies or clinical trials. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidate or any future product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenue will be materially impaired.

In addition, even if we were to obtain approval, the approval of the indication for our product candidate by such regulatory authorities may, among other things, be more limited than we request. Such regulatory authorities may not approve the price we intend to charge for our product, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. These regulatory authorities may also require the label to contain warnings, contraindications, or precautions that limit the commercialization of that product. Any of these scenarios could compromise the commercial prospects for our product candidate or any future product candidates.

If serious adverse or unacceptable side effects are identified during the development of IV Tramadol or our future product candidates, we may need to abandon or limit our development of some of our product candidates.

If our product candidate or future product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. In our industry, many compounds that initially showed promise in early stage testing have later been found to cause undesirable side effects that prevented further development of the compound. In the event that our preclinical or clinical trials reveal a high and unacceptable severity and prevalence of side effects, our trials could be delayed, suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development or deny approval of our product candidate or future product candidates for any or all targeted indications. The FDA could also issue a letter requesting additional data or information prior to making a final decision regarding whether or not to approve a product candidate. The number of requests for additional data or information issued by the FDA in recent years has increased, and resulted in substantial delays in the approval of several new drugs. Undesirable side effects caused by our product candidate or future product candidates could also result in the inclusion of serious risk information in our product labeling, application of burdensome post-market requirements, or the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing and generating revenues from the sale of our product candidate. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial and could result in potential product liability claims.

For example, some of the adverse events observed in the IV Tramadol clinical trials completed to date include nausea, dizziness, drowsiness, tiredness, sweating, vomiting, dry mouth, somnolence and hypotension.

Additionally, if one or more of our current or future product candidates receives marketing approval, and we or others later identify undesirable side effects caused by this product, a number of potentially significant negative consequences could result, including:

- regulatory authorities may require the addition of serious risk-related labeling statements, specific warnings, precautions, or contraindication;

- regulatory authorities may suspend or withdraw their approval of the product, or require the suspension of manufacturing, or the recall of the product from the market;
- regulatory authorities may require implementation of burdensome post-market risk mitigation strategies and practices;
- we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product; or
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining marketing approval and market acceptance of our product candidate or future product candidates or could substantially increase our commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from its sale.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel.

We may not be able to attract or retain qualified management and commercial, scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our employees, consultants, or third-party partners may engage in misconduct or other improper activities, including those that result in noncompliance with certain regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees, consultants, or third-party partners could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee, consultant, or third-party misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation, as well as civil and criminal liability. The precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other civil and/or criminal sanctions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. Although we believe that the safety procedures for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of contamination or injury resulting from our use of 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.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

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

We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company" as that term is used in the JOBS Act, and may remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of the initial public offering of our common stock, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our outstanding common stock that are held by non-affiliates exceeds $700 million as of the prior June 30, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this Annual Report on Form 10-K;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have elected to take advantage of this extended transition period.

We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non-voting common shares held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than $100 million during the most recently completed fiscal year and our voting and non-voting common shares held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure, are exempt from the auditor attestation requirements of Section 404, and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors.

We have elected to take advantage of certain of the reduced reporting obligations. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile.

We are a "controlled company" within the meaning of NASDAQ listing standards and, as a result, qualify for, and rely on, exemptions from certain corporate governance requirements. You will not have the same protections afforded to stockholders of companies that are subject to such requirements.

We are a "controlled company" within the meaning of NASDAQ listing standards. Under these rules, a company of which more than 50% of the voting power is held by an individual, a group or another company is a "controlled company" and may elect not to comply with certain corporate governance requirements of NASDAQ, including (i) the requirement that a majority of the Board of Directors consist of independent directors, (ii) the requirement that we have a nominating and corporate governance committee that is composed entirely of independent directors with a written charter addressing the committee's purpose and responsibilities and (iii) the requirement that we have a compensation committee that is composed entirely of independent directors with a written charter addressing the committee's purpose and responsibilities. We intend to rely on some or all of these exemptions.

Accordingly, you will not have the same protections afforded to stockholders of companies subject to all of the corporate governance requirements of NASDAQ.

Certain of our officers and directors serve in similar roles with our parent company, affiliates, related parties and other parties with whom we transact business; ongoing and future relationships and transactions between these parties could result in conflicts of interest.

We share directors and/or officers with certain of our parent company, affiliates, related parties or other companies with which we transact business, and such arrangements could create conflicts of interest in the future, including with respect to the allocation of corporate opportunities. While we believe that we have put in place policies and procedures to identify such conflicts and that any existing agreements that may give rise to such conflicts and any such policies or procedures were negotiated at arm's length in conformity with fiduciary duties, such conflicts of interest may nonetheless arise. The existence and consequences of such potential conflicts could expose us to lost profits, claims by our investors and creditors, and harm to our results of operations.

Risks Pertaining to Our Finances

We have incurred significant losses since our inception. We expect to incur losses for the foreseeable future, and may never achieve or maintain profitability.

We are an emerging growth company with a limited operating history. We have focused primarily on in-licensing and developing IV Tramadol, with the goal of supporting regulatory approval for this product candidate. We have incurred losses since our inception in February 2015.

These losses, among other things, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect to continue to incur significant operating losses for the foreseeable future. We also do not anticipate that we will achieve profitability for a period of time after generating material revenues, if ever. If we are unable to generate revenues, we will not become profitable and may be unable to continue operations without continued funding. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the timing or amount of increased expenses or when or if, we will be able to achieve profitability. In addition, the Company cannot be certain that additional funding will be available on acceptable terms, or at all.

Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if:

- IV Tramadol or other future product candidates are approved for commercial sale, due to the necessity in establishing adequate commercial infrastructure to launch such candidate or candidates without substantial delays, including hiring, sales and marketing personnel, and contracting with third parties for warehousing, distribution, cash collection and related commercial activities;
- we are required by the FDA, or foreign regulatory authorities, to perform studies in addition to those currently expected;
- there are any delays in completing our clinical trials or the development of any of our product candidates;
- we execute other collaborative, licensing or similar arrangements and the timing of payments we may make or receive under these arrangements;
- there are variations in the level of expenses related to our future development programs;
- there are any product liability or intellectual property infringement lawsuits in which we may become involved; and
- there are any regulatory developments affecting IV Tramadol or the product candidates of our competitors.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from our development stage product, and we do not know when, or if, we will generate any revenue. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- obtain regulatory approval for IV Tramadol, or any other product candidates that we may license or acquire;
- manufacture commercial quantities of IV Tramadol or other product candidates, if approved, at acceptable cost levels; and
- develop a commercial organization and the supporting infrastructure required to successfully market and sell IV Tramadol or other product candidates, if approved.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress our value and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in our value could also cause you to lose all or part of your investment.

Our short operating history makes it difficult to evaluate our business and prospects.

We were incorporated on February 9, 2015, and have only been conducting operations with respect to IV Tramadol since February 17, 2015. We have not yet demonstrated an ability to successfully obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions about our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

In addition, as a young business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to expand our capabilities to support commercial activities. We may not be successful in adding such capabilities.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any past quarterly period as an indication of future operating performance.

There is substantial doubt about our ability to continue as a going concern, which may hinder our ability to obtain future financing.

