UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K/A

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

August 15, 2023
Date of Report (Date of earliest event reported)

CervoMed Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-24477**	**30-0645032**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**
20 Park Plaza, Suite 424 Boston, Massachusetts		**02116**
(Address of principal executive offices)		**(Zip Code)**

Registrant's telephone number, including area code: (617) 744-4400

Not applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.001 par value	CRVO	NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

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. ☐

Explanatory Note

On August 16, 2023, the Delaware corporation formerly known as "Diffusion Pharmaceuticals Inc." completed its previously announced merger transaction in accordance with the terms and conditions of the Agreement and Plan of Merger, dated as of March 30, 2023 (the "Merger Agreement"), by and among Diffusion Pharmaceuticals Inc. ("Diffusion"), Dawn Merger Sub Inc., a wholly owned subsidiary of Diffusion ("Merger Sub"), and EIP Pharma, Inc. ("EIP"), pursuant to which Merger Sub merged with and into EIP, with EIP surviving the merger as a wholly owned subsidiary of Diffusion (the "Merger"). Additionally, on August 16, 2023, the Company changed its name from "Diffusion Pharmaceuticals Inc." to "CervoMed Inc." (the "Company").

On August 17, 2023, the Company filed a Current Report on Form 8-K (the "Original Form 8-K") reporting, among other items, the consummation of the Merger. This Amendment No. 1 to Current Report on Form 8-K amends the Original Form 8-K to (i) include a correction to the number of Exchange Shares (as that term is defined in the Original Form 8-K) under Item 2.01 of the Original Form 8-K and (ii) provide the Company's Business section, Risk Factors section, and Management's Discussion and Analysis of Financial Condition and Results of Operations section under Item 8.01, which were excluded from the Original Form 8-K in reliance on the instructions to such Item.

Item 2.01 Completion of Acquisition or Disposition of Assets

The third sentence of the third paragraph of Item 2.01 of the Original Form 8-K is hereby amended and restated in its entirety to read as set forth below:

"At the Effective Time, each outstanding share of EIP capital stock (after giving effect to (i) the automatic conversion of all shares of EIP preferred stock into shares of EIP common stock, (ii) the conversion of EIP's convertible notes into shares of EIP common stock, and excluding any shares held as treasury stock by EIP or held or owned by Diffusion or any subsidiary of Diffusion or EIP and any dissenting shares) was converted into the right to receive 0.1151 shares of Diffusion common stock, which resulted in the issuance by Diffusion of an aggregate of 4,314,033 shares of Diffusion common stock to the stockholders of EIP (the "Exchange Shares"). Immediately following the Effective Time, there were 5,674,250 shares of the Company issued and outstanding."

Item 8.01. Other Events

The Company's Business section, the Company's Risk Factors section and the Company's Management's Discussion and Analysis of Financial Condition and Results of Operations section are filed herewith as Exhibits 99.1, 99.2 and 99.3, respectively, and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	**Description**
99.1	Business Section of CervoMed Inc.
99.2	Risk Factors Section of CervoMed Inc.
99.3	Management's Discussion and Analysis of Financial Condition and Results of Operations of EIP Pharma, Inc. as of and for the period ended June 30, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: September 29, 2023

CervoMed Inc.

By: /s/ William Tanner, Ph.D.
Name: William Tanner, Ph.D.
Title: Chief Financial Officer

MANAGEMENT'S DISCUSSION AND ANALYSIS OF EIP PHARMA'S FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing in Exhibit 99.2 to the Current Report on Form 8-K, filed by CervoMed Inc. ("CervoMed") with the SEC on August 9, 2023. Some of the information contained in this discussion and analysis or set forth in our prospectus filed with the United States Securities and Exchange Commission ("SEC") on July 13, 2023 contains forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. As a result of many factors, including those factors set forth in the "Risk Factors" section included as Exhibit 99.2 to the Form 8-K of which this Exhibit 99.1 is also a part, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. You should carefully read the "Risk Factors" section included as Exhibit 99.2 to the accompanying Form 8-K, as well as the other information included in our prospectus, dated July 13, 2023, and other filings with the SEC, to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements.

On August 16, 2023, subsequent to the date of the financial information included in the discussion below, we (i) completed the previously announced merger transaction (the "Merger") between our wholly owned subsidiary, Dawn Merger Inc., and EIP Pharma, Inc. ("EIP") and, (ii) immediately thereafter, changed our corporate name from "Diffusion Pharmaceuticals Inc," ("Diffusion") to "CervoMed Inc." Accordingly, unless the context otherwise requires, all references in this section to "we," "our," or "us," refer to the business of EIP for all dates and periods prior to August 16, 2023 and to the business of CervoMed for all dates and periods subsequent to (and including) August 16, 2023.

Overview

We are a clinical stage therapeutics company that is developing treatments for acute and chronic neurodegenerative diseases of the brain and the Central Nervous System ("CNS"), such as Dementia with Lewy Bodies ("DLB"), and other neurologic indications. In DLB, for which there are no approved therapies and no disease-modifying drugs in Phase 3 clinical development, we believe we are one of the leaders in the industry, as we are the only company that we are aware of with an asset that, in that disease, has shown statistically significant positive effects compared to placebo in a Phase 2a clinical trial and has entered a Phase 2b clinical evaluation. Our novel approach focuses on reducing the impact of inflammation in the brain, or neuroinflammation, which we believe is a key factor in the manifestation of neurodegenerative disease. Chronic activation of the enzyme p38α in the neurons (nerve cells) within the brains of people with neurodegenerative diseases is believed to impair how neurons communicate through synapses (the connections between neurons). This impairment, termed synaptic dysfunction, leads to deterioration of cognitive and motor abilities. Left untreated, synaptic dysfunction can result in neuronal loss that leads to devastating disabilities, institutionalization and, ultimately, death. We believe that inhibiting p38α activity in the brain, by interfering with key pathogenic drivers of disease, has the potential to improve cognitive and motor function observed in early-stage neurodegenerative diseases. We also believe it is possible to modify the course of these diseases by delaying permanent synaptic dysfunction and neuron death.

We are developing an oral therapy, neflamapimod, that penetrates the blood-brain barrier and inhibits activity of p38α in the neuron. Based on preclinical and clinical work to date, we believe if neflamapimod is given in the early stages of neurodegenerative diseases, it may reverse synaptic dysfunction and improve neuron health. In preclinical studies, neflamapimod has been shown to reverse the neurodegenerative process in the basal forebrain cholinergic ("BFC") system, the specific region of the brain that is the site of the major pathology in DLB. We have obtained positive Phase 2a clinical data in DLB, specifically, statistically significant improvement compared to placebo on measures of dementia severity and functional mobility (walking ability). In addition, we previously obtained and our Phase 2 clinical data in Alzheimer's Disease ("AD") that provides supportive clinical data demonstrating blood-brain-barrier penetration, target engagement, and identification of dose-response.

Our next step in the clinical development of neflamapimod is the conduct of our recently initiated Phase 2b placebo-controlled clinical trial intended to confirm the Phase 2a results and provide the data necessary to finalize design of a Phase 3 clinical trial, the general framework of which has been agreed upon with the U.S. Food and Drug Administration ("FDA"). The Phase 2b trial is estimated to be fully funded by an awarded grant from the National Institute of Health's National Institute on Aging ("NIA") and was initiated in the second quarter of 2023, with data-readout planned for the second half of 2024.

Building on what we learned in our Phase 2a trial, the Phase 2b trial, known as RewinD-LB, is a double-blind, 16-week study in 160 patients with early stage DLB randomized 1:1 to 40mg neflamapimod or placebo TID. Patients in both the neflamapimod and placebo groups who complete the main, randomized, double-blinded, 16-week phase of the study will receive neflamapimod on an open label basis for an additional 32 weeks. Key distinctions from Phase 2a trial include (1) the use of a single daily dose regimen of neflamapimod (40mg TID), (2) use of the CDR-SB, a measure of dementia severity, as a primary endpoint, and (3) the exclusion of patients with AD co-pathology, assessed by ptau181 levels in the blood). Clinical trial simulations indicate with the incorporation of these changes from our Phase 2a trial, the RewinD-LB study is designed to have >95%, approaching 100%, statistical power to detect significant improvement over placebo on the CDR-SB.

EIP Financial Summary as of and for the Period Ended June 30, 2023

To date, we have not had any products approved for sale and have not generated any revenue from product sales. We do not expect to generate revenue from product sales until such time, if ever, that we are able to successfully complete the development and obtain marketing approval for one of our product candidates. We have never been profitable, and we will continue to require additional capital to develop neflamapimod and fund operations for the foreseeable future. We have incurred net losses in each year since inception and expect to continue to incur net losses for the foreseeable future. Our ability to generate product revenue will depend on the successful development and eventual commercialization of neflamapimod. EIP's net losses were $1.8 million and $3.0 million for the three months and six months ended June 30, 2023, respectively. As of June 30, 2023, EIP had an accumulated deficit of $55.3 million. Substantially all such net losses have resulted from costs incurred in connection with research and development programs and from general and administrative costs associated with operations. We expect our expenses will increase in connection with our ongoing activities, as we:

- advance neflamapimod through clinical trials, including our ongoing Phase 2b trial for DLB, through to initiation of a Phase 3 trial in DLB;
- hire additional personnel;
- operate as a public company;
- require the manufacture of supplies for our nonclinical studies and clinical trials; and
- obtain, maintain, expand, and protect our intellectual property portfolio.

EIP's losses from operations and accumulated deficit, as well as the additional capital needed to fund operations within one year of June 30, 2023, raise substantial doubt about EIP's ability to continue as a going concern, prior to giving effect to the Merger subsequently completed on August 16, 2023. However, based on our current operating plan, we believe that EIP's existing cash and cash equivalents on hand as of June 30, 2023, along with the remaining funds to be received from the NIA grant and the cash acquired from Diffusion in the Merger, will enable us to fund our operating expenses and capital expenditure requirements through at least 12 months from June 30, 2023.

We expect to incur substantial expenditures in the foreseeable future for the development of neflamapimod and will require additional financing to continue this development. EIP's financial statements as of and for the period June 30, 2023 have been prepared on a basis that assumes that EIP will continue as a going concern, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might be necessary should we be unable to continue as a going concern.

Recent Developments

Amendments to EIP Convertible Notes

On June 16, 2023, EIP and the noteholders of those certain (i) convertible promissory notes of EIP, dated as of December 4, 2021, as amended, and (ii) convertible promissory notes of EIP, dated as of December 10, 2021, as amended (collectively, the "EIP Convertible Notes") amended the terms and conditions of the EIP Convertible Notes to, among other things, establish a fixed conversion price of $1.47 with respect to the Merger or, with respect to any reverse merger transaction other than the Merger, 70% of the price per share of EIP common stock, par value 0.001 ("EIP Common Stock") as determined in good faith by the EIP board of directors at the time of the execution and delivery by EIP of a definitive agreement providing for a reverse merger.

In addition, the EIP Convertible Notes, dated December 10, 2021 were amended to provide that, to the extent the conversion of such notes in the Merger were to result in the holder beneficially owning more than 9.99% of our outstanding voting stock, such holder would be granted pre-funded warrants in lieu of common stock for the conversion of any principal and accrued but unpaid interest in excess of 9.99%.

In connection with the closing of the Merger, all outstanding EIP Convertible Notes converted into shares of EIP Common Stock at the fixed conversion price of $1.47, which shares of EIP Common Stock were subsequently converted into the right to receive shares of CervoMed common stock (or pre-funded warrants in lieu thereof) upon the closing of the Merger.

July 2023 EIP Share Issuance

On July 10, 2023, EIP sold and issued an aggregate of 551,020 shares of EIP Common Stock to Joshua Boger, an existing EIP stockholder, and Frank Zavrl, a non-employee director of EIP and, following completion of the Merger, CervoMed, for aggregate gross proceeds of $810,000.

Based on the exchange ratio in the Merger of 0.1151, the purchase price of $1.47 per share of EIP Common Stock equates to a purchase price of approximately $12.77 per share of CervoMed common stock subsequently received as Merger consideration.

Closing of Merger

On March 30, 2023, we entered into a merger agreement (the "Merger Agreement") with EIP, pursuant to which EIP merged with an into our wholly owned subsidiary, with EIP surviving the merger. The Merger closed on August 16, 2023. Additionally, in connection with the closing of the Merger, we changed our name from "Diffusion Pharmaceuticals Inc." to "CervoMed Inc."

Impact of COVID-19

The COVID-19 pandemic continues to evolve. While it appears its most severe effects have subsided, COVID-19 could re-emerge or new public health threats could appear. The future impact of the COVID-19 pandemic or a similar health disruption is highly uncertain and subject to change. We cannot predict the full extent of potential delays or impacts on our business, our clinical trials, health care systems, third parties with whom we engage or the global economy as a whole, but if we or any of the third parties with whom we engage, including personnel at contract manufacturing organizations and other third parties with whom we conduct business, were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timeline presently planned could be materially and adversely impacted. Overall, we recognize the challenges of product development during a pandemic, and we will continue to closely monitor events as they develop and plan for alternative and mitigating measures if needed.

Components of EIP Results of Operations as of and for the Period Ended June 30, 2023

Revenue

EIP has not generated any revenue from product sales and we do not expect to do so in the near future. As of June 30, 2023, total cash funding of $4.3 million was received by EIP from the NIA grant. The total revenue recognized from the NIA grant was $1.7 million and $3.1 million for the three and six months ended June 30, 2023, respectively. The funding that has not been recognized as revenue, $1.2 million as of June 30, 2023, has been recorded as deferred revenue.

Research and Development Expenses

Research and development expenses account for a significant portion of our operating expenses. We recognize research and development expenses as incurred. Research and development expenses consist primarily of costs incurred for the discovery and development of our product candidates, which include:

- expenses incurred under agreements with third-party contract organizations, preclinical testing organizations, and consultants;
- costs related to production of clinical materials, including fees paid to contract manufacturers;
- vendor expenses related to the execution of preclinical studies and clinical trials;

- personnel-related expenses, including salaries, benefits, and stock-based compensation for personnel engaged in research and development functions;
- costs related to the preparation of regulatory submissions;
- third-party license fees; and
- expenses for rent and other supplies.

Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors, collaborators, and third-party service providers. Non-refundable advance payments made by us for future research and development activities are capitalized and expensed as the related goods are delivered and as services are performed.

Specific program expenses include expenses associated with the development of our lead product candidate, neflamapimod, which recently initiated a Phase 2b clinical trial for treatment of subjects with DLB. Personnel or other operating expenses incurred for our research and development programs primarily relate to salaries and benefits, stock-based compensation, and facility expenses.

At this time, we cannot reasonably estimate or know the nature, timing, and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, neflamapimod, or for any other product candidates that we may develop or acquire. We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development ("R&D") activities related to developing neflamapimod such as conducting larger clinical trials, seeking regulatory approval and incurring expenses associated with hiring personnel to support other R&D efforts. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of product candidates, including neflamapimod, is highly uncertain.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel-related costs, including stock-based compensation for our personnel in executive, finance and accounting, and other administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters, professional fees paid for accounting, auditing, consulting, and tax services, insurance costs, and facility costs.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development activities and as we begin development activities pursuant to the NIA grant. We also anticipate that we will incur increased expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC and those of any national securities exchange on which our securities are traded, legal, auditing, additional insurance expenses, investor relations activities, and other administrative and professional services.

Other Income (Expense)

Other income (expense) consists of interest earned on our cash and cash equivalents and the change in fair value of the EIP Convertible Notes.

EIP Results of Operations as of and for the Period Ended June 30, 2023

Comparison of Three Months Ended June 30, 2023 and 2022

	Three Months ended June 30,		Change	
	2023	2022	$	%
Grant revenue	$ 1,719,944	$ -	$ 1,719,944	100%
Operating expenses				
Research and development	1,958,388	256,825	1,701,563	663%
General and administrative	1,414,303	493,335	920,968	187%
Total Operating Expenses	3,372,691	750,160	2,622,531	350%
Loss from operations	(1,652,747)	(750,160)	(902,587)	120%
Other income (expense)				
Other income (expense)	(212,211)	(5)	(212,206)	4,244,120%
Interest income	17,707	7,222	10,485	145%
Interest expense	-	1	(1)	(100)%
Total other income (expense)	(194,504)	7,218	(201,722)	(-2,795)%
Net loss	$ (1,847,251)	$ (742,942)	$ (1,104,309)	149%

Grant Revenue

Grant revenue was $1.7 million for the three months ended June 30, 2023, compared to $0 for the three months ended June 30, 2022. The increase of $1.7 million was a result of a $21.0 million grant awarded to us by the NIA in January 2023 to support a Phase 2b study of neflamapimod in DLB.

Research and Development Expenses

Research and development expenses were $2.0 million for the three months ended June 30, 2023, compared to $1.7 million for the three months ended June 30, 2022. The increase of $0.3 million was primarily driven by increased clinical activity.

General and Administrative Expenses

General and administrative expenses were $1.4 million for the three months ended June 30, 2023, compared to $0.5 million for the three months ended June 30, 2022. The increase of $0.9 million was primarily due to an increase in legal, accounting and other professional fees of $0.8 million and an increase in other general and administrative expense, primarily related to public/investor relations, of $0.1 million.

Other Income (Expense)

Other income (expense) was $(212,211) for the three months ended June 30, 2023, compared to $(5) for the three months ended June 30, 2022. The expense increase of $0.2 million was primarily due to adjustments to the fair value of the EIP Convertible Notes for the three months ended June 30, 2023.

Interest Income

Interest income was $17,707 for the three months ended June 30, 2023, compared to $7,222 for the three months ended June 30, 2022. The increase of $10,485 was primarily due to higher interest rates.

Interest expense

Interest expense was $0 for the three months ended June 30, 2023, compared to $1 for the three months ended June 30, 2022.

Comparison of Six Months Ended June 30, 2023 and 2022

	Six Months ended June 30,		Change	
	2023	**2022**	**$**	**%**
Grant revenue	$ 3,127,812	$ -	$ 3,127,812	100%
Operating expenses				
Research and development	3,791,662	625,241	3,166,421	506%
General and administrative	3,053,234	1,007,416	2,045,818	203%
Total Operating Expenses	6,844,896	1,632,657	5,212,239	319%
Loss from operations	(3,717,084)	(1,632,657)	(2,084,427)	128%
Other income (expense)				
Other income (expense)	644,368	(1,769,005)	2,413,373	100%
Interest income	53,111	8,655	44,456	514%
Interest expense	-	(17)	17	(100)%
Total other income (expense)	697,479	(1,760,367)	2,457,846	100%
Net loss	$ (3,019,605)	$ (3,393,024)	$ 373,419	(11)%

Grant Revenue

Grant revenue was $3.1 million for the six months ended June 30, 2023, compared to $0 for the six months ended June 30, 2022. The increase of $3.1 million was a result of a $21.0 million grant awarded to us by the NIA in January 2023 to support a Phase 2b study of neflamapimod in DLB.

Research and Development Expenses

Research and development expenses were $3.8 million for the six months ended June 30, 2023, compared to $0.6 million for the six months ended June 30, 2022. The increase of $3.2 million was primarily driven by increased clinical activity.

General and Administrative Expenses

General and administrative expenses were $3.1 million for the six months ended June 30, 2023, compared to $1.0 million for the six months ended June 30, 2022. The increase of $2.1 million was primarily due to an increase in legal, accounting and other professional fees of $1.7 million and an increase in other general and administrative expense, primarily related to public/investor relations, of $0.3 million.

Other Income

Other income was $0.6 million for the six months ended June 30, 2023, compared to an expense of $1.8 million for the six months ended June 30, 2022. The increase of $2.4 million was primarily due to adjustments to the fair value of the EIP Convertible Notes.

Interest Income

Interest income was $53,111 for the six months ended June 30, 2023, compared to $8,665 for the six months ended June 30, 2022. The increase of $44,456 was primarily due to higher interest rates.

Interest expense

Interest expense was $0 for the six months ended June 30, 2023, compared to $17 for the six months ended June 30, 2022.

Liquidity and Capital Resources of EIP

Sources of Liquidity

From the date of EIP's inception through June 30, 2023, EIP's operations had primarily been financed through the issuance of common stock, convertible preferred stock and convertible debt financings. As of June 30, 2023 (and without giving pro forma effect to the Merger subsequently completed on August 16, 2023 or the proceeds from the issuance of EIP Common Stock in July 2023), EIP had approximately $0.6 million of cash and cash equivalents. EIP has incurred net operating losses since inception and has not generated positive cash flows from operations. As of June 30, 2023, EIP had an accumulated deficit of approximately $55.3 million. In January 2023, EIP was awarded a $21.0 million grant from the NIA to support the Phase 2b study of neflamapimod in DLB, which is expected to be received over a three-year period. As of June 30, 2023, total cash funding of $4.3 million had been received from the NIA grant.

Our primary uses of cash are to fund our operations, which consist primarily of research and development expenditures related to our programs and, to a lesser extent, general and administrative expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

The total principal and accrued interest of EIP convertible debt of $11.5 million, which had a fair value of $11.8 million as of June 30, 2023, was scheduled to become due in December 2023 pursuant to its terms. However, in connection with closing of the Merger in August 2023, all previously outstanding convertible debt of EIP was converted into the right to receive shares of CervoMed common stock. EIP's losses from operations, negative operating cash flows and accumulated deficit, as well as the additional capital needed to fund operations within one year of the issuance date of EIP's financial statements for the period ended June 30, 2023, raise substantial doubt about EIP's ability to continue as a going concern, prior to giving effect to the subsequent closing of the Merger on August 16, 2023. However, based on our current operating plan, we believe that EIP's existing cash and cash equivalents on hand as of June 30, 2023, along with the remaining funds to be received from the NIA grant and the cash acquired from Diffusion in the Merger, will enable us to fund our operating expenses and capital expenditure requirements through at least 12 months from June 30, 2023.

We expect to incur substantial expenditures in the foreseeable future for the development of our product candidates and will require additional financing to continue this development. The unaudited financial statements included as Exhibit 99.2 to CervoMed's Current Report on Form 8-K, filed with the SEC on August 9, 2023, have been prepared on a basis that assumes that EIP will continue as a going concern, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might be necessary should EIP be unable to continue as a going concern.

Future Funding Requirements

Any product candidates we may develop may never achieve commercialization, and we anticipate that we will continue to incur losses for the foreseeable future. We expect that our research and development expenses, general and administrative expenses, and capital expenditures will continue to increase. In addition, we expect to incur costs associated with operating as a public company. As a result, 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 or other capital sources, including potential collaborations, licenses and other similar arrangements. Our primary uses of capital are, and we expect will continue to be, costs related to clinical research, manufacturing and development services; compensation and related expenses; costs relating to the build-out of our headquarters, other offices and laboratories; license payments or milestone obligations that may arise; laboratory expenses and costs for related supplies; manufacturing costs; legal and other regulatory expenses and general overhead costs.

Based on our current operating plan, we believe that EIP's existing cash and cash equivalents on hand as of June 30, 2023, along with the remaining funds to be received from the NIA grant and the cash acquired from Diffusion in the Merger, will enable us to fund our operating expenses and capital expenditure requirements to the end of 2024. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. We will continue to require additional financing to advance our current product candidates through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. We will continue to seek funds through equity offerings, debt financings or other capital sources, including potential collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise capital, we will need to delay, reduce or terminate planned activities to reduce costs, including our development or commercialization activities for neflamapimod. We might also be required to seek funds through arrangements with third parties that require us to relinquish certain of our rights to neflamapimod or otherwise agree to terms unfavorable to us.

Because of the numerous risks and uncertainties associated with research, development and commercialization of product candidates, we are unable to estimate the exact amount of our operating capital requirements. Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the enrollment, progress, timing, costs and results of the Phase 2b trial for neflamapimod in patients with DLB, as well as additional development plans for neflamapimod in other disease indications, such as Recovery after Anterior Circulation Ischemic Stroke and Early Onset Alzheimer's Disease;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities;
- our ability to reach certain milestone events set forth in our collaboration agreements and the timing of such achievements, triggering our obligation to make applicable payments;
- the hiring of additional clinical, scientific and commercial personnel to pursue our development plans, as well the increased costs of internal and external resources as to support our operations as a public reporting company;
- the cost and timing of securing manufacturing arrangements for clinical or commercial production;
- the cost of establishing, either internally or in collaboration with others, sales, marketing and distribution capabilities to commercialize neflamapimod, if approved;
- the cost of filing, prosecuting, enforcing, and defending our patent claims and other intellectual property rights, including defending against any patent infringement actions brought by third parties against us;

- the ability to receive additional non-dilutive funding, including grants from organizations and foundations;
- our ability to establish strategic collaborations, licensing or other arrangements with other parties on favorable terms, if at all; and
- the extent to which we may in-license or acquire other product candidates or technologies.