Our unaudited interim condensed financial statements as of September 30, 2021 have been prepared under the assumption that we will continue as a going concern for the next twelve months. As of September 30, 2021, we had cash and cash equivalents of $0.6 million and an accumulated deficit of $76.1 million. We do not believe that our cash and cash equivalents are sufficient for the next twelve months. As a result of our financial condition and other factors described herein, there is substantial doubt about our ability to continue as a going concern. Our ability to continue as a going concern will depend on our ability to obtain additional funding, as to which no assurances can be given. We continue to analyze various alternatives, including amending existing lines of credit, debt or equity financings or other arrangements. Our future success depends on our ability to raise capital and/or implement the various strategic alternatives discussed above. We cannot be certain that these initiatives or raising additional capital, whether through selling additional debt or equity securities or obtaining a line of credit or other loan, will be available to us or, if available, will be on terms acceptable to us. If we issue additional securities to raise funds, these securities may have rights, preferences, or privileges senior to those of our common stock, and our current shareholders may experience dilution. If we are unable to obtain funds when needed or on acceptable terms, we may be required to curtail our current development programs, cut operating costs, forego future development and other opportunities or even terminate our operations.

We do not have any products that are approved for commercial sale and therefore do not expect to generate any revenues from product sales in the foreseeable future, if ever.

We have not generated any product related revenues to date. To obtain revenues from sales of our product candidates, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing and marketing products with commercial potential. We may never succeed in these activities, and we may not generate sufficient revenues to continue our business operations or achieve profitability.

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all. If we fail to raise the necessary additional capital, we may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

Our operations have consumed substantial amounts of cash since inception. We expect to significantly increase our spending to advance the clinical development of IV Tramadol and launch and commercialize any additional product candidates for which we receive regulatory approval, including building our own commercial organizations to address certain markets. We will require additional capital for the further development and potential commercialization of IV Tramadol or other potential product candidates, as well as to fund our other operating expenses and capital expenditures, and cannot provide any assurance that we will be able to raise funds to complete the development of our product.

We cannot be certain that additional funding will be available on acceptable terms, or 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 or discontinue the development or commercialization of one or more of our product candidates. We may also seek collaborators for product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available. Any of these events could significantly harm our business, financial condition and prospects.

Our future funding requirements will depend on many factors, including, but not limited to:

- the potential for delays in our efforts to seek regulatory approval for our product candidate, and any costs associated with such delays;
- the costs of establishing a commercial organization to sell, market and distribute our product candidates;
- the rate of progress and costs of our efforts to prepare for the submission of an NDA for any product candidates that we may in-license or acquire in the future, and the potential that we may need to conduct additional clinical trials to support applications for regulatory approval;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with our product candidates, including any such costs we may be required to expend if our licensors are unwilling or unable to do so;

- the cost and timing of securing sufficient supplies of our product candidate from our contract manufacturers in preparation for commercialization;
- the effect of competing technological and market developments;
- the terms and timing of any collaborative, licensing, co-promotion or other arrangements that we may establish;
- if one or more of our product candidates are approved, the potential that we may be required to file a lawsuit to defend our patent rights or regulatory exclusivities from challenges by companies seeking to market generic versions of one or more of our product candidates; and
- the success of the commercialization of one or more of our product candidates.

In order to carry out our business plan and implement our strategy, we may need to obtain additional financing and may choose to raise additional funds through strategic collaborations, licensing arrangements, public or private equity or debt financing, bank lines of credit, asset sales, government grants, or other arrangements. We cannot be sure that any additional funding, if needed, will be available on terms favorable to us or at all. Furthermore, any additional equity or equity-related financing may be dilutive to our stockholders, and debt or equity financing, if available, may subject us to restrictive covenants and significant interest costs. If we obtain funding through a strategic collaboration or licensing arrangement, we may be required to relinquish our rights to our product candidate or marketing territories.

Our inability to raise capital when needed would harm our business, financial condition and results of operations, and could cause our stock value to decline or require that we wind down our operations altogether.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish proprietary rights.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, grants and license and development agreements in connection with any collaborations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing and preferred equity 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.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market any potential product candidates that we would otherwise prefer to develop and market ourselves.

We will continue to incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

We are a listed and traded public company. As a public company, we incur significant legal, accounting and other expenses under the Sarbanes-Oxley Act of 2002, as well as rules subsequently implemented by the Securities and Exchange Commission, or SEC, and the rules of any stock exchange on which we may become listed. These rules impose various requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and appropriate corporate governance practices. Our management and other personnel have devoted and will continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified persons to serve on our Board of Directors, our Board committees or as executive officers.

The Sarbanes-Oxley Act of 2002 requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. As a result, we are required to periodically perform an evaluation of our internal controls over financial reporting to allow management to report on the effectiveness of those controls, as required by Section 404 of the Sarbanes-Oxley Act. However, while we remain either a non-accelerated filer and/or an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we have engaged in a process to document and evaluate our internal control over financial reporting. These efforts to comply with Section 404 and related regulations have required, and continue to require, the commitment of significant financial and managerial resources. While we anticipate maintaining the integrity of our internal controls over financial reporting and all other aspects of Section 404, we cannot be certain that a material weakness will not be identified when we test the effectiveness of our control systems in the future. If a material weakness is identified, we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources, costly litigation or a loss of public confidence in our internal controls, which could have an adverse effect on the market price of our stock.

If we fail to satisfy applicable listing standards, including compliance with the minimum market value of listed securities requirement, our common stock may be delisted from the NASDAQ Capital Market.

On September 2, 2021, we received a letter from the Listing Qualifications Department of the NASDAQ Stock Market notifying us that, based upon its review for the last 30 consecutive business days, we did not meet the continuing listing requirements of NASDAQ Marketplace Rule 5550(b)(2), which requires that we maintain a minimum market value of listed securities of at least $35 million. NASDAQ also informed us that we did not meet the requirements of Listing Rules 5550(b)(1) and 5550(b)(3). The notification from the NASDAQ Stock Market does not have an immediate effect on the listing of our common stock and our common stock will continue to trade on the NASDAQ under the symbol “ATXI”. Under NASDAQ’s Listing Rules, we have 180 calendar days from the date of the notification to regain compliance, which will expire on March 1, 2022. If, at any time during this period, the market value of our common stock closes at $35 million or more for a minimum of 10 consecutive business days, we will regain compliance with this requirement. If we are unable to regain compliance during the 180-day period, we will receive an additional notification that our securities are subject to delisting. We could, at that time, request a hearing to remain on the NASDAQ Capital Market, which request will ordinarily suspend such delisting determination until a decision is made by NASDAQ subsequent to the hearing.

There can be no assurances, however, that we will be successful in regaining compliance with the continued listing requirements and maintaining the listing of our common stock on the NASDAQ Capital Market. Delisting from the NASDAQ could adversely affect our ability to raise additional financing through the public or private sale of equity securities, would significantly affect the ability of investors to trade our securities and would negatively affect the value and liquidity of our common stock. Delisting could also have other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest and fewer business development opportunities. If our common stock is delisted by the NASDAQ the price of our common stock may decline and our common stock may be eligible to trade on the OTC Bulletin Board, another over-the-counter quotation system, or on the pink sheets where an investor may find it more difficult to dispose of their common stock or obtain accurate quotations as to the market value of our common stock. Further, if we are delisted, we would incur additional costs under requirements of state “blue sky” laws in connection with any sales of our securities. These requirements could severely limit the market liquidity of our common stock and the ability of our stockholders to sell our common stock in the secondary market.

In the event we were to pursue a bankruptcy reorganization under the U.S. Bankruptcy Code, we would be subject to the risks and uncertainties associated with bankruptcy proceedings, including the potential delisting of our common stock from trading on Nasdaq.