A change in the outcome of any of these or other variables could significantly alter the costs and timing associated with the development of neflamapimod. Furthermore, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

Cash Flows

	Six Months ended June 30,	
	2023	**2022**
Net cash used in:		
Operating activities	$ (3,443,795)	$ (1,309,289)
Net decrease in cash and cash equivalents	$ (3,443,795)	$ (1,309,289)

Net Cash Used in Operating Activities

For the six months ended June 30, 2023, cash used in operating activities was $3.4 million. The net cash outflow from operations primarily resulted from net loss of $3.0 million and change in fair value of convertible debt of $0.6 million, offset by a non-cash charge of $0.1 million for stock-based compensation and changes in operating assets and liabilities of $0.1 million.

For the six months ended June 30, 2022, cash used in operating activities was $1.3 million. The net cash outflow from operations primarily resulted from net loss of $3.4 million, offset by a change in fair value of convertible debt of $1.8 million, a non-cash charge of $0.2 million for stock-based compensation, contributed capital in lieu of executive compensation of $0.1 million and a change in operating assets and liabilities of $0.1 million.

Net Cash Provided by Financing Activities

There was no cash provided by financing activities during the six months ended June 30, 2023 and June 30, 2022.

Net Cash Provided by Investing Activities

There was no cash provided by investing activities during the six months ended June 30, 2023 and June 30, 2022.

Contractual Obligations and Other Commitments

We enter into contracts in the normal course of business with third-party contract organizations for clinical trials, non-clinical studies and manufacturing, and other services for operating purposes. The amount and timing of contractual obligations may vary based on the timing of services.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Critical Accounting Polices and Estimates

Management’s discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions, and any such differences may be material. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management’s judgments and estimates. We believe the following are our more significant estimates and judgments used in the preparation of our financial statements.

Research and Development Costs

Research and development costs are expensed as incurred and consist primarily of new product development. Research and development costs include salaries and benefits, consultants' fees, process development costs and stock-based compensation, as well as fees paid to third parties that conduct certain research and development activities on our behalf.

A substantial portion of our ongoing research and development activities are conducted by third-party service providers. We record accrued expenses for estimated preclinical study and clinical trial expenses. Estimates are based on the services performed pursuant to contracts with research institutions, contract research organizations in connection with clinical studies, investigative sites in connection with clinical studies, vendors in connection with preclinical development activities, and contract manufacturing organizations in connection with the production of materials for clinical trials. Further, we accrue expenses related to clinical trials based on the level of subject enrollment and activity according to the related agreement. We monitor subject enrollment levels and related activity to the extent reasonably possible and make judgments and estimates in determining the accrued balance in each reporting period. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development.

If we underestimate or overestimate the level of services performed or the costs of these services, actual expenses could differ from estimates. To date, we have not experienced significant changes in our estimates of preclinical studies and clinical trial accruals.

Stock-based Compensation

Stock-based compensation for employee and non-employee awards is measured on the grant date based on the fair value of the award and recognized on a straight-line basis over the requisite service period. The fair value of stock options to purchase common stock are measured using the Black-Scholes option pricing model. We account for forfeitures as they occur. The fair value of stock options is determined by us using the methods and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment and estimation by management.

Expected Term. The expected term represents the period that stock-based awards are expected to be outstanding. We use the "simplified method" to estimate the expected term of stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the contractual term of ten years and the weighted-average vesting term of our stock options, taking into consideration multiple vesting tranches. We utilize this method due to lack of historical data and the plain-vanilla nature of our stock-based awards.

Expected Volatility. We have limited information on the volatility of common stock as the shares are not actively traded on any public markets. The expected volatility is derived from the historical stock volatilities of comparable peer public companies within our industry. These companies are considered to be comparable to our business over a period equivalent to the expected term of the stock-based awards.

Risk-Free Interest Rate. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the date of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the stock options expected term.

Expected Dividend Rate. The expected dividend is zero as we have not paid, nor do we anticipate paying, any dividends on our stock options in the foreseeable future.

As of June 30, 2023, the grant date fair value of EIP Common Stock was typically determined by EIP's board of directors with the assistance of management and a third party valuation specialist. Following the completion of the Merger, our board of directors will determine the fair value of each share of underlying common stock based on the closing price of our common stock as reported on the date of each equity grant.

Valuation of EIP Convertible Notes

The fair value of the EIP Convertible Notes as of June 30, 2023 and December 31, 2022 were estimated as the combination of a zero-coupon bond and a call option. The combined values for each of the EIP Convertible Notes as of June 30, 2023 and December 31, 2022 were then weighted by the probability of completing a financing or reverse merger. This approach resulted in the classification of the EIP Convertible Notes as of June 30, 2023 and December 31, 2022 as Level 3 of the fair value hierarchy (see Note 8 to the unaudited financial statements included as Exhibit 99.2 to CervoMed's Current Report on Form 8-K, filed with the SEC on August 9, 2023). The assumptions utilized to value the EIP Convertible Notes as of June 30, 2023 were an estimated term of 0.13 years, volatility of 69.0% and a market yield of 54.0% and 5.4% for completing a financing or reverse merger, respectively. The measurement of fair value incorporates expected future cash flows associated with interest payments; as such, there is no separate accrual for interest accrued but not yet paid.

In connection with the closing of the Merger, all outstanding EIP Convertible Notes converted into shares of EIP Common Stock at the fixed conversion price of $1.47, which shares of EIP Common Stock were subsequently converted into the right to receive shares of CervoMed common stock (or pre-funded warrants in lieu thereof) upon closing of the Merger.

Quantitative and Qualitative Disclosures about Market Risk

Interest Rate Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. The primary objective of our investment activities is to preserve capital to fund our operations. We also seek to maximize income from our investments without assuming significant risk.

EIP had cash and cash equivalents of $0.6 million as of June 30, 2023 (without giving pro forma effect to the completion of the Merger in August 2023 or proceeds from the issuance of EIP Common Stock in July 2023), which included bank deposits and money market funds. Such interest-earning instruments carry a degree of interest rate risk. However, historical fluctuations in interest income have not been significant for us.

Foreign Currency Risk

Our expenses are generally denominated in U.S. dollars. However, we have entered into a limited number of contracts with vendors for research and development services with payments denominated in foreign currencies, including the Euro. We are subject to foreign currency transaction gains or losses on our contracts denominated in foreign currencies. To date, foreign currency transaction gains and losses have not been material to our financial statements, and we have not had a formal hedging program with respect to foreign currency.

Effects of Inflation

We believe that inflation and changing prices have had a moderate impact on our results of operations for the period presented herein.

Recently Adopted Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in the notes to our financial statements appearing in Exhibit 99.2 to CervoMed's Current Report on Form 8-K, filed with the SEC on August 9, 2023.

Exhibit 99.2

Risks Related to CervoMed Inc.

Investing in CervoMed Inc. (the "Company," "we" or "us") securities involves a high degree of risk. Set forth below are certain material risks and uncertainties known to us that could adversely affect our business, financial condition, or results of operations or could cause our actual results to differ materially from our expectations expressed in our filings with the U.S. Securities and Exchange Commission (the "SEC") and other public statements. The occurrence of the events contemplated by one or more of the factors we describe below could cause the market price of our securities to decline, resulting in the loss of all or part of any investment in our common stock. Furthermore, other risks that are currently unknown to us or that we currently believe to be immaterial may also, nevertheless, adversely affect our business, financial condition, or results of operations in a way that is material.

You should carefully consider the risk factors set forth below as may updated by our subsequent filings under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), together with all other information in our filings with the SEC, including the unaudited financial information included as Exhibit 99.2 to our Current Report on Form 8-K filed with the SEC on August 9, 2023, Management's Discussion and Analysis of Financial Condition and Results of Operations filed as Exhibit 99.1 to the Current Report on Form 8-K to which these Risk Factors are attached, and our Quarterly Report on Form 10-Q for the period ended June 30, 2023, filed with the SEC on August 8, 2023, before making any investment decisions. Furthermore, the risks and uncertainties described below and in the documents mentioned above are not the only ones the Company faces. Additional risks and uncertainties not presently known to the Company or that we currently believe to be immaterial could, nevertheless, adversely affect the Company's business, operating results and financial condition, as well as adversely affect the value of an investment in the Company's securities, and the occurrence of any of these risks might cause you to lose all or part of your investment.

Risks Related to the Company's Business, Financial Position and Capital Requirements

The Company currently does not have, and may never have, any products that generate significant revenues.

The Company is a clinical stage company focused on developing treatments for degenerative diseases of the brain, and currently has no products that are approved for commercial sale, and it is possible it may never be able to develop a marketable product. To date, the Company has not generated any revenues from its lead product candidate, neflamapimod, or from any other product candidate. The Company cannot guarantee that neflamapimod, or any other product candidate that it may develop or acquire in the future, will ever become marketable products.

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drug products are subject to extensive regulation in the United States ("U.S.") and in other countries. Before the U.S. Food and Drug Administration ("FDA") and other regulatory authorities in the European Union and elsewhere will approve neflamapimod for commercialization, the Company must demonstrate that its drug satisfies rigorous standards of safety and efficacy for each of its intended uses. In order to compete effectively, the Company's drugs must be easy to administer, cost-effective and economical to manufacture on a commercial scale. The Company may not achieve any of these objectives.

The Company initiated a Phase 2b randomized double-blind placebo-controlled clinical study of neflamapimod in subjects with Dementia with Lewy Bodies ("DLB") in the second quarter of 2023 and anticipates completing enrollment in the study in the first half of 2024. The Company cannot be certain that this Phase 2b trial or any future clinical development of neflamapimod will be successful, or that it will receive the regulatory approvals required to commercialize that drug candidate for any intended use, or that any future research and drug discovery programs undertaken by the Company will yield a drug candidate suitable for investigation through clinical trials. Even if the Company is able to successfully develop neflamapimod through approval and commercialization, any revenues from sales of the drug will not materialize for several years, if at all.

The Company is a clinical-stage biopharmaceutical company, and it has incurred significant losses since its inception. The Company expects its net losses to continue for the foreseeable future. The Company is not currently profitable and may never achieve or sustain profitability. The Company is unable to predict the extent of future losses or when it might become profitable, if ever.

Investment in pharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval, and become commercially viable. EIP has incurred net losses since its inception, and as of June 30, 2023, it had an accumulated deficit of approximately $55.3 million (without giving effect to the Merger (as defined below)). The Company expects to incur net losses for the foreseeable future as it incurs significant clinical development costs related to the advancement of neflamapimod. The Company has not commercialized any products and has never generated revenue from neflamapimod or any other product. In order to obtain revenues from any product candidate, the Company must succeed, either alone or in collaboration with others, in developing, obtaining regulatory approval for, and manufacturing and marketing drugs with significant market potential. The Company may never succeed in these activities and may never generate revenues that are significant enough to achieve profitability.

The Company expects to incur significant additional operating losses for at least the next several years as it advances neflamapimod through clinical development, conduct clinical trials, seek regulatory approval and commercialize neflamapimod, if it is ultimately approved for marketing. The costs of advancing product candidates into each clinical phase tend to increase substantially over the clinical development process. Therefore, the total costs to advance neflamapimod to marketing approval in even a single jurisdiction will be substantial. Because of the numerous risks and uncertainties associated with pharmaceutical product development, the Company is unable to accurately predict the timing or amount of increased expenses, or when or if it will be able to begin generating revenue from the commercialization of neflamapimod, let alone achieve or maintain profitability.

The amount of the Company's future net losses will depend, in part, on the rate of future growth of its expenses and its ability to generate revenues. If the Company is unable to develop and commercialize one or more product candidates, either alone or through collaborations, or if revenues from any product that receives marketing approval are insufficient, it will not achieve profitability. Even if the Company does achieve profitability, it may not be able to sustain it, which could materially and adversely affect its business.

The Company will require additional capital to fund its operations. If the Company fails to obtain necessary financing on acceptable terms, or if at all, it may not be able to complete the development and commercialization of neflamapimod.

The Company expects to spend substantial amounts to complete the development of, seek regulatory approvals for, and commercialize neflamapimod, if it is ultimately approved for marketing. These expenditures will include costs related to the recently initiated Phase 2b clinical trial of neflamapimod in DLB and costs associated with its license agreement with Vertex Pharmaceuticals Incorporated ("Vertex"), under which the Company is obligated to make certain payments in connection with the achievement of specified events.

Until such time, if ever, that the Company can generate sufficient product revenue and achieve profitability, it expects to seek to finance future cash needs through equity or debt financings and/or corporate collaboration, licensing arrangements and grants. Based upon the Company's current operating plan, the Company believes that the Company's existing cash and cash equivalents and a grant from the National Institute on Aging ("NIA") will enable the Company to fund its operating expenses and capital expenditure requirements for at least the next 12 months. The Company's estimates and expectations regarding its cash runway are based on assumptions that may prove to be incorrect, and changing circumstances could cause it to consume capital faster or in different ways than the Company currently expects. For example, the Company's recently initiated Phase 2b trial for neflamapimod may be more expensive, time-consuming, or difficult to implement than the Company currently anticipates. Because the length of time and activities associated with the successful development of neflamapimod is highly uncertain, the Company is unable to estimate the actual funds it will require to complete research and development and ultimately commercialize its drug candidate for one or more indications.

The Company's future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the enrollment, progress, timing, costs and results of the Company's recently initiated Phase 2b trial for neflamapimod in patients with DLB, as the Company has additional development plans for neflamapimod in other disease indications;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities;
- the Company's ability to reach certain milestone events set forth in its agreement with Vertex and the timing of such achievements, triggering the Company's obligation to make applicable payments;
- the hiring of additional clinical, scientific and operational personnel to pursue the Company's development plans, as well the increased costs of internal and external resources as to support the Company's transition to a public reporting company;
- the cost and timing of securing manufacturing arrangements for clinical or commercial production;
- the cost of establishing, either internally or in collaboration with others, sales, marketing and distribution capabilities to commercialize neflamapimod, if approved;
- the cost of filing, prosecuting, enforcing, and defending the Company's patent claims and other intellectual property rights, including defending against any patent infringement actions brought by third parties against the Company;
- the Company's ability to establish collaborations with other parties on favorable terms, if at all; and
- the extent to which the Company may in-license or acquire other product candidates or technologies.

The Company may raise additional capital in the future through a variety of sources, including public or private equity offerings, debt financings, grant funding, or strategic collaborations and licensing arrangements. Adequate additional financing may not be available to The Company on acceptable terms, or at all. The Company's failure to raise capital as and when needed would have a negative effect on its financial condition and its ability to pursue its business strategy. If the Company is unable to secure additional capital in sufficient amounts or on terms acceptable to the Company, it may have to delay, scale back or discontinue its development or commercialization activities for neflamapimod.

Further, to the extent that the Company raises additional capital through the sale of common stock or securities convertible or exchangeable into common stock, its stockholder's ownership interest in the Company will be diluted. In addition, any debt financing may subject the Company to fixed payment obligations and covenants limiting or restricting its ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If the Company raises additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, the Company may have to relinquish certain valuable intellectual property or other rights to its product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to it. Even if the Company were to obtain sufficient funding, there can be no assurance that it will be available on terms acceptable to the Company or its stockholders.

The Phase 2b clinical study is funded by a non-dilutive grant that is subject to certain conditions for funding in subsequent years.

The Company's recently initiated Phase 2b clinical study is funded by a grant from the National Institute of Health's National Institute on Aging (the "NIA"). The funds for the study will be disbursed over the course of the study as costs are incurred. While the funds for the first year of the study have already been allocated, the awarded funds future year total cost support are subject to the availability of funds (i.e., the NIA is funded by Congress in subsequent fiscal years) and the Company's demonstration of progress in the project that is in line with the timelines provide in the grant. If such funds are no longer available, including due to a government shutdown that prohibits the disbursal of such funds, or the Company fails to demonstrate such progress, the Company's ability to continue its clinical programs may be impaired and delayed, and the Company may otherwise need to seek additional financing.

The Company could be subject to audit and repayment of its non-dilutive NIA grant.

In connection with the NIA grant, the Company may be subject to routine audits by certain government agencies. As part of an audit, these agencies may review the Company's performance, cost structures and compliance with applicable laws, regulations, policies and standards and the terms and conditions of the applicable NIA grant. If any of the Company's expenditures are found to be unallowable or allocated improperly or if the Company has otherwise violated terms of such NIA grant, the expenditures may not be reimbursed and/or it may be required to repay funds already disbursed. Any audit by the NIA may result in a material adjustment to the Company's results of operations and financial condition and harm the Company's ability to operate in accordance with its business plan. Additionally, negative results in any of its planned clinical trials of neflamapimod that are funded with an NIA grant may result in the Company's failure to receive additional NIA grants to fund future clinical trials.

The Company may expend its limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because the Company has limited financial resources, it intends to focus on developing neflamapimod and future product candidates for specific indications that the Company identifies as most likely to succeed, in terms of both regulatory approval and commercialization. As a result, the Company may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. The Company's resource allocation decisions may cause the Company to fail to capitalize on viable commercial products or profitable market opportunities. Its spending on current and future research and development programs and on product candidates for specific indications may not yield any commercially viable products. If the Company does not accurately evaluate the commercial potential or target market for a particular product candidate, it may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for the Company to retain sole development and commercialization rights to such product candidate.

The Company may be required to make significant payments to Vertex in connection with the Company's license agreement.

In August 2012, the Company entered into an Option and License Agreement with Vertex, which the Company amended in April 2014 and November 2015 (collectively, the "Vertex Agreement"). Pursuant to the terms of the Vertex Agreement, the Company acquired an exclusive license to develop and commercialize neflamapimod for the diagnosis, treatment, and prevention of Alzheimer's disease ("AD") and other central nervous system ("CNS") disorders.

Under the Vertex Agreement, the Company is subject to significant potential future obligations, including payment of development milestones and royalties on net product sales, as well as other material obligations. The Vertex Agreement sets forth specific regulatory and product approval events and the related payments that the Company would be obligated to make to Vertex if and when such events occur.

The terms of the Vertex Agreement also provide that the Company will make royalty payments to Vertex in the event aggregate net sales for a commercialized licensed product meet specified thresholds, subject to adjustment in the event of certain events, such as the absence of a valid patent claim or if fees are due to a third party for a license necessary for the development, manufacture, sale or use of a licensed product. Such royalties will be on a sliding scale as a percentage of net sales, depending on the amount of net sales in the applicable years. The Company is also obligated to make a milestone payment to Vertex upon net sales reaching a certain specified amount in any 12-month period.

The first expected milestone events concern filing of a new drug application ("NDA") with the FDA for marketing approval of a licensed product in the U.S., or a similar filing for a non-U.S. major market. Thus, although the Company does not expect any milestone or royalty payments to be due in the immediate future, these potential obligations represent significant cash amounts that it may ultimately be obligated to pay. The Company does not know that it will have sufficient funds available to meet its obligations if and when these payments become due. The obligation to pay some or all of these milestone and royalty amounts may materially harm the Company's development efforts, as well as its overall financial condition.

The Company has identified material weaknesses in its internal control over financial reporting which, if not corrected, could affect the reliability of the Company's financial statements and have other adverse consequences. The Company may identify additional material weaknesses in its internal controls over financing reporting which it may not be able to remedy in a timely manner.

In connection with the audit of the Company's financial statements for the year ended December 31, 2022, material weaknesses in the Company's internal control over financial reporting were identified in relation to: (i) the Company's newly acquired subsidiary, EIP Pharma, Inc.'s ("EIP") valuation and recording of significant complex transactions, specifically related to the valuation of its convertible notes (which have subsequently been converted) and the recording of accrued interest and related interest expense in connection therewith; and (ii) the absence of effective controls regarding the accurate identification, evaluation and proper recording of various expense accounts at year-end.

A material weakness is a deficiency or combination of deficiencies in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our consolidated financial statements would not be prevented or detected on a timely basis. The identified material weaknesses, if not corrected, could result in a material misstatement to the Company's consolidated financial statements that may not be prevented or detected. Given that EIP operated as a private company prior to August 16, 2023, it may not have the necessary formalized processes to effectively implement review controls within its internal control over financial reporting.

The material weaknesses will not be considered remediated until a remediation plan has been fully implemented, the applicable controls operate for a sufficient period of time, and it has been concluded, through testing, that the newly implemented and enhanced controls are operating effectively. The Company currently expects to commence the remediation plan during 2023 by adding additional review procedures by qualified personnel over complex accounting matters and expense accounts. The Company cannot predict the success of such efforts or the outcome of its assessment of the remediation efforts. The Company's efforts may not remediate this material weakness in its internal control over financial reporting, or additional material weaknesses may be identified in the future. In addition, the Company plans to adopt Diffusion Pharmaceutical Inc.'s financial reporting processes. A failure to appropriately integrate financial reporting processes between the two companies, and to implement and maintain effective internal control over financial reporting could result in errors in the Company's financial statements that could result in a restatement of the Company's financial statements and could cause the Company to fail to meet our reporting obligations, any of which could diminish investor confidence in us and cause a decline in the price of the Company's common stock.

The Company and its independent registered public accounting firm were not required to perform an evaluation of its internal control over financial reporting as of December 31, 2022 in accordance with the provisions of the Sarbanes-Oxley Act. Accordingly, the Company cannot assure you that it has identified all material weaknesses or that there will not be additional material weaknesses in the future.

The Company will incur costs and demands upon management as a result of complying with the laws, rules and regulations affecting public companies.

The Company will incur significant legal, accounting and other expenses that the Company did not incur as a private company, including costs associated with public company reporting requirements. The Company will also incur costs associated with corporate governance requirements, including requirements under the laws, rules and regulations of the U.S. Securities and Exchange Commission ("SEC"), as well as the rules and regulations of The Nasdaq Stock Market LLC ("Nasdaq"). These laws, rules and regulations are expected to increase the Company's legal and financial compliance costs and to make some activities more time-consuming and costly. For example, the Company's management team consists of a number of executive officers, some of whom have not previously managed and operated a public company. These executive officers and other personnel will need to devote substantial time to gaining expertise regarding operations as a public company and compliance with applicable laws and regulations. These laws, rules and regulations also may make it difficult and expensive for the Company to obtain directors' and officers' liability insurance. As a result, it may be more difficult for the Company to attract and retain qualified individuals to serve on the Company's board of directors or as executive officers of the Company, which may adversely affect investor confidence in the Company and could cause the Company's business or stock price to suffer.

The Company's future success depends in large part on the Company's ability to retain its key employees, as well as its ability to attract, train and motivate qualified personnel. The Company may also encounter difficulties in managing its growth, which could disrupt its operations.

The Company has a small number of full and part-time employees, and it is highly dependent on the principal members of its management team, including its President and Chief Executive Officer, John Alam, M.D. Although the Company has employment agreements or offer letters with its executive officers and certain key employees, these agreements do not prevent them from terminating their services at any time.

Competition in the biotechnology industry for skilled and experienced employees is intense, particularly in the greater Boston, Massachusetts area where the Company's headquarters is located. The Company also faces competition for the hiring of scientific and clinical personnel from universities and research institutions, many of which are near the Company's headquarters. The loss of the services of any member of the Company's senior management, clinical development or scientific staff may significantly delay or prevent the achievement of drug development and other business objectives and could have a material adverse effect on the Company's business, operating results and financial condition.

The Company also relies on consultants and advisors to assist it in formulating and executing its business strategy. All of the Company's consultants and advisors are either self-employed or employed by other organizations, and they may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations, which may affect their ability to contribute to the Company.

As the Company continues to develop neflamapimod for the treatment of DLB, and also to expand into clinical trials for other CNS disorders, the Company expects to experience significant growth in the number of employees and the scope of its operations. This strategy will require it to recruit additional clinical development, regulatory, scientific, and technical personnel, as well as sales and marketing personnel if the Company's drug is approved. If the Company is unable to attract, retain and motivate a sufficient number of highly qualified personnel to match its growth, its ability to further develop and commercialize neflamapimod, or any future product candidates the Company may develop or acquire, will be limited.

The Company may also be required to implement and improve managerial, operational and financial systems to manage its potential growth. Due to its limited financial and personnel resources, the Company may not be able to effectively manage the expansion of its operations or recruit and train additional qualified personnel. The expansion of the Company's operations may lead to significant costs and may divert its management and business development resources. Any inability to manage growth could delay the execution of the Company's business plans or disrupt its operations.

Consumers may sue the Company for product liability, which could result in substantial liabilities that exceed its available resources and damage its reputation.

Researching, developing, and commercializing drug products entail significant product liability risks. The use of neflamapimod or any other product candidates the Company may develop in clinical trials and the sale of any products for which it obtains marketing approval exposes it to the risk of product liability claims. Product liability claims might be brought against the Company by clinical trial participants, patients, healthcare providers, pharmaceutical distributors or others selling or otherwise coming into contact with its product candidates or future commercial products. The Company has obtained limited product liability insurance coverage for its clinical trials, which the Company believes to be reasonable given its current operations. However, the Company's insurance coverage may not reimburse the Company or may not be sufficient to reimburse it for any expenses or losses it may suffer.

Although the Company currently has limited product liability insurance that covers its clinical trials, it will need to increase and expand this coverage as it commences larger scale trials, as well as if neflamapimod is ultimately approved for commercial sale. This insurance may be extremely expensive or may not fully cover the Company's potential liabilities. Inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of neflamapimod, if it is approved. Product liability claims could have a material adverse effect on the Company's business and results of operations.