We continue to experience significant financial and operating challenges that present substantial doubt as to our ability to continue as a going concern. If we continue to experience financial and operating challenges or are unsuccessful or unable to raise additional capital, there is risk that it will be necessary for us to commence reorganization proceedings. In the event we were to pursue such a restructuring, our operations, our ability to develop and execute our business plan and our continuation as a going concern would be subject to the risks and uncertainties associated with bankruptcy proceedings, including, among others: the high costs of bankruptcy proceedings and related fees; our ability to maintain the listing of our common stock on the Nasdaq Capital Market; our ability to obtain sufficient financing to allow us to emerge from bankruptcy and execute our business plan post-emergence, and our ability to comply with terms and conditions of that financing; our ability to maintain our relationships with our lenders, counterparties, vendors, suppliers, employees and other third parties; our ability to maintain contracts that are critical to our operations on reasonably acceptable terms and conditions; the ability of third parties to use certain limited safe harbor provisions of the U.S. Bankruptcy Code to terminate contracts without first seeking bankruptcy court approval; and the actions and decisions of third parties who have claims and/or interests in our bankruptcy proceedings that may be inconsistent with our operational and strategic plans. Any reorganization effected under the U.S. Bankruptcy Code will result in a total loss of your investment in our common stock.

In addition, if we were to commence bankruptcy proceedings, our shares of common stock would likely be delisted from trading on Nasdaq. Nasdaq rules provide that securities of a company that trades on Nasdaq may be delisted in the event that such company seeks bankruptcy protection. In response to a Chapter 11 filing, Nasdaq would likely issue a delisting letter immediately following such a filing. If Nasdaq were to issue such a letter, we would have the opportunity to appeal the determination during which time the delisting would be stayed, but if we did not appeal or otherwise were not successful in our appeal, our common stock would soon thereafter be delisted and our common stock could be traded in the over-the-counter markets. Any delisting of our common stock could result in a substantial decline in the value of our common stock including, among other reasons, for the reduced liquidity of our common stock.

Risks Pertaining to Reliance on Third Parties

If IV Tramadol is approved and our contract manufacturer fails to produce the product in the volumes that we require on a timely basis, to produce the product according to the applicable quality standards and requirements, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the commercialization of this product candidate, lose potential revenues or be unable to meet market demand.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls, and the use of specialized processing equipment. We have entered into a development and supply agreement for the completion of pre-commercialization manufacturing development activities and the manufacture of commercial supplies of IV Tramadol. Any termination or disruption of this relationship may materially harm our business and financial condition, and impact any commercialization efforts for this product candidate.

In order to meet anticipated demand for IV Tramadol, if this product candidate is approved, we currently have one manufacturer to provide us clinical and commercial supply of IV Tramadol in accordance with the CGMP requirements. We also may plan to qualify a backup manufacturer, in order to ensure an alternative source and to mitigate any potential supply issues.

All of our contract manufacturers must comply with strictly enforced federal, state and, where applicable, foreign regulations, including CGMP requirements enforced by the FDA through its inspectional authority over facilities under the FDCA, as well requirements for controlled substance handling and security requirements enforced by DEA, and while we exercise oversight of our suppliers, we have limited direct control over their compliance with these regulations, as reflected in day-to-day operations. Any failure to comply with applicable regulations may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval, and would limit the availability of our product. Any quality or compliance issue, manufacturing defect or error discovered after products have been produced and distributed could result in even more significant consequences, including costly recall procedures, re-stocking costs, damage to our reputation and potential for product liability claims.

If the commercial manufacturers upon whom we rely to manufacture IV Tramadol, and any other product candidates we may in-license, fail to deliver sufficient commercial quantities on a timely basis at commercially reasonable prices, we would likely be unable to meet demand for our products and we would lose potential revenues.

We rely, and expect to continue to rely, on third parties to conduct our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials or complying with applicable regulatory requirements.

We have relied on third party contract research organizations and clinical research organizations to conduct some of our preclinical studies and all of our clinical trials for IV Tramadol and may do so any future product candidates. We may continue to rely on third parties, such as contract research organizations, clinical research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct preclinical studies and clinical trials. The agreements with these third parties might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that could delay our product development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our legal and regulatory product development responsibilities. For example, we will remain responsible for ensuring that each of our preclinical studies and clinical trials are conducted in accordance with the general investigational plan and protocols for the trial and for ensuring that our preclinical studies are conducted in accordance with good laboratory practice, or GLP, as appropriate. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of our clinical research organizations fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable or unacceptable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted using products manufactured and produced in accordance with CGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

The third parties with whom we have contracted to help perform our preclinical studies or clinical trials may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidate and will not be able to, or may be delayed in our efforts to, potentially successfully commercialize our product candidate.

If any of our relationships with these third-party contract research organizations or clinical research organizations terminates, we may not be able to enter into arrangements with alternative contract research organizations or clinical research organizations or to do so on commercially reasonable terms. Switching or adding additional contract research organizations or clinical research organizations involves additional cost and requires extensive training and management time and focus. In addition, there is a natural transition period when a new contract research organization or clinical research organization commences work. As a result, delays could occur, which could compromise our ability to meet our desired development timelines. Though we carefully manage our relationships with our contract research organizations or clinical research organizations, there can be no assurance that we will not encounter challenges or delays in the future.

We contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and expect to continue to do so for potential commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our potential product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own any manufacturing facilities or personnel. We rely, and expect to continue to rely, on third party manufacturers to manufacture our product candidate for preclinical and clinical testing, as well as for commercial manufacture, once our product candidate receives marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidate or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or potential commercialization efforts.

We may be unable to establish any agreements with such third party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third party manufacturers, reliance on third party manufacturers entails additional risks, including, but not necessarily limited to:

- reliance on the third party for regulatory compliance and quality assurance;
- raw material or active ingredient shortages from suppliers the third party has qualified for our product;
- the possible breach of the manufacturing agreement by the third party;
- manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

The facilities used by our contract manufacturers to manufacture our product candidate is subject to registration requirements, and inspection by the FDA. A pre-approval inspection may be conducted after the submission of an application to the FDA. Although we will have oversight over our suppliers and manufacturers, we do not directly control the manufacturing operations and processes at these facilities, and therefore rely on, our contract manufacturers to ensure full compliance with CGMP regulations with respect to the day-to-day operations related to the manufacture of our product candidates. Third party manufacturers may, following an inspection, be subject to a Form FDA-483 or similar inspectional findings, or a Warning Letter, or may not otherwise be able to comply with the CGMP regulations or similar regulatory requirements outside the United States. The failure of our third-party manufacturers to comply with applicable regulations directly impacts our compliance and could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

IV Tramadol and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There may be a limited number of manufacturers that both operate under CGMP regulations and are capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. We may incur added costs and delays in identifying and qualifying any replacement manufacturers.

The DEA restricts the importation of a controlled substance finished drug product when the same substance is commercially available in the United States, which could reduce the number of potential alternative manufacturers for IV Tramadol.

Our current and anticipated future dependence upon others for the manufacture of our product candidate may adversely affect our future profit margins and our ability to potentially commercialize any products that receive marketing approval on a timely and competitive basis.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or potential commercialization of our products, producing additional losses and depriving us of potential product revenue.

We rely on clinical data and results obtained by third parties that could ultimately prove to be inaccurate or unreliable.

As part of our strategy to mitigate development risk, we sought to develop a product candidate with a validated mechanism of action, and we utilize biomarkers to assess potential clinical efficacy early in the development process. This strategy necessarily relies upon clinical data and other results obtained by third parties that may ultimately prove to be inaccurate or unreliable. Further, such clinical data and results may be based on products or product candidates that are significantly different from our product candidate or future product candidates. If the third-party data and results we rely upon prove to be inaccurate, unreliable or not applicable to our product candidate or future product candidate, we could make inaccurate assumptions and conclusions about our product candidates and our research and development efforts could be compromised and called into question during the review or any marketing applications we submit.