The Company's employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

The Company is exposed to the risk of fraud, misconduct or other illegal activity by its employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and negligent conduct that fails to: comply with the laws of the FDA, European Medicines Agency ("EMA") and other comparable foreign regulatory authorities; provide true, complete and accurate information to the FDA, EMA and other comparable foreign regulatory authorities; comply with manufacturing standards the Company has established; comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to the Company. If the Company obtains FDA approval of any of its product candidates and begins commercializing those products in the United States, its potential exposure under such laws will increase significantly, and its costs associated with compliance with such laws are also likely to increase. In particular, research, sales, marketing, education and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of subject recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to the Company's reputation. The Company has adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by employees and third parties, and the precautions the Company takes to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting it from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against the Company, and the Company is not successful in defending itself or asserting its rights, those actions could have a significant impact on its business, including the imposition of significant fines or other sanctions.

If the Company seeks to enter into collaborative arrangements or strategic alliances for its drug candidates, but fails to enter into and maintain successful relationships, it may have to reduce or delay its drug development activities or increase its expenditures.

An important element of a biotechnology company's strategy for developing, manufacturing and commercializing its drug candidates may be to enter into strategic alliances with pharmaceutical companies or other industry participants to advance its programs and enable it to maintain its financial and operational capacity. Biotechnology companies at the Company's stage of development sometimes rely upon collaborative arrangements or strategic alliances to complete the development and commercialization of drug candidates, particularly after the Phase 2 stage of clinical testing.

To date, the Company has not entered into any collaborative arrangements or strategic alliances, and it may face significant competition in seeking such relationships. In addition, such arrangements may place the development of the Company's drug candidates outside its control, require the Company to relinquish important rights, or may otherwise be on terms unfavorable to the Company. The Company may not be able to negotiate collaborations and alliances on acceptable terms, if at all. If the Company enters into a collaborative arrangement and it proves to be unsuccessful, the Company may have to delay, or limit the size or scope of, certain of its drug development activities.

Alternatively, if the Company elects to fund drug development or research programs on its own, it will have to increase its expenditures and will need to obtain additional funding, which may not be available to the Company on acceptable terms, if at all.

The Company's business is subject to complex and evolving U.S. and foreign laws and regulations relating to privacy and data protection. These laws and regulations are subject to change and uncertain interpretation, and could result in claims, changes to its business practices, or monetary penalties, and otherwise may harm the Company's business.

A wide variety of provincial, state, national, and international laws and regulations apply to the collection, use, retention, protection, disclosure, transfer and other processing of personal data. These data protection and privacy-related laws and regulations are evolving and may result in ever-increasing regulatory and public scrutiny and escalating levels of enforcement and sanctions. For example, the European Union General Data Protection Regulation ("GDPR") which became fully effective on May 25, 2018, imposes stringent data protection requirements and provides for penalties for noncompliance of up to the greater of €20 million or four percent of worldwide annual revenues. The GDPR and many other laws and regulations relating to privacy and data protection are still being tested in courts, and they are subject to new and differing interpretations by courts and regulatory officials. The Company is working to comply with the GDPR and other privacy and data protection laws and regulations that apply to it, and the Company anticipates needing to devote significant additional resources to complying with these laws and regulations. It is possible that the GDPR or other laws and regulations relating to privacy and data protection may be interpreted and applied in a manner that is inconsistent from jurisdiction to jurisdiction or inconsistent with the Company's current policies and practices.

The Company's actual or perceived failure to adequately comply with applicable laws and regulations relating to privacy and data protection, or to protect personal data and other data the Company processes or maintains, could result in regulatory fines, investigations and enforcement actions, penalties and other liabilities, claims for damages by affected individuals, and damage to the Company's reputation, any of which could materially affect its business, financial condition, results of operations and growth prospects.

The Company's internal computer systems, or those of its vendors, collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of its product development programs, compromise sensitive information related to its business or prevent it from accessing critical information, potentially exposing it to liability or otherwise adversely affecting its business.

The Company's internal computer systems and those of its current and any future third-party vendors, collaborators and other contractors or consultants are vulnerable to damage, interruption or data theft from computer viruses, computer hackers, malicious code, employee theft or misuse, ransomware, social engineering (including phishing attacks), denial-of-service attacks, sophisticated nation-state and nation-state-supported actors, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Cybersecurity incidents, which may not be immediately or ever detected, are increasing in frequency and evolving in nature. Additionally, due to geopolitical tensions related to Russia's invasion of Ukraine, the risk of cyber-attacks may be elevated.

While the Company seeks to protect its information technology systems from system failure, accident and security breach, if such an event were to occur and cause interruptions in its operations, it could result in a disruption of the Company's development programs and its business operations, whether due to a loss of its trade secrets or other proprietary information or other disruptions. For example, the loss of clinical trial data from future clinical trials could result in delays in the Company's regulatory approval efforts and significantly increase its costs to recover or reproduce the data. If the Company were to experience a significant cybersecurity breach of its information systems or data, the costs associated with the investigation, remediation and potential notification of the breach to counterparties and data subjects could be material. In addition, the Company's remediation efforts may not be successful. If it does not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, it could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary information. In addition, in response to the recent COVID-19 pandemic, a majority of the Company's workforce began to work remotely, which has continued and is now considered its normal business. This could increase the Company's cyber security risk, create data accessibility concerns, and make the Company more susceptible to communication disruption.

To the extent that any disruption or security breach were to result in a loss of, or damage to, the Company's or its third-party vendors', collaborators' or other contractors' or consultants' data or applications, or inappropriate disclosure of confidential or proprietary information, the Company could incur liability including litigation exposure, penalties and fines, the Company could become the subject of regulatory actions or investigations, its competitive position could be harmed and the further development and commercialization of its product candidates could be delayed. Any of the above could have a material adverse effect on the Company's business, financial condition, results of operations or prospects. While the Company maintains cyber-liability insurance (covering security and privacy matters), such insurance may not be adequate to cover any losses experienced as a result of a cybersecurity incident.

Unfavorable global economic conditions could adversely affect the Company's business, financial condition or results of operations.

The Company's results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, in 2008, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets and, more recently, the COVID-19 pandemic caused significant volatility and uncertainty in U.S. and international markets. A severe or prolonged economic downturn, or additional global financial crises, could result in a variety of risks to the Company's business, including weakened demand for its product candidates, if approved, or its ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain the Company's suppliers, possibly resulting in supply disruption. Any of the foregoing could harm the Company's business and it cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact its business.

U.S. federal income tax reform could adversely affect the Company's business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect the Company or holders of its common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, on March 27, 2020, former President Trump signed into law the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act") which included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 coronavirus outbreak, including temporary beneficial changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters. Additionally, on December 22, 2017, former President Trump signed into law the Tax Cuts and Jobs Act of 2017 ("TCJA"), which significantly reformed the Code. The TCJA included significant changes to corporate and individual taxation, some of which could adversely impact an investment in the Company's common stock. Under the TCJA, in general, NOLs generated in taxable years beginning after December 31, 2017 may offset no more than 80 percent of such year's taxable income and there is no ability for such NOLs to be carried back to a prior taxable year. The CARES Act modified the TCJA with respect to the TCJA's limitation on the deduction of NOLs and provided that NOLs arising in taxable years beginning after December 31, 2017 and before January 1, 2021 may be carried back to each of the five taxable years preceding the tax year of such loss, but NOLs arising in taxable years beginning after December 31, 2020 may not be carried back. In addition, the CARES Act eliminated the limitation on the deduction of NOLs to 80 percent of current year taxable income for taxable years beginning before January 1, 2021 (but reinstated the limitation for taxable years beginning after December 31, 2020). As a result of such limitations, the Company may be required to pay federal income tax in some future year notwithstanding that it had a net loss for all years in the aggregate. Future changes in tax laws could have a material adverse effect on the Company's business, cash flow, financial condition or results of operations. The Company urges investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in the Company's Common Stock.

The Company faces risks associated with increased political uncertainty.

The recent invasion of Ukraine by Russia and the sanctions, bans and other measures taken by governments, organizations and companies against Russia and certain Russian citizens in response thereto has increased the political uncertainty in Europe and has strained the relations between Russia and a significant number of governments, including the U.S. The duration and outcome of this conflict, any retaliatory actions taken by Russia and the impact on regional or global economies is unknown but could have a material adverse effect on the Company's business, financial condition and results of its operations.

Risks Related to the Company's Product Development and Regulatory Approval

The Company is heavily dependent on the success of its lead product candidate, neflamapimod, which is still under clinical development. If neflamapimod does not receive regulatory approval or is not successfully commercialized, the Company's business will be materially harmed.

The Company has invested almost all of its efforts and financial resources to date in the development of neflamapimod for the treatment of DLB. To date, the Company has not initiated or completed a pivotal clinical trial, obtained marketing approval for any product candidate, manufactured a commercial scale product or arranged for a third party to do so on its behalf, or conducted sales and marketing activities necessary for successful product commercialization. The Company's future success is substantially dependent on its ability to successfully complete clinical development of, obtain regulatory approval for, and successfully commercialize neflamapimod for this indication and additional indications, which may never occur.

The Company expects a substantial portion of its efforts and expenditures over the next few years will be devoted to the advancement of neflamapimod. In order to be successful, the Company will require additional clinical development, management of clinical and manufacturing activities, regulatory approval in multiple jurisdictions, securing manufacturing supply, building a commercial organization, and significant marketing efforts, among other requirements, before it can generate any revenues from commercial sales. The Company cannot be certain that it will be able to successfully complete any or all of these activities.

The Company has not submitted an NDA to the FDA or comparable applications to other regulatory authorities for neflamapimod, and it does not expect to be in a position to do so for several years, if ever. Significant additional clinical testing and research will be required before it can file such applications seeking approval of neflamapimod for the treatment of DLB, or in any other indications that the Company may pursue. If the Company is unable to obtain the necessary regulatory approvals for neflamapimod, it will not be able to commercialize its drug. This would materially adversely affect the Company's financial position, and the Company may not be able to generate sufficient revenue to continue its business.

The development and commercialization of drug products is subject to extensive regulation, and the regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time-consuming, and inherently unpredictable. There is no guarantee that the Company's planned clinical trials for neflamapimod to treat patients with DLB, or in any other indications that the Company may pursue, will be successful. If the Company is ultimately unable to obtain regulatory approval for its lead product candidate on a timely basis, if at all, its business will be substantially harmed.

The development and commercialization of drug products is subject to extensive regulation, and the regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time-consuming, and inherently unpredictable. If the Company is ultimately unable to obtain regulatory approval for its lead product candidate neflamapimod on a timely basis, if at all, its business will be substantially harmed.

Clinical trials are expensive and can be difficult to design and implement. Such trials can take many years to complete, and their outcomes are inherently uncertain. Failure can occur at any stage during the clinical trial process. The Company may experience difficulties in initiating and completing the clinical trials that it intends to conduct, and the Company does not know whether such trials will enroll patients on time, need to be redesigned, or be completed on schedule, if at all. In connection with clinical trials, the Company faces significant risks, including that its product candidate may not prove to be efficacious; patients may suffer adverse effects for reasons that may or may not be related to the product candidate being tested; the results may not confirm the positive results of its earlier preclinical studies and clinical trials; and the results may not meet the level of statistical significance required by the FDA or other regulatory agencies.

In the Company's clinical studies to date, the Company has obtained positive clinical data for neflamapimod treatment in patients with DLB. Its Phase 2a data for neflamapimod demonstrated improvement vs. placebo in dementia severity and motor function. Based on the encouraging results of its Phase 2a studies, the Company initiated a confirmatory, hypothesis-testing Phase 2b randomized double-blind placebo-controlled clinical study of neflamapimod in subjects with DLB in the second quarter of 2023. The Company's Phase 2b trial may not be successful or the FDA may disagree with the Company's interpretation of the clinical trial data or how those data inform the design of a potentially pivotal Phase 3 clinical trial for the Company's lead indication.

Even if the Company's initial clinical trials results are confirmed in this Phase 2b clinical proof-of-concept ("POC") trial, the Company will still need to successfully complete additional clinical trials, including a Phase 3 trial, before it is prepared to submit an NDA for regulatory approval of neflamapimod in patients with DLB, assuming that the data collected from the Company's clinical trials are deemed sufficient to support the submission of an NDA. The Company cannot predict with any certainty if or when it might complete its development efforts and submit an NDA for regulatory approval of neflamapimod, or whether any such NDA will be approved by the FDA. An NDA or comparable foreign submission seeking marketing approval for neflamapimod also may not be accepted by FDA or foreign regulatory authorities due to, among other reasons, the content or formatting of the submission.

This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in the Company's failure to obtain regulatory approval to market neflamapimod for any of its planned indications, which would significantly harm the Company's business, results of operations, and prospects. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for a new product candidate. As a result, the Company may be required to conduct additional nonclinical studies, alter its proposed clinical trial designs, or conduct additional clinical trials to satisfy the regulatory authorities in each of the jurisdictions in which it hopes to conduct clinical trials and develop and market its products, if approved. Further, even if the Company believes the data collected from its clinical trials are promising, such data may not be sufficient to support approval by the FDA or any comparable foreign regulatory authority.

The Company has concentrated its research and development efforts on the treatment of DLB, a disease that has seen limited success in drug development. In addition, its rationale for neflamapimod in the treatment of DLB is based on a scientific understanding of the disease that may be wrong.

There have been limited efforts by biopharmaceutical and pharmaceutical companies to develop treatments for DLB and there are no therapies available for patients that have been approved with a specific indication to treat DLB. Only symptomatic therapies that are approved for other diseases, generally either AD or Parkinson's disease, are currently utilized to manage patients with DLB. In addition, many potential disease-modifying therapies have been evaluated in other neurodegenerative diseases, particularly in AD, and these have encountered challenges in their development and, as a result, only recently two disease-modifying treatments to treat AD have been approved in the United States.

The Company's approach to the treatment of DLB focuses in large part on neflamapimod's ability to inhibit the intra-cellular enzyme p38α. The expression of p38α is considered to be a critical contributor in the toxicity of inflammation, alpha-synuclein, amyloid-beta and tau to neurons and synapses, which the Company and other scientific experts believe leads to synaptic dysfunction. Synaptic dysfunction, specifically impaired synaptic plasticity, leads to disruption of episodic memory and is a significant event in the development and symptomatology of DLB.

Neflamapimod blocks the effects of inflammation and other stress-inducers on neurons and synapses by inhibiting p38α. In targeting synaptic dysfunction in this manner, the Company believes neflamapimod has the potential to not only slow disease progression, but also reverse existing memory deficits in patients with DLB; that is, to both prevent further decline and improve cognitive function. In the Company's clinical studies to date, neflamapimod treatment in patients with DLB has led to statistically significant improvement in cognition, motor function, and cognition & function, which appear to be the best clinical measures of DLB.

However, the Company cannot be certain that its approach will lead to the development of approvable or marketable products. To date the only drugs approved by the FDA to treat DLB have addressed the disease's symptoms. In addition, there has never been an approval of a drug in DLB and therefore, there are no regulatory precedents for endpoints in that indication. Consequently, the FDA has a limited set of products to rely upon in evaluating neflamapimod. This could result in a longer than expected regulatory review process, increased expected development costs or the delay or prevention of commercialization of neflamapimod for the treatment of DLB.

The Company has no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for its future viability.

The Company has not yet demonstrated, either on its own or through collaboration with third parties, an ability to successfully complete a large-scale, pivotal clinical trial, obtain marketing approval, manufacture a commercial product, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about its future success or viability may not be as accurate as they could be if the Company had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

In addition, as a business with a limited operating history, the Company may encounter unforeseen expenses, complications, delays and other known and unknown factors. If it is able to successfully develop neflamapimod, the Company may eventually need to transition from a company with a research focus to a company capable of supporting commercial activities. The Company may not be successful in such a transition and, as a result, its business may be adversely affected.

As the Company continues to build its business, the Company expects that its financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond its control. Accordingly, investors should not rely upon the results of any particular quarterly or annual period as indications of the Company's future operating performance.

Safety issues with neflamapimod or with any other product candidate the Company may develop or acquire in the future, or with product candidates or approved products of third parties that are similar to the Company's product candidates, could give rise to delays in the regulatory approval process, restrictions on labeling or product withdrawal after approval, if any.

Results of any clinical trial the Company conducts could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Serious adverse events or undesirable side effects caused by neflamapimod, or any other product candidates the Company may develop or acquire, could cause it or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. In addition, many compounds that have initially showed promise in clinical or earlier stage testing are later found to cause undesirable or unexpected side effects that prevented further development of the compound. Further, problems with product candidates or approved products marketed by third parties that utilize the same therapeutic target or that belong to the same therapeutic class as neflamapimod or any future product candidates could adversely affect the development, regulatory approval and commercialization of the Company's product candidates.

To date, neflamapimod has been evaluated in 217 patients, at doses up to 750 mg twice a day, and up to 24 weeks of treatment. The adverse effects (side effects) seen in more than 5% of neflamapimod-treated patients include headache (10% in neflamapimod-treated patients vs. 5% in placebo recipients), diarrhea (10% vs. 5%), abdominal pain (6% vs. 5%), respiratory infection (5% vs. 5%), and falls (5% vs. 5%); these events were generally were mild and in all but one case (a case of diarrhea and abdominal pain) did not lead to treatment discontinuation. In addition, increased levels of certain "liver enzymes" in the blood are a well-known dose-dependent side effect of p38 MAPK inhibitors. These liver enzymes, aspartate aminotransferase and alanine aminotransferase, are proteins are commonly produced in the liver, the measurements of which can help doctors evaluate liver function. With neflamapimod, during 12 weeks of dosing at 250mg BID (i.e., four-fold higher daily dosing than in the recently initiated Phase 2b trial) in 44 subjects with rheumatoid arthritis, elevations in such liver enzymes levels were noted in six subjects (14%). Additionally, in one subject (1%) participating in the Reverse-SD 24-week trial in mild AD, ALT and AST levels increased to three times the upper limit of normal.

After the Company acquired an exclusive license from Vertex to develop and commercialize neflamapimod for the treatment of AD and other CNS disorders, the Company submitted an investigational new drug ("IND") application, to the FDA's Division of Neurology Products ("DNP") in February 2015. The DNP cleared the Company's clinical trial application in March 2015. However, in August 2015, following a standard review of the long-term animal toxicity studies, the DNP placed a partial clinical hold on Phase 2a Study 303 and any subsequent studies proposed under the IND, limiting administration of neflamapimod to doses that lead to plasma drug levels which provide at least a 10-fold safety margin to the plasma drug levels in animals that in long-term animal toxicity studies had previously led to minimal or equivocal findings in the liver, bone marrow and CNS. A partial clinical hold means that FDA suspends part of the clinical work requested under the IND (e.g., a specific protocol or part of a protocol is not allowed to proceed); however, other protocols or parts of the protocol are allowed to proceed under the IND. Under DNP's partial clinical hold that remains in effect for the neflamapimod IND, the agency limited administration of neflamapimod to doses that lead to plasma drug levels that provide a ten-fold safety margin to human subjects, based on the plasma drug levels in animals that had previously led to minimal or equivocal toxicity findings. the Company's current understanding of plasma drug levels achieved with neflamapimod in humans means that its investigational dosing in the United States is limited by this partial clinical hold to no more than 40 mg three times daily in patients weighing 60kg (132 lbs.) or more. the Company's recently initiated Phase 2b clinical study is being conducted at 40mg three times daily (limited to patients weighing 60kg or more within the United States, and not so limited outside the US).

Our current plans across our indications do not envision surpassing this dose level, and the Company does not expect this partial clinical hold to impact our ongoing and planned clinical trials. With respect to the adverse effects discussed above, the patients were asymptomatic, there were no associated increases in bilirubin, and the elevations resolved with treatment discontinuation. Liver enzyme abnormalities were not observed in the Phase 2a trial of neflamapimod in DLB. However, as the Company continues the development and clinical trials of neflamapimod, treatment-related serious adverse events ("SAEs") may arise in the future. Side effects that are deemed to be drug-related could affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Undesirable side effects in one of the Company's clinical trials for neflamapimod in one indication could adversely affect enrollment in clinical trials, regulatory approval and commercialization of the Company's product candidate in other indications. These side effects may not be appropriately recognized or managed by the treating medical staff. In addition, discovery of previously unknown class effect problems may prevent or delay clinical development and commercial approval of product candidates or result in restrictions on permissible uses after their approval. If the Company or others identify undesirable side effects caused by the mechanisms of action of a product candidate or a class of product candidates, the FDA may require the Company to conduct additional clinical trials, or to implement a Risk Evaluation and Mitigation Strategy program ("REMS program") prior to commercial approval. Alternatively, regulatory authorities may not approve the product candidate or, as a condition of approval, require specific warnings and contraindications or place certain limitations on how the Company can promote the drug. Following a potential future drug product approval, regulatory authorities might also withdraw such approval and require the Company to take its drug off the market. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients, rare and severe side effects of neflamapimod or future product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If neflamapimod, or any other product candidates the Company may develop or acquire, receives marketing approval and the Company or others identify undesirable side effects caused by such product candidates (or any other similar products) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such product candidates;
- regulatory authorities may require the addition of labeling statements, such as a "Boxed" Warning or a contraindication;
- the Company may be required to change the way such product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the product candidates;
- FDA may require a REMS plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools, and regulatory authorities in other jurisdictions may require comparable risk mitigation plans;
- the Company may be subject to regulatory investigations and government enforcement actions;
- the FDA or a comparable foreign regulatory authority may require the Company to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety and efficacy of the product;

- the Company may decide to recall such product candidates from the marketplace after they are approved;
- the Company could be sued and held liable for injury caused to individuals exposed to or taking its product candidates; and
- the Company's reputation may suffer.

Any failure or delay in commencing or completing clinical trials or obtaining regulatory approvals for neflamapimod would delay the Company's commercialization prospects, substantially increase the costs of commercializing neflamapimod, and severely harm the Company's business and financial condition.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. The Company may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of neflamapimod or any other product candidates the Company may develop or acquire.

The risk of failure in drug development is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, the Company must complete nonclinical development and conduct extensive clinical trials to demonstrate the safety and efficacy of its product candidates in humans. Clinical trials are expensive, difficult to design and implement and can take several years to complete, and their outcomes are inherently uncertain. Failure can occur at any time during the clinical trial process. Nonclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in nonclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. It is impossible to predict when or if neflamapimod will prove to be effective or safe for any indication in humans or will receive marketing approval.

The Company may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent its ability to receive marketing approval or commercialize neflamapimod for any indication. Clinical trials may be delayed, suspended or prematurely terminated because costs are greater than the Company anticipates or for a variety of other reasons, such as:

- delay or failure in reaching agreement with the FDA or a comparable foreign regulatory authority on a trial design that the Company is able to execute;
- delay or failure in obtaining authorization to commence a trial, including approval from the appropriate IRB or ethics committee at each clinical site to conduct testing of a candidate on human subjects, or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- delays in reaching, or failure to reach, agreement on acceptable terms with prospective trial sites and prospective clinical research organizations ("CROs"), the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- inability, delay or failure in identifying and maintaining a sufficient number of trial sites, many of which may already be engaged in other clinical programs;
- inability, delay or failure in identifying, recruiting, and training suitable clinical investigators;
- delay or failure in recruiting, screening, and enrolling suitable subjects to participate in a trial;
- delay or failure in having subjects complete a trial or return for post-treatment follow-up;
- delays caused by operational issues at clinical trial sites;

- changes to the clinical trial protocols and/or changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;

- clinical sites and investigators deviating from the clinical protocol, failing to conduct the trial in accordance with Good Clinical Practices or other regulatory requirements, or dropping out of a trial;

- failure to initiate or delay of or inability to complete a clinical trial as a result of the authorizing IND or foreign clinical trial application being placed on temporary or permanent clinical hold by the FDA or comparable foreign regulatory authority;

- lack of adequate funding to continue a clinical trial, including unforeseen costs due to enrollment delays, requirements to conduct additional clinical trials and increased expenses associated with the services of the Company's CROs and other third parties, or the cost of clinical trials being greater than the Company anticipated;

- delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of neflamapimod or the Company's future product candidates for use in clinical trials or the inability to do any of the foregoing;

- developments on trials conducted by competitors for related technology that raises FDA or foreign regulatory authority concerns about risk to patients of the technology broadly;

- clinical trials of the Company's product candidates may produce negative or inconclusive results, and the Company may decide, or regulators may require it, to conduct additional nonclinical studies, clinical trials or abandon product development programs;

- the number of patients required for clinical trials of the Company's product candidates may be larger than the Company anticipates, enrollment in these clinical trials may be slower than it anticipates or participants may drop out of these clinical trials at a higher rate than it anticipates;

- the Company's third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to the Company in a timely manner, or at all;

- regulators, the IRB or a Data Safety Monitoring Board if one is used for the Company's clinical trials, may require that the Company suspend or terminate its clinical trials for various reasons, including noncompliance with regulatory requirements, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, or a finding that the participants are being exposed to unacceptable health risks;

- the supply or quality of the Company's product candidates or other materials necessary to conduct clinical trials of the Company's product candidates may be insufficient or inadequate;

- transfer of manufacturing processes to larger-scale facilities operated by a contract manufacturing organization ("CMO"), and delays or failure by the Company's CMOs or the Company to make any necessary changes to such manufacturing process;

- the FDA or comparable foreign regulatory authorities may require the Company to submit additional data or impose other requirements before permitting it to initiate a clinical trial; or

- changes in governmental regulations or administrative actions.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of marketing approval for neflamapimod or any other future product candidates. Further, the FDA or comparable foreign regulatory authorities may disagree with the Company's clinical trial design and the Company's interpretation of data from clinical trials or may change the requirements for approval even after the FDA has reviewed and commented on the design for the Company's clinical trials.