Risks Pertaining to Regulatory Approval Process

We may not receive regulatory approval for IV Tramadol, or our approval may be significantly delayed due to scientific or regulatory reasons.

We continue to pursue regulatory approval. We have filed a Formal Dispute Resolution Request (FDRR) in accordance with the FDRR process that exists within the FDA's Center for Drug Evaluation and Research (CDER) for resolving scientific and/or medical disputes between CDER and sponsors that cannot be resolved at the division level. The FDA has significant regulatory discretion, and even where we have submitted information, responses, data and scientific rationales for our positions, the FDA may not accept these responses or may otherwise conclude that we have not fully satisfied their concerns. Even by escalating above the division level by utilizing the FDA's Formal Dispute Resolution process, there is no guarantee that the FDA will accept our FDRR for review, and if they do, that the FDA's agrees with our proposed outcome. There is no guarantee that the FDA will agree with our position, consider the deficiencies cited in the CRLs resolved, or grant regulatory approval. If the FDA agrees to hear our appeal, there is no guarantee that we will successfully establish a path forward regarding the unresolved issues identified by the scientific and technical reviewers. The FDRR process, itself, is inherently uncertain, and could lead to further delays, if the FDA declines to accept the request, decides to issue of an interim response, determines that a decision on the appeal must be made at a different level of management, or believes that new information has been introduced, and decides not to hear the appeal on the grounds that the FDA will only hear an appeal based on the same information that was relied upon to make the original decision.

Even if IV Tramadol receives regulatory approval, which may not occur, it and any other products we may market will remain subject to substantial regulatory scrutiny.

IV Tramadol and any other product candidates we may license or acquire will also be subject to ongoing regulatory and compliance requirements, including regular inspections by the FDA and other regulatory authorities. These requirements relate to, among others, labeling, packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information and reports, registration and listing requirements, ongoing CGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping of the drug.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance programs to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and off-label information and if we do not market our products for only their approved indications and on-label information, we may be subject to enforcement action for off-label marketing as well as false claims liability. Violations of the FDCA relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our product, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such product, operations, manufacturers or manufacturing processes;
- restrictions or new requirements related to the promotion, labeling or marketing of a product;

- restrictions on product distribution or use, including import and export restrictions;
- requirements to conduct post-marketing studies or clinical trials;
- Form FDA-483 findings, or warning letters;
- recall of the product, or withdrawal of the product from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- fines, restitution or disgorgement of profits;
- suspension or withdrawal of marketing or regulatory approvals;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our product;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies, as well as policies of the DEA, who has jurisdiction over controlled substances and opioids, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidate. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained.

We will need to obtain FDA approval of any proposed product brand names, and any failure or delay associated with such approval may adversely impact our business.

A pharmaceutical product candidate cannot be marketed in the United States or many other countries until we have completed a rigorous and extensive regulatory review processes, including obtaining the approval of a brand name. Any brand names we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the U.S. Patent and Trademark Office, or USPTO. The FDA typically conducts a review of proposed product brand names, including an evaluation of potential for confusion with other product names. The FDA may also object to a product brand name if it believes the name inappropriately implies medical claims. If the FDA objects to any of our proposed product brand name, we may be required to adopt an alternative brand name for our product candidate. If we adopt an alternative brand name, we would lose the benefit of our existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product brand name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to potentially commercialize our product candidate.

Our current and future relationships with customers and third-party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors, distributors, retailers, marketers and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and similar state or foreign laws which may constrain the business or financial arrangements and relationships through which we sell, market and distribute any product candidates for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by U.S. federal and state governments and by governments in foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include, but are not necessarily limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs, such as Medicare and Medicaid;

- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which impose criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent, making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government, or the knowing retention of an overpayment from government health care programs; the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose obligations on covered healthcare providers, health plans, and healthcare clearinghouses, as well as their business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Open Payments program, which requires manufacturers of certain drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to "payments or other transfers of value" made to physicians, which is defined to include doctors, dentists, optometrists, podiatrists and chiropractors, and certain teaching hospitals and applicable manufacturers to report annually to CMS ownership and investment interests held by the physicians and their immediate family members. Data collection began on August 1, 2013 with requirements for manufacturers to submit reports to CMS by March 31, 2014 and 90 days after the end of each subsequent calendar year. Disclosure of such information was made by CMS on a publicly available website beginning in September 2014; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with

current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, which could have a material adverse effect on our business. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including our collaborators, is found not to be in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also materially affect our business.

Regulatory approval for any approved product is limited by the FDA to those specific indications and conditions for which clinical safety and efficacy have been demonstrated.

Any regulatory approval is limited to the specific labeled indication(s) for which a product is deemed to be safe and effective by the FDA. In addition to the FDA approval required for new formulations, any new indication for an approved product also requires FDA approval. If we are not able to obtain FDA approval for any desired future indications for our product, our ability to effectively potentially market and sell our product may be reduced and our business may be adversely affected.

While physicians may choose to prescribe drugs for uses that are not described in the product's approved labeled indication, or for uses that differ from those tested in clinical studies, and thus the basis for approval by the regulatory authorities, our ability to promote the products is limited to those indications that are specifically approved by the FDA. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. Regulatory authorities in the United States generally do not regulate the practice of medicine by physicians with respect to their choice of treatments. Regulatory authorities do, however, restrict communications by pharmaceutical companies in terms of their ability to promote off-label uses or disseminate off-label information. If our promotional activities fail to comply with these requirements, we may be subject to regulatory, compliance, or enforcement action by, these authorities. In addition, our failure to follow FDA requirements relating to promotion and advertising may result in a Warning Letter, cause the FDA to suspend or withdraw an approved product from the market, require a recall, require the issuance of corrective advertising, institute fines, or could result in disgorgement of money, operating restrictions, injunctions or civil or criminal prosecution by the government, any of which could harm our reputation and business.

If the DEA decides to reschedule Tramadol from a Schedule IV controlled substance to a more restrictive Schedule, IV Tramadol could lose its competitive advantage, and our related clinical development and regulatory approval could be delayed or prevented.

In July 2014, the DEA classified Tramadol as a Schedule IV controlled substance. In comparison, other opioids, which have a high potential for abuse, are classified as Schedule I and II controlled substances. If approved, IV Tramadol will be the only intravenous Schedule IV opioid on the market. However, in the current environment where the opioid epidemic is a recognized problem in the United States, there is a possibility that the DEA could reschedule Tramadol to a more restrictive classification (Schedule I, II or III). Such a rescheduling, or other similar action by DEA, would severely impair IV Tramadol's current competitive advantage over traditional opioids and may affect our ability to potentially market IV Tramadol as a safe alternative pain management product.

Risks Pertaining to the Commercialization of Product Candidate

Current and future legislation and regulation may increase the difficulty and cost for us to obtain marketing approval of, and to commercialize, our product candidate and may affect the prices we are able to obtain.

In the United States, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidate, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and certain disabled people and introduced a reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this law provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this law and future laws could decrease the coverage and price that we will receive for any approved products. While the MMA only applies to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Therefore, any limitations in reimbursement that results from the MMA may result in reductions in payments from private payors.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively the ACA, became law. The ACA is a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the ACA of importance to our potential product candidate are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biological products;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability to drugs dispensed to Medicaid managed care organization enrollees;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under 340B Drug Pricing Program;
- new requirements to report financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

The Supreme Court upheld the ACA in the main challenge to the constitutionality of the law in 2012. Specifically, the Supreme Court held that the individual mandate and corresponding penalty was constitutional because it would be considered a tax by the federal government. The Supreme Court also upheld federal subsidies for purchasers of insurance through federally facilitated exchanges in a decision released in June 2015.

At the end of 2017, Congress passed the Tax Cuts and Jobs Act, which repealed the penalty for individuals who fail to maintain minimum essential health coverage as required by the ACA. Following this legislation, Texas and 19 other states filed a lawsuit alleging that the ACA is unconstitutional as the individual mandate was repealed, undermining the legal basis for the Supreme Court's prior decision. On December 14, 2018, Texas Federal District Court Judge Reed O'Connor issued a ruling declaring that the ACA in its entirety is unconstitutional. Upon appeal, the Fifth Circuit upheld the district court's ruling that the individual mandate is unconstitutional. However, the Fifth Circuit remanded the case back to the district court to conduct a more thorough assessment of the constitutionality of the entire ACA despite the individual mandate being unconstitutional. The Supreme Court agreed to hear the case on appeal from the Fifth Circuit on March 2, 2020 and held oral arguments on November 10, 2020. While this lawsuit has no immediate legal effect on the ACA and its provisions, it is ongoing and the outcome may have a significant impact on our business.

The Bipartisan Budget Act of 2018, the "BBA," which set government spending levels for Fiscal Years 2018 and 2019, revised certain provisions of the ACA. Specifically, beginning in 2019, the BBA increased manufacturer point-of-sale discounts off negotiated prices of applicable brand drugs in the Medicare Part D coverage gap from 50% to 70%, ultimately increasing the liability for brand drug manufacturers. Further, this mandatory manufacturer discount applied to biosimilars beginning in 2019.

The 116th Congress explored legislation intended to address the cost of prescription drugs. Notably, the major committees of jurisdiction in the Senate (Finance Committee, Health, Education, Labor and Pensions Committee, and Judiciary Committee), have marked up legislation intended to address various elements of the prescription drug supply chain. Proposals include a significant overhaul of the Medicare Part D benefit design, addressing patent loopholes, and efforts to cap increases in drug prices. On December 12, 2019, the House of Representatives passed broad legislation that would, among other provisions, require HHS to negotiate drug prices and impose price caps. Failure by a manufacturer to reach an agreement with HHS on the negotiated price could result in significant penalties for prescription drug manufacturers. The 117th Congress convened on January 3, 2021, and could reintroduce many of the bills targeting drug prices. While we cannot predict what proposals may ultimately become law, the elements under consideration could significantly change the landscape in which the pharmaceutical market operates.

The Trump Administration took several regulatory steps to redirect ACA implementation. The Department of Health and Human Services (HHS) finalized a hospital payment reduction for drugs acquired through the 340B Drug Pricing Program.

Under the Trump Administration, HHS finalized several proposals aimed at lowering drug prices for Medicare beneficiaries and increasing price transparency. For example, the Trump Administration issued an interim final rule on November 27, 2020 implementing a "Most Favored Nation" payment model for Part B drugs that applies international reference pricing to determine reimbursement for certain drugs paid by Medicare Part B. The interim final rule was enjoined by federal courts prior to its implementation date of January 1, 2021, and the lawsuit is ongoing. In addition, HHS, in conjunction with the FDA, finalized four pharmaceutical importation pathways in September 2020: (1) regulations establishing importation of pharmaceuticals from Canada by wholesalers and pharmacists; (2) FDA guidance permitting manufacturers to import their own pharmaceuticals that were originally intended for marketing in other countries; (3) a request for proposals from private sector entities to import prescription drugs for personal use under existing statutory authority; and (4) a request for proposals from private sector entities to reimport insulin under existing statutory authority. Further, on November 11, 2020, the Trump Administration issued a final rule that changes the permissible structure of drug rebates and discounts between drug manufacturers and third-party payors (including pharmacy benefit managers that negotiate drug prices on behalf of such third-party payors). This final rule, often referred to as the "Rebate Rule," could have significant direct and indirect impacts on drug pricing in both government and commercial markets. With respect to price transparency, the Trump Administration promulgated regulations that require hospitals and third-party payors to disclose prices of items and services, which may impact negotiated rates in the commercial market.

On January 20, 2021, Joe Biden was inaugurated as the 46th president of the United States. As a presidential candidate, Mr. Biden indicated support for several policies aimed at lowering drug prices, including government price negotiation, drug importation, international reference pricing, and price increase controls. The incoming Biden Administration may continue, modify, or repeal many of the drug pricing policies proposed and finalized by the Trump Administration. While we cannot predict which policies the Biden Administration may support and enforce, the policies finalized in the months prior to the beginning of Mr. Biden's term, if continued, could significantly change the landscape in which the pharmaceutical market operates and significantly impact our ability to effectively market and sell our products.

There have been, and likely will continue to be, legislative and regulatory proposals at the federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare products and services. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any products for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

In addition, governments may impose price controls, which may adversely affect our future profitability. In January 2020, President Trump signed into law the U.S.-Mexico-Canada (USMCA) trade deal into law. As enacted, there are no commitments with respect to biological product intellectual property rights or data protection, which may create an unfavorable environment across these three countries

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the payment that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government healthcare programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to potentially generate revenue, attain profitability, or commercialize our product.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals, if any, of our product candidate, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing conditions and other requirements.

Public concern regarding the safety of opioid drug products such as IV Tramadol could delay or limit our ability to obtain regulatory approval, result in the inclusion of serious risk information in our labeling, negatively impact market performance, or require us to undertake other activities that may entail additional costs.

In light of widely publicized events concerning the safety risk of certain drug products, the FDA, members of Congress, the Government Accountability Office, medical professionals and the general public have raised concerns about potential controlled substance drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and the establishment of risk management programs. The Food and Drug Administration Amendments Act of 2007, or FDAAA, grants significant expanded authority to the FDA much of which is aimed at improving the safety of drug products before and after approval. In particular, the new law authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information and require risk evaluation and mitigation strategies for certain drugs, including certain currently approved drugs. It also significantly expands the federal government's clinical trial registry and results databank, which we expect will result in significantly increased government oversight of clinical trials. Under the FDAAA, companies that violate these and other provisions of the new law are subject to substantial civil monetary penalties, among other regulatory, civil and criminal penalties. The increased attention to drug safety issues may result in a more cautious approach by the FDA in its review of data from our clinical trials. Data from clinical trials may receive greater scrutiny, particularly with respect to safety, which may make the FDA or other regulatory authorities more likely to require additional preclinical studies or clinical trials. If the FDA requires us to conduct additional preclinical studies or clinical trials prior to approving IV Tramadol, our ability to obtain approval of this product candidate will be delayed. If the FDA requires us to provide additional clinical or preclinical data following the approval of IV Tramadol, the indications for which this product candidate is approved may be limited or there may be specific warnings or limitations on production dosing, and our efforts to commercialize IV Tramadol may be otherwise adversely impacted.

Rising public, medical, Congressional, and agency concern around the prescription of controlled substance drug products to patients and a growing movement to reduce the use of opioid drug products, to develop abuse-deterrent products, and to prevent dependence also could negatively impact our ability to commercialize and generate revenue from IV Tramadol if it is approved for marketing in the United States. Congress has enacted several laws intended to address opioid use disorder, including the Comprehensive Addiction and Recovery Act (CARA) in 2016, the 21 st Century Cures Act (Cures Act) in 2016, and the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act (the SUPPORT Act) in 2018. These laws primarily focus on funding for treatment, research, and education, but also include provisions intended to encourage reduction in opioid use, such as funding for research on non-opioid pain treatments. Other legislative and administrative measures at the state and federal level include, or may include in the future, restrictions and limitations on opioid prescribing, limitations on opioid doses dispensed per episode of care, labeling requirements specific to opioids, limitations on FDA approval of opioids, assessment of fees against opioid manufacturers, or reimbursement disincentives specific to opioids.