If the Company is required to conduct additional clinical trials or other nonclinical studies of neflamapimod in various disease conditions beyond those that the Company currently contemplates, if it is unable to successfully complete clinical trials of the Company's product candidates or other studies, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, the Company may:

- be delayed in obtaining marketing approval for its product candidates;
- not obtain marketing approval for its product candidates at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings that would reduce the potential market for its products or inhibit its ability to successfully commercialize the Company's products;
- be subject to additional post-marketing restrictions or requirements, including post-marketing testing; or
- have the product removed from the market after obtaining marketing approval.
- the Company is also required to register certain clinical trials and post the results of completed clinical trials on a government-sponsored database, such as ClinicalTrials.gov in the United States, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Enrollment and retention of participants in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside the Company's control.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on the Company's ability to enroll a sufficient number of research participants who remain in the study until its conclusion. The Company may encounter delays in enrolling, or be unable to enroll, a sufficient number of individuals to complete any of its clinical trials, and even once enrolled the Company may be unable to retain a sufficient number of participants to complete any of its trials. Subject enrollment and retention in clinical trials depends on many factors, including:

- the eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the nature of the trial protocol;
- the proximity of potential subjects to clinical sites;
- the existing body of safety and efficacy data with respect to the product candidate;
- the Company's ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies;

- competing clinical trials being conducted by other companies or institutions; and
- the risk that participants enrolled in clinical trials will drop out of the trials before completion.

Furthermore, any negative results the Company may report in clinical trials may make it difficult or impossible to recruit and retain subjects in other clinical trials of that same product candidate. Delays or failures in planned enrollment or retention of clinical trial subjects, including in our ongoing Phase 2b trial, may result in increased costs or program delays, which could have a harmful effect on the Company's ability to develop a product candidate or could render further development impossible.

If the Company is unable to take full advantage of regulatory programs designed to expedite drug development or provide other incentives, its development programs may be adversely impacted.

There are a number of incentive programs administered by the FDA and other regulatory bodies to facilitate development of drugs in areas of unmet medical need. For example, neflamapimod received a Fast Track designation in October 2019 from the FDA for investigation as a treatment of DLB. Fast Track designation is granted by FDA, in response to a sponsor's request, upon a determination that the product candidate is intended to treat a serious or life-threatening disease or condition and has the potential to address an unmet medical need, meaning it could provide a therapeutic option for patients where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast Track designation and other available FDA programs do not change the standards for approval but may expedite the development or approval process for certain drug candidates.

Neflamapimod may not qualify for or maintain designations under this or other incentive programs under any of the FDA's existing or future programs to expedite drug development in areas of unmet medical need. the Company's inability to fully take advantage of these incentive programs may require the Company to run larger trials, incur delays, lose opportunities that may not otherwise be available to it, and incur greater expense in the development of its product candidates.

Results of preclinical studies and early clinical trials may not be indicative of results obtained in later trials. In addition, preliminary, topline and interim data from the Company's clinical trials that the Company may announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

The results of preclinical studies and early clinical trials of a product candidate, including neflamapimod, may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry, both generally and in the DLB treatment space in particular, have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Even if the Company's clinical trials for neflamapimod are completed as planned, including a future Phase 3 trial, the Company cannot be certain that their results will support the safety and efficacy sufficient to obtain regulatory approval.

In addition, from time-to-time the Company may announce or publish preliminary, topline, or interim data from its clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. the Company also makes assumptions, estimations, calculations and conclusions as part of its analyses of data, and it may not have received or had the opportunity to fully and carefully evaluate all data. Preliminary and interim data are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or interim data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data the Company previously published. As a result, preliminary and interim data are not necessarily predictive of final results and should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm the Company's business prospects. Accordingly, the results from the completed preclinical studies and clinical trials for the Company's product candidates may not be predictive of the results the Company may obtain in later stage trials. Its clinical trials may produce negative or inconclusive results, and the Company may decide, or regulators may require it, to conduct additional clinical trials.

Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain approval from the FDA, the EMA or other regulatory agencies for their products. Others, including regulatory agencies, may not accept or agree with the Company's assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate and the Company in general.

In addition, the information the Company chooses to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. Others may not agree with what the Company determines is the material or otherwise appropriate information to include in its disclosure, and any information the Company determines not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding neflamapimod, a future product candidate, or its business. If the interim, preliminary, or topline data that the Company reports differ from later, final or actual results, or if others, including the FDA and comparable foreign regulatory authorities, disagree with the conclusions reached, the Company's ability to obtain approval for, and commercialize our product candidates may be harmed, which could harm its business, financial condition, results of operations and prospects.

The Company relies on third parties to conduct, supervise and monitor its clinical trials. If those third parties do not successfully carry out their contractual duties, or if they perform in an unsatisfactory manner, the Company's business will be harmed.

Although the Company designs and manages its preclinical studies and clinical trials, it does not currently have the ability to conduct clinical trials for neflamapimod on its own. The Company has relied, and will continue to rely, on third parties such as contract research organizations, medical institutions, and clinical investigators to ensure the proper and timely conduct of its clinical trials. The Company's reliance on CROs for clinical development activities limits its control over these activities, but it remains responsible for ensuring that each of the Company's trials is conducted in accordance with the applicable protocol, legal and regulatory and scientific standards. The Company does not control these third parties, and they may not devote sufficient time and resources to the Company's projects, or their performance may be substandard, resulting in clinical trial delays or suspensions, delays in submission of our marketing applications or failure of a regulatory authority to accept our applications for filing. There is no assurance that the third parties the Company engages will be able to provide the functions, tests, activities or services as agreed upon, or provide them at the agreed upon price and timeline or to the Company's requisite quality standards, including due to geopolitical events, natural disasters, public health emergencies or pandemics, or poor workforce relations or human capital management.

The Company and its CROs are required to comply with the Good Laboratory Practice requirements for preclinical studies and GCP requirements for clinical trials, which are regulations and guidelines enforced by the FDA and are also required by comparable foreign regulatory authorities. If the Company or its CROs fail to comply with GCP requirements, the clinical data generated in its clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require the Company to perform additional clinical trials before approving its marketing applications. There is also no assurance these third parties will not make errors in the design, management or retention of the Company's data or data systems. Any failures by such third parties could lead to a loss of data, which in turn could lead to delays in clinical development and obtaining regulatory approval. Third parties may not pass FDA or other regulatory audits, which could delay or prohibit regulatory approval. In addition, the cost of such services could significantly increase over time. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, regulatory approval of current and future product candidates may be delayed, prevented or cost significantly more than expected, all of which could have a material adverse effect on the Company's business, financial condition, results of operations and prospects.

If the Company's CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to the Company's clinical protocols or regulatory requirements or for any other reason, the Company's clinical trials may be extended, delayed or terminated, and it may not be able to obtain regulatory approval for, or successfully commercialize any product candidate that it develops. As a result, the Company's financial results and the commercial prospects for neflamapimod would be harmed, its costs could increase, and its ability to generate revenue could be delayed.

The Company has employed several different contract research organizations for clinical trial services. Although the Company believes there are numerous alternatives to provide these services, in the event that it seeks a new CRO, the Company may not be able to enter into replacement arrangements without delays or incurring additional expenses. Switching or adding additional CROs involves substantial cost and requires management's time and focus. In addition, there is a natural transition period when a new CRO commences work. Though the Company intends to carefully manage its relationships with its CROs, there can be no assurance that the Company will not encounter challenges or delays in the future or that these delays or challenges will not have an adverse impact on its business, financial condition and prospects.

The Company's reliance on third parties for the production of neflamapimod may result in delays in the Company's clinical trials or regulatory approvals and may impair the development and ultimate commercialization of neflamapimod, which would adversely impact the Company's business and financial position.

The Company has no manufacturing facilities and does not have extensive experience in the manufacturing of drugs or in designing drug-manufacturing processes. The Company currently relies on third parties for the manufacture of drug substance, the manufacture of drug product, and the packaging of drug product for clinical use. This reliance on contract manufacturers and suppliers subjects the Company to inherent uncertainties related to product safety, availability, security and cost. Holders of NDAs, or other forms of FDA approvals, or those distributing a regulated product under their own name, are ultimately responsible for compliance with manufacturing obligations even if the manufacturing is conducted by a third party.

The Company further intends to rely on third-party CMOs for the production of commercial supply of neflamapimod if its drug is ultimately approved. If CMOs cannot successfully manufacture drug substance and drug product for the Company's neflamapimod program, or any other product candidate that the Company may develop or acquire in the future, in conformity to its specifications and the applicable regulatory requirements, the Company will not be able to secure or maintain regulatory approval for the use of that product candidate in clinical trials, or for commercial distribution of that product candidate, if approved. Additionally, any problems the Company experiences with any such CMOs could delay the manufacturing of its product candidates, which could harm its results of operations. All drug manufacturers and packagers are required to operate in accordance with FDA-mandated current good manufacturing practices ("cGMPs"). A failure of any of the Company's current or future contract manufacturers to establish and follow cGMPs and to document their adherence to such practices may lead to significant delays in obtaining regulatory approval of product candidates or the ultimate launch of products based on the Company's product candidates into the market. In the event of such failure, the Company could also face fines, injunctions, civil penalties, and other sanctions. Further, if the FDA or comparable foreign regulatory authority finds deficiencies with or does not approve a CMO's facilities for the future commercial manufacture of neflamapimod, or if it withdraws any such approval or finds deficiencies in the future, the Company may need to find alternative manufacturing facilities, which would delay its development program and significantly impact its ability to obtain regulatory approval for or commercialize neflamapimod.

If any facility of the Company's third-party drug manufacturers or suppliers were to suffer an accident or a force majeure event such as war, missile or terrorist attack, earthquake, major fire or explosion, major equipment failure or power failure lasting beyond the capabilities of its backup generators or similar event, the Company could be materially adversely affected and any of its clinical trials could be materially delayed. Such an extended shut down may force the Company to procure a new research and development facility or another manufacturer or supplier, which could be time-consuming. During this period, the Company may be unable to receive investigational neflamapimod supplies or any other product candidates it may develop or acquire.

The recently initiated Phase 2b clinical trial is being conducted with a drug substance (the active pharmaceutical ingredient ("API")) already manufactured in 2019 at a third-party CMO. In addition, the Company has sufficient drug substance available to cover the anticipated needs for Phase 3 in DLB. This drug substance was manufactured at an established commercial contract manufacturing organization that is approved for and manufactures drug both for investigational use and marketed products. The Company anticipates utilizing the company for clinical trials beyond the Phase 3 clinical trial in DLB, as well potentially for commercial use. However, supplies of the neflamapimod drug substance could be interrupted from time to time, and the Company cannot be certain that alternative supplies could be obtained within a reasonable timeframe, at an acceptable cost, or at all. In addition, a disruption in the supply of drug substance could delay the commercial launch of the Company's product candidates, if approved, or result in a shortage in supply, which would impair its ability to generate revenues from the sale of our product candidates. Growth in the costs and expenses of raw materials may also impair the Company's ability to cost effectively manufacture its product candidates.

The Company also currently relies on a third-party CMO (different than that for the API) for the manufacture of our neflamapimod drug product. The Company has used the same manufacturer for its neflamapimod drug product in all our clinical trials to date. If neflamapimod is ultimately approved for commercial sale, the Company expects to continue to rely on third-party contractors for manufacturing the drug product. Although the Company intends to do so prior to any commercial launch, it has not yet entered into long-term agreements for the commercial supply of either drug substance or drug product with its current manufacturing providers, or with any alternate manufacturers.

While the Company believes that there are multiple alternative sources available for manufacturing of both drug substance and drug product in its neflamapimod program, the Company may not be able to enter into replacement arrangements without delays or additional expenditures. It cannot estimate these delays or costs with certainty but, if they were to occur, they could cause a delay in the Company's development and commercialization efforts.