We expect intense competition for IV Tramadol, and new products may emerge that provide different or better therapeutic alternatives for our targeted indications.

The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. We face, and will continue to face, competition in the development and marketing of IV Tramadol from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. There can be no assurance that developments by others will not render IV Tramadol obsolete or noncompetitive. Furthermore, new developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical industry at a rapid pace. These developments may render IV Tramadol obsolete or noncompetitive.

IV Tramadol will compete with well-established products with similar indications. Competing products available for the management of pain include Ofirmev (IV acetaminophen) and IV formulations of NSAIDs such as Dyloject (diclofenac), Toradol (ketorolac), Anjeso (meloxicam) and Caldolor (ibuprofen). In addition, we also expect to compete with agents such as Exparel, a liposome injection of bupivacaine indicated for administration into the surgical site to produce postsurgical analgesia. In addition to approved products, there are a number of product candidates in development for the management of acute pain. The late-stage pain development pipeline is replete with reformulations and fixed-dose combination products of already available therapies. Among specific drug classes, opioid analgesics and NSAIDs represent the greatest number of agents in development. Most investigational opioids that have reached the later stages of clinical development are new formulations of already marketed opioids. Likewise, investigational NSAIDs — mostly lower dose injectable reformulations of already approved compounds — are another significant area of late-stage drug development in the postoperative pain space.

Competitors may seek to develop alternative formulations of IV centrally acting synthetic opioid analgesics for our targeted indications that do not directly infringe on our in-licensed patent rights. The commercial opportunity for IV Tramadol could be significantly harmed if competitors are able to develop alternative formulations outside the scope of our in-licensed patents. Compared to us, many of our potential competitors have substantially greater:

- capital resources;
- development resources, including personnel and technology;
- clinical trial experience;
- regulatory experience;
- expertise in prosecution of intellectual property rights; and
- manufacturing, distribution and sales and marketing experience.

As a result of these factors, our competitors may obtain regulatory approval of their products more rapidly than we are able to or may obtain patent protection or other intellectual property rights that limit our ability to develop or potentially commercialize IV Tramadol. Our competitors may also develop drugs that are more effective, safe, useful and less costly than ours and may be more successful than us in manufacturing and marketing their products.

If the government or third-party payors fail to provide adequate coverage and payment rates for IV Tramadol or any future products we may license or acquire in the future, if any, or if hospitals choose to use therapies that are less expensive, our potential revenue and prospects for profitability will be limited.

Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower-cost drugs and may be incorporated into existing payments for other services. In both domestic and foreign markets, our sales of any future products will depend in part upon the availability of coverage and reimbursement from third party payors. Such third-party payors include government health programs such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. In particular, many U.S. hospitals receive a fixed reimbursement amount per procedure for certain surgeries and other treatment therapies they perform. Because this amount may not be based on the actual expenses the hospital incurs, hospitals may choose to use therapies which are less expensive when compared to our product candidate or future product candidates. Accordingly, IV Tramadol or any other product candidates that we may in-license or acquire, if approved, will face competition from other therapies and drugs for these limited hospital financial resources. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to the satisfaction of hospitals, other target customers and their third-party payors. Such studies might require us to commit a significant amount of management time and financial and other resources. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by implementation of recently promulgated regulations that permit importation of drugs from countries where they may be sold at lower prices than in the United States. Our future product might not ultimately be considered cost-effective. Adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

If IV Tramadol does not achieve broad market acceptance, the potential revenues that we generate from its sales will be limited.

The commercial success of IV Tramadol, if approved, will depend upon its acceptance by the medical community, the ability to ensure that the drug is included in hospital formularies, and coverage and reimbursement for IV Tramadol by third party payors, including government payors. The degree of market acceptance of IV Tramadol or any other product candidate we may license or acquire would depend on a number of factors, including, but not necessarily limited to:

- the efficacy and safety as demonstrated in clinical trials;
- the safety and use of IV Tramadol in its intended patient population;
- the timing of market introduction of such product candidate as well as competitive products;
- the clinical indications for which the drug is approved;
- acceptance by physicians, major operators of cancer clinics and patients of the drug as a safe and effective treatment;
- the safety of such product candidate seen in a broader patient group (i.e., real world use);
- the availability, cost and potential advantages of alternative treatments, including less expensive generic drugs;
- the availability of adequate reimbursement and pricing by third party payors and government authorities;
- the relative convenience and ease of administration of the product candidate for clinical practices;
- the product labeling or product insert required by the FDA or regulatory authority in other countries, including any contradictions, warnings, drug interactions, or other precautions;
- the approval, availability, market acceptance and reimbursement for a companion diagnostic, if any;
- the prevalence and severity of adverse side effects;
- the effectiveness of our sales and marketing efforts;

- changes in the standard of care for the targeted indications for our product candidate or future product candidates, which could reduce the marketing impact of any superiority claims that we could make following FDA approval; and

- potential advantages over, and availability of, alternative treatments.

If any product candidate that we develop does not provide a treatment regimen that is as beneficial as, or is not perceived as being as beneficial as, the current standard of care or otherwise does not provide patient benefit, that product candidate, if approved for commercial sale by the FDA or other regulatory authorities, likely will not achieve market acceptance. Our ability to effectively promote and potentially sell IV Tramadol and any other product candidates we may license or acquire in the hospital marketplace will also depend on pricing and cost effectiveness, including our ability to produce a product at a competitive price and achieve acceptance of the product onto hospital formularies, as well as our ability to obtain sufficient third-party coverage or reimbursement. Since many hospitals are members of group purchasing organizations, which leverage the purchasing power of a group of entities to obtain discounts based on the collective buying power of the group, our ability to potentially attract customers in the hospital marketplace will also depend on our ability to effectively potentially promote our product candidate to group purchasing organizations. We will also need to demonstrate acceptable evidence of safety and efficacy, as well as relative convenience and ease of administration. Market acceptance could be further limited depending on the prevalence and severity of any expected or unexpected adverse side effects associated with our product candidate. If our product candidate is approved but does not achieve an adequate level of acceptance by physicians, health care payors and patients, we may not potentially generate sufficient revenue from this product, and we may not become or remain profitable. In addition, our efforts to educate the medical community and third-party payors on the benefits of our product candidate may require significant resources and may never be successful.

If we are unable to establish sales, and marketing capabilities or to enter into agreements with third parties to market and sell our product candidate, we may not be successful in commercializing our product candidate if and when it is approved.

We currently do not have a marketing or sales organization for the marketing and sales of pharmaceutical products since we currently have no drug products for sale, and only one drug product candidate, IV Tramadol. In order to potentially commercialize any product candidate that receives marketing approval, we would need to build out marketing, sales, managerial and other non-technical capabilities or enter into agreements with third party contract organizations to perform these services, and we may not be successful in doing so. In the event of successful development and regulatory approval of IV Tramadol or another product candidate, we might have to build a targeted specialist sales force to market or co-promote the product. There are risks involved with establishing our own sales and marketing capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our potential efforts to successfully commercialize our future product, if any, using our own sales and marketing capabilities include, but are not necessarily limited to:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;

- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;

- the lack of complementary or other products to be offered by sales personnel, which may put us at a competitive disadvantage from the perspective of sales efficiency relative to companies with more extensive product lines; and

- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

As an alternative to establishing our own sales force, we may choose to partner with third parties that have well-established direct sales forces to sell, market and distribute our products. There are risks involved with partnering with third party sales forces, including ensuring adequate training on the product, regulatory, and compliance requirements associated with promotion of the product.