Although the Company generally has not, and does not intend to, begin a clinical trial unless it believes it has on hand, or will be able to obtain, a sufficient supply of neflamapimod to complete the clinical trial, any significant delay in the supply of neflamapimod drug substance or drug product could considerably delay conducting the Company's clinical trials and potential regulatory approval of its product candidates.

Further, third-party suppliers, manufacturers, or distributors may not perform as agreed or may terminate their agreements with the Company, including due to the effects related to geopolitical events, natural disasters, public health emergencies or pandemics, such as the COVID-19 pandemic, or force majeure events that affect their facilities or ability to perform. Any significant problem that the Company's suppliers, manufacturers, distributors or regulatory service providers experience could delay or interrupt supply of materials necessary to produce the Company's product candidates. Failure to obtain the needed quantities of the Company's product candidates could have a material and adverse effect on its business, financial condition, results of operations and prospects.

If the Company changes the manufacturers of its product candidates, it may be required to conduct comparability studies evaluating the manufacturing processes of the product candidates.

The FDA and other regulatory agencies maintain strict requirements governing the manufacturing process for prescription drug products that would apply to the Company's product candidates, if approved. For example, when a manufacturer seeks to make any change to the manufacturing process, the FDA typically requires the applicant to conduct non-clinical and, depending on the magnitude of the changes, potentially clinical comparability studies that evaluate the potential differences in the product candidates resulting from the change in the manufacturing process. If the Company were to change manufacturers of its drug substance or drug product during or after the clinical trials and regulatory approval process for neflamapimod or any of its other product candidates, the Company will be required to conduct comparability studies assessing product candidates manufactured at the new manufacturing facility. Further, manufacturing changes are generally categorized as having either a substantial, moderate, or minimal potential to adversely affect the identity, strength or quality of the drug product as they may relate to the safety or effectiveness of the product, and if a change has a substantial potential to have an adverse effect on the drug product, an applicant must submit and receive FDA approval of a prior approval supplemental application before the product made with the manufacturing change is distributed. Other forms of notice to FDA are also required for manufacturing changes that have a moderate or minimal potential to have an adverse effect on the drug product's safety or effectiveness. Regardless of the type of manufacturing change, the methods used and the facilities and controls used for the manufacture, processing, packaging, or holding of human drugs must comply with applicable cGMP regulations.

Delays in designing and completing a comparability study to the satisfaction of the FDA or other regulatory agencies could delay or preclude the Company's development plans and, thereby, delay the Company's ability to receive marketing approval or limit its revenue and growth, once approved. In addition, in the event that the FDA or other regulatory agencies do not accept non-clinical comparability data, the Company may need to conduct a study involving dosing of patients comparing the two products. That study may result in a delay in the approval or launch of any of its product candidates.

Any product candidate for which the Company obtains marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and the Company may be subject to penalties if it fails to comply with regulatory requirements or if it experiences unanticipated problems with its products, when and if any of them are approved.

If the FDA or a comparable foreign regulatory authority approves neflamapimod or any of the Company's future product candidates for marketing, activities such as the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. The FDA or a comparable foreign regulatory authority may also impose requirements for costly post-marketing nonclinical studies or clinical trials (often called "Phase 4 trials") and post-marketing surveillance to monitor the safety or efficacy of the product. If the Company or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, production problems or issues with the facility where the product is manufactured or processed, such as product contamination or significant not-compliance with applicable cGMPs, a regulator may impose restrictions on that product, the manufacturing facility or the Company. If the Company or its third-party providers, including the Company's CMOs, fail to comply fully with applicable regulations, then the Company may be required to initiate a recall or withdrawal of its products.

The Company must also comply with requirements concerning advertising and promotion for any of its product candidates for which it obtains marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, the Company will not be able to promote any products it develops for indications or uses for which they are not approved. The FDA and other agencies closely oversee the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products, and if the Company promotes its products beyond their approved indications, it may be subject to enforcement actions or prosecution arising from that off-label promotion. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws. Accordingly, to the extent the Company receives marketing approval for neflamapimod, the Company and its CMOs and other third-party partners will continue to expend time, money and effort in all areas of regulatory compliance, including promotional and labeling compliance, manufacturing, production, product surveillance, and quality control. If the Company is not able to comply with post-approval regulatory requirements, it could have marketing approval for any of its products withdrawn by regulatory authorities and its ability to market any future products could be limited, which could adversely affect its ability to achieve or sustain profitability. Thus, the cost of compliance with post-approval regulations may have a negative effect on the Company's operating results and financial condition.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay marketing approval of the Company's product candidates. If the Company is slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if it is not able to maintain regulatory compliance, it may lose any marketing approval that it may have obtained, which would adversely affect the Company's business, prospects and ability to achieve or sustain profitability.

If the Company is unable to establish sales, marketing and distribution capabilities either on its own or in collaboration with third parties, it may not be successful in commercializing neflamapimod, if approved.

The Company does not currently have any infrastructure for the sales, marketing or distribution of an approved drug product, and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market and successfully commercialize neflamapimod, if approved, the Company must build its sales, distribution, marketing, managerial and other non-technical capabilities, or make arrangements with third parties to perform these services.

There are significant expenses and risks involved in establishing the Company's own sales, marketing and distribution functions, including the Company's ability to hire, retain and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Alternatively, to the extent that the Company depends on third parties for such services, any revenues it receives will depend upon the efforts of those third parties, and there can be no assurance that such efforts will be successful.

If the Company is unable to establish adequate sales, marketing and distribution capabilities, either on its own or in collaboration with others, the Company will not be successful in commercializing neflamapimod, if it is ultimately approved, and it may never become profitable. The Company will be competing with companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, the Company may be unable to compete successfully against these more established companies.

Risks Related to the Company's Commercialization Plans

The Company's business operations are subject to applicable healthcare laws and regulations. If neflamapimod is approved, the Company will also be subject to stringent regulation and ongoing regulatory obligations and restrictions, which could delay its marketing and commercialization activities and also expose it to penalties if the Company fails to comply with applicable regulations.

Although the Company does not currently have any products on the market, once it begins commercializing neflamapimod or any other future product candidates, it will be subject to additional healthcare statutory and regulatory requirements and oversight by federal and state governments as well as foreign governments in the jurisdictions in which the Company conducts its business. Physicians, other healthcare providers and third-party payors will play a primary role in the recommendation, prescription and use of any product candidates for which the Company obtains marketing approval. The Company's future arrangements with such third parties may expose the Company to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which it markets, sells and distributes any products for which the Company obtains marketing approval. Restrictions under applicable domestic and foreign healthcare laws and regulations include the following:

- the U.S. 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 a federal healthcare program such as Medicare and Medicaid; a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- U.S. federal false claims, false statements and civil monetary penalties laws, including the U.S. federal False Claims Act, which impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government; actions may be brought by the government or a whistleblower and may include an assertion that a claim for payment by federal healthcare programs for items and services which results from a violation of the federal Anti-Kickback Statue constitutes a false or fraudulent claim for purposes of the False Claims Act;

- the U.S. federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") that imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- analogous state and foreign laws and regulations relating to healthcare fraud and abuse, 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;

- the U.S. federal physician payment transparency requirements, sometimes referred to as the "Sunshine Act," which requires manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report to the Centers for Medicare & Medicaid Services ("CMS"), information related to physician payments and other transfers of value to physicians, certain advanced non-physician health care practitioners, and teaching hospitals, as well as the ownership and investment interests of physicians and their immediate family members;

- analogous state and foreign laws that require pharmaceutical companies to track, report and disclose to the government or the public information related to payments, gifts, and other transfers of value or remuneration to physicians and other healthcare providers, marketing activities or expenditures, or product pricing or transparency information, or that require pharmaceutical companies to implement compliance programs that meet certain standards or to restrict or limit interactions between pharmaceutical manufacturers and members of the healthcare industry;

- the U.S. federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under federal healthcare programs;

- HIPAA, which imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information; and

- state and foreign laws that govern the privacy and security of health information in certain circumstances, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business. Efforts to ensure that the Company's business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of health care reform, especially in light of the lack of applicable precedent and regulations. Any action against the Company for violation of these laws, even if the Company successfully defends against it, could cause the Company to incur significant legal expenses and divert our management's attention from the operation of its business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a health care company may run afoul of one or more of the requirements. If the FDA or a comparable foreign regulatory authority approves any of the Company's product candidates, the Company will be subject to an expanded number of these laws and regulations and will need to expend resources to develop and implement policies and processes to promote ongoing compliance. It is possible that governmental authorities will conclude that the Company's 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, resulting in government enforcement actions.

If the Company's operations are found to be in violation of any of these laws or any other governmental regulations that may apply to the Company, it may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from federal healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of the Company's operations. If any of the physicians or other healthcare providers or entities with whom the Company expects to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from federal healthcare programs.

Even if neflamapimod or any other product candidate the Company develops receives marketing approval, it may fail to achieve the level of acceptance necessary for commercial success.

If neflamapimod, or any other product candidate the Company may develop or acquire in the future, receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, health care professionals, patients, third-party payors and others in the medical community. If the Company's drug does not achieve an adequate level of acceptance, the Company may not generate significant product revenues or become profitable. The degree of market acceptance will depend on a number of factors, including but not limited to:

- the ability to provide acceptable evidence of efficacy and potential advantages compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the Company's ability to offer its drug for sale at competitive prices, which may be subject to regulatory control;
- the availability of third-party insurance coverage and adequate reimbursement;
- the availability of alternative treatments and the cost of a new treatment in relation to those alternatives, including any similar generic treatments;
- the relative convenience and ease of administration of a new treatment compared to alternatives, and the prevalence and severity of any side effects of a new treatment;
- the strength and effectiveness of the Company's sales, marketing and distribution capabilities, either internally or in collaboration with others;
- any restrictions on the use of the Company's product together with other medications; and
- any restrictions on the distribution of the Company's product such as those imposed under a mandatory REMS program.

If neflamapimod or any other product candidate that the Company may develop in the future does not provide a treatment regimen that is at least as beneficial as the current standard of care or otherwise does not provide some additional patient benefit over the current standard of care, that product will not achieve market acceptance, and the Company will not generate sufficient revenues to achieve profitability. Because the Company expects sales of its product candidates, if approved, to generate substantially all of its revenues for the foreseeable future, the failure of the Company's product candidates to find market acceptance would materially harm its business.

If the market opportunity for any product candidate that the Company develops is smaller than it believes, its revenue may be adversely affected and its business may suffer.

The Company intends to initially focus its product candidate development on treatments for various CNS and neurodegenerative indications. The addressable patient populations that may benefit from treatment with the Company's product candidates, if approved, are based on its estimates. These estimates, which have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations and market research, may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these CNS and neurodegenerative diseases. Any regulatory approval of the Company's product candidates would be limited to the therapeutic indications examined in the Company's clinical trials and as determined by the FDA, which would not permit the Company to market its products for any other therapeutic indications not expressly reviewed and approved as safe and effective. Additionally, the potentially addressable patient population for the Company's product candidates may not ultimately be amenable to treatment with the Company's product candidates. Even if the Company receives regulatory approval for any of its product candidates, such approval could be conditioned upon label restrictions that materially limit the addressable patient population. The Company's market opportunity may also be limited by future competitor treatments that enter the market. If any of the Company's estimates prove to be inaccurate, the market opportunity for any product candidate that the Company or its strategic partners develop could be significantly diminished and have an adverse material impact on its business.

The Company faces substantial competition from other biotechnology and pharmaceutical companies, and its operating results will suffer if it fails to compete effectively.

The biotechnology and pharmaceutical industries are highly competitive and subject to significant and rapid technological change. If neflamapimod is approved, it will face intense competition from a variety of businesses, including large, fully integrated pharmaceutical companies, specialty pharmaceutical companies, biopharmaceutical companies in the United States and other jurisdictions, academic institutions and governmental agencies and public and private research institutions. These organizations may have significantly greater resources than the Company does. They may also conduct similar research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing and marketing of products that may compete with neflamapimod.

Currently, there are a limited number of companies and disease modifying approaches for DLB. However, given the potential market opportunity for the treatment of DLB and other neurodegenerative diseases, an increasing number of established pharmaceutical firms and smaller biotechnology/biopharmaceutical companies are pursuing a range of potential therapies for these diseases in various stages of clinical development. In addition to these current and potential competitors, the Company anticipates that more companies will enter the DLB market in the future. The Company's potential competitors could have significantly greater financial resources, as well as drug development, manufacturing, marketing, and sales expertise. They may also be able to develop and commercialize products that are safer, more effective, less expensive, more convenient, easier to administer