If we breach the agreement under which we license rights to IV Tramadol, we could lose the ability to continue to develop and potentially commercialize this product candidate.

In February 2015, Fortress obtained an exclusive license to IV Tramadol for the U.S. market from Revogenex Ireland Ltd., or Revogenex, pursuant to the License Agreement; Fortress subsequently transferred the License Agreement to us. Because we have in-licensed the rights to this product candidate from a third party, if there is any dispute between us and our licensor regarding our rights under the License Agreement, our ability to develop and potentially commercialize this product candidate may be adversely affected. Any uncured, material breach under the License Agreement could result in our loss of exclusive rights to our product candidate and may lead to a complete termination of our related product development efforts.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for IV Tramadol or other product candidates we may license or acquire and may have to limit their commercialization.

The use of IV Tramadol and any other product candidates we may license or acquire in clinical trials and the sale of any products for which we obtain marketing approval expose us to the risk of product liability claims. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Product liability claims might be brought against us by consumers, health care providers or others using, administering or selling our products. If we cannot successfully defend ourselves against these claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- decreased demand for any product candidates or products that we may develop;
- initiation of investigations by regulators;
- impairment of our business reputation;
- costs of related litigation;
- substantial monetary awards to patients or other claimants;
- loss of revenues;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize our product candidate or future product candidates.

We have limited product liability insurance coverage for our clinical trials. However, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. When needed, we intend to potentially expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for our product candidate in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

Risks Pertaining to Intellectual Property and Potential Disputes Thereof

If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection in the United States with respect to IV Tramadol or any other product candidates that we may license or acquire and the methods we use to manufacture them, as well as successfully defending these patents and trade secrets against third party challenges. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidate. We will only be able to protect our technologies from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

The patent prosecution process is expensive and time-consuming, and we may not be able to 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 our research and development output before it is too late to obtain patent protection. If our licensors or we fail to obtain or maintain patent protection or trade secret protection for IV Tramadol or any other product candidate we may license or acquire, third parties could use our proprietary information, which could impair our ability to compete in the market and adversely affect our ability to generate revenues and achieve profitability. Moreover, should we enter into other collaborations we may be required to consult with or cede control to collaborators regarding the prosecution, maintenance and enforcement of our patents. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, no consistent policy regarding the breadth of claims allowed in pharmaceutical or biotechnology patents has emerged to date in the United States. The patent situation outside the United States is even more uncertain. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after a first filing, or in some cases at all. Therefore, we cannot know with certainty whether we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. In the event that a third party has also filed a U.S. patent application relating to our product candidates or a similar invention, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a material adverse effect on our U.S. patent position. As a result, the issuance, scope, validity, enforceability and commercial value of our or any of our licensors' patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. For example, the federal courts of the United States have taken an increasingly dim view of the patent eligibility of certain subject matter, such as naturally occurring nucleic acid sequences, amino acid sequences and certain methods of utilizing same, which include their detection in a biological sample and diagnostic conclusions arising from their detection. Such subject matter, which had long been a staple of the biotechnology and biopharmaceutical industry to protect their discoveries, is now considered, with few exceptions, ineligible in the first place for protection under the patent laws of the United States. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents (if any) or in those licensed from third parties.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and affect the validity, enforceability, scope or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-to-file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material, adverse effect on our business and financial condition.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, inter parties review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, PTAB trial, proceeding or litigation could reduce the scope of, render unenforceable, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent does not foreclose challenges to its inventorship, scope, validity or enforceability. Therefore, our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates 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.

The patent rights that we have in-licensed covering the infusion time and pharmacokinetics, or PK, profile for IV Tramadol are limited to a specific IV formulation of centrally acting synthetic opioid analgesic, and our market opportunity for this product candidate may be limited by the lack of patent protection for the active ingredient itself and other formulations that may be developed by competitors.

The active ingredients in IV Tramadol have been generic in the United States for a number of years. While we believe that the patent estate covering IV Tramadol (including but not limited to U.S. Patent Nos. 8,895,622; 9,561,195, 9,566,253 9,962,343, 10,406,122, 9,693,949, 9,968,551, 9,980,900, 10,022,321,10,537,521, 10,624,842, 10,751,277, 10,751,278, 10,751,279, 10,646,433, 10,729,644, 10,729,645, and 10,617,635) provides strong protection, our market opportunity would be limited if a generic manufacturer could obtain regulatory approval for another IV formulation of tramadol and commercialize it without infringing our patents.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, rendered unenforceable, or interpreted narrowly.

We may become involved in other types of legal proceedings related to our intellectual property that could result in the invalidation or unenforceability of our patents and could be expensive and time consuming, regardless of the outcome.

Any party can challenge the validity of our patents in post-grant proceedings at the PTAB, which include *inter partes* review and *post-grant* review proceedings. Although these proceedings are more limited, and therefore are often less expensive, than district court litigation, they can still require substantial resources. If the PTAB finds that our patents are unpatentable, we will be unable to enforce those patents against our competitors. Additionally, our competitors may bring other administrative challenges to our patents before the USPTO, including opposition, derivation, interference, *ex parte* reexamination, and *inter partes* reexamination proceedings. These proceedings may prevent our patent applications from issuing, or for patents that are already issued, an unsuccessful outcome will render the patent unenforceable.

If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in any litigation would harm our business.

Our ability to develop, manufacture, market and potentially sell IV Tramadol or any other product candidates that we may license or acquire depends upon our ability to avoid infringing the proprietary rights of third parties. Numerous U.S. and foreign patents and pending patent applications, which are owned by third parties, exist in the general fields of pain treatment and cover the use of numerous compounds and formulations in our targeted markets. Because of the uncertainty inherent in any patent or other litigation involving proprietary rights, we and our licensors may not be successful in defending intellectual property claims by third parties, which could have a material adverse effect on our results of operations. Regardless of the outcome of any litigation, defending the litigation may be expensive, time-consuming and distracting to management. In addition, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that IV Tramadol may infringe. There could also be existing patents of which we are not aware that IV Tramadol may inadvertently infringe.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. If a third party claims that we infringe on their patents or misappropriated their technology, we could face a number of issues, including:

- infringement and other intellectual property claims which, with or without merit, can be expensive and time consuming to litigate and can divert management's attention from our core business;
- substantial damages for past infringement which we may have to pay if a court decides that our product infringes on a competitor's patent;
- a court prohibiting us from selling or licensing our product unless the patent holder licenses the patent to us, which it would not be required to do;
- if a license is available from a patent holder, we may have to pay substantial royalties or grant cross licenses to our patents; and
- redesigning our processes so they do not infringe, which may not be possible or could require substantial funds and time.

We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights that are important or necessary to the development and potential commercialization of our product. It may be necessary for us to use the patented or proprietary technology of third parties to potentially commercialize our product, in which case we would be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are currently party to a license agreement for IV Tramadol. In the future, we may become party to licenses that are important for product development and potential commercialization. If we fail to comply with our obligations under current or future license and funding agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product or utilize any technology that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could materially and adversely affect the value of a product candidate being developed under any such agreement or could restrict our drug discovery activities. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

To the extent we operate in foreign jurisdictions, we may be exposed to increased risk associated with the potential theft of technology and intellectual property.

Our U.S. patents can be enforced against those who make, use, offer to sell, or sell our licensed patented inventions within the U.S., or against those who import our licensed patented inventions within the U.S. We may depend on foreign intellectual property rights to

prevent competitors from manufacturing and selling our products outside of the U.S. without our authorization. Foreign laws and regulations may not protect our patent rights and trade secret rights to the same extent as U.S. law. It is also possible that we may be required to compromise protections or waive rights in order to conduct business in a foreign jurisdiction. Such restrictions may limit our ability to profitably compete in those markets.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent protection for our product candidate or future product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position, particularly where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We limit disclosure of such trade secrets where possible but we also seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who do have access to them, such as our employees, our licensors, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and may unintentionally or willfully disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

General Risks

Our business and operations could be adversely affected by the effects of health epidemics, including the ongoing COVID-19 pandemic.

Any potential future clinical trials may experience delays in patient enrolment, potentially due to prioritization of hospital resources toward the COVID-19 pandemic, or concerns among patients about participating in clinical trials during a public health emergency. The COVID-19 pandemic is affecting the operations of government entities, such as the FDA, as well as contract research organizations, third-party manufacturers, and other third-parties upon whom we rely. As a result of "shelter-in-place" orders, quarantines or similar orders or restrictions to control the spread of COVID-19, many companies, including our own, have implemented work-from-home policies for their employees. The effects of these stay at home orders and work-from-home policies may be negatively impacting productivity, resulting in delays in our timelines. The extent of the impact on our operations depends in part on the time these restrictions remain in place, and whether restrictions are reinstated as a result of a rising surge in COVID-19 cases. These and similar disruptions in our operations could negatively impact our business, operating results and financial condition.

The spread of COVID-19 has also led to disruption and volatility in the global capital markets, which increases the cost of, and adversely impacts access to, capital and increases economic uncertainty. To the extent the COVID-19 pandemic adversely affects our business, financial results and value of our common stock, it may also affect our ability to access capital and obtain financing, which could in the future negatively affect our liquidity.

The global pandemic of COVID-19 continues to evolve rapidly, and the ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full impact of potential delays or effects on our business, , our ability to access the capital markets, or supply chains or on the global economy as a whole. However, these effects could have a material impact on our operations, and we will continue to monitor the COVID-19 situation closely.

Our results of operations and liquidity needs could be materially negatively affected by market fluctuations and economic downturn.

Our results of operations could be materially negatively affected by economic conditions generally, both in the United States and elsewhere around the world. Continuing concerns over inflation, energy costs, geopolitical issues, the availability and cost of credit, the U.S. mortgage market and residential real estate market in the United States have contributed to increased volatility and diminished expectations for the economy and the markets going forward. These factors, combined with volatile oil prices, declining business and consumer confidence and increased unemployment, have precipitated an economic recession and fears of a possible depression. Domestic and international equity markets continue to experience heightened volatility and turmoil. These events and the continuing market upheavals may have an adverse effect on us. In the event of a continuing market downturn, our results of operations could be adversely affected by those factors in many ways, including making it more difficult for us to raise funds if necessary, and our stock price may further decline.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Any system failure, accident or security breach that causes interruptions in our operations could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed clinical trials for IV Tramadol could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liability and the further development of our product candidate may be delayed.

The occurrence of a catastrophic disaster could damage our facilities beyond insurance limits or we could lose key data which could cause us to curtail or cease operations.

We are vulnerable to damage and/or loss of vital data from natural disasters, such as earthquakes, tornadoes, power loss, fire, health epidemics and pandemics, floods and similar events, as well as from accidental loss or destruction. If any disaster were to occur, our ability to operate our businesses could be seriously impaired. We have property, liability and business interruption insurance that may not be adequate to cover losses resulting from disasters or other similar significant business interruptions, and we do not plan to purchase additional insurance to cover such losses due to the cost of obtaining such coverage. Any significant losses that are not recoverable under our insurance policies could seriously impair our business, financial condition and prospects. Any of the aforementioned circumstances, including without limitation the emerging COVID-19 virus, may also impede our employees' and consultants' abilities to provide services in-person and/or in a timely manner; hinder our ability to raise funds to finance our operations on favorable terms or at all; and trigger effectiveness of "force majeure" clauses under agreements with respect to which we receive goods and services, or under which we are obligated to achieve developmental milestones on certain timeframes. Disputes with third parties over the applicability of such "force majeure" clauses, or the enforceability of developmental milestones and related extension mechanisms in light of such business interruptions, may arise and may become expensive and time-consuming.

We may become involved in securities class action litigation that could divert management's attention and harm our business.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of biotechnology and pharmaceutical companies. These broad market fluctuations may cause the market price of our stock to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant stock price volatility in recent years and due to the significant stock price decline we experienced following the announcement of the CRL. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management's attention and resources, which could adversely affect our business.

Item 2. Recent Sales of Unregistered Securities.

N/A.

Item 3. Defaults Upon Senior Securities.

N/A.

Item 4. Mine Safety Disclosures.

N/A.

Item 5. Other Information.

N/A.

Item 6. Financial Statements and Exhibits

Exhibit No.	Description
31.1	Certification of Chief Executive Officer of Avenue Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002, dated November 15, 2021.
31.2	Certification of Principal Financial Officer of Avenue Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002, dated November 15, 2021.
32.1	Certification of Chief Executive Officer of Avenue Therapeutics, Inc. pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, dated November 15, 2021.
32.2	Certification of Principal Financial Officer of Avenue Therapeutics, Inc. pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, dated November 15, 2021.
101	The following financial information from the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2021, formatted in Extensible Business Reporting Language (XBRL): (i) the Condensed Balance Sheets, (ii) the Condensed Statements of Operations, (iii) the Condensed Statements of Stockholders' Equity, (iv) the Condensed Statements of Cash Flows, and (v) Notes to the Condensed Financial Statements.

SIGNATURES

Pursuant to the requirements of the 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.

Avenue Therapeutics, Inc.
(Registrant)

Date: November 15, 2021

By: /s/ Lucy Lu, M.D.
Lucy Lu, M.D.
President, Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.1

Certification of
Principal Executive Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Lucy Lu, M.D., certify that:

1. I have reviewed this report on Form 10-Q of Avenue Therapeutics, 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 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, 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 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 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.

/s Lucy Lu, M.D.
Lucy Lu, M.D.
President, Chief Executive Officer and Director
(Principal Executive Officer)
November 15, 2021

Exhibit 31.2

Certification of
Principal Financial Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Joseph Vazzano, certify that:

1. I have reviewed this report on Form 10-Q of Avenue Therapeutics, 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 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, 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 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 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.

/s/ Joseph Vazzano
Joseph Vazzano
Chief Financial Officer
(Principal Financial Officer)
November 15, 2021

Exhibit 32.1

Certification of
Principal Executive Officer
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

I, Lucy Lu, M.D., Chief Executive Officer of Avenue Therapeutics, Inc. (the "Company"), in compliance with Section 906 of the Sarbanes-Oxley Act of 2002, hereby certify that, to the best of my knowledge, the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2021 (the "Report") filed with the Securities and Exchange Commission:

- Fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

/s/ Lucy Lu, M.D.
Lucy Lu, M.D.
President, Chief Executive Officer and Director
(Principal Executive Officer)
November 15, 2021

Exhibit 32.2

Certification of
Principal Financial Officer
Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

I, Joseph Vazzano, Principal Financial Officer of Avenue Therapeutics, Inc. (the "Company"), in compliance with Section 906 of the Sarbanes-Oxley Act of 2002, hereby certify that, to the best of my knowledge, the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2021 (the "Report") filed with the Securities and Exchange Commission:

- Fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

/s/ Joseph Vazzano
Joseph Vazzano
Chief Financial Officer
(Principal Financial Officer)
November 15, 2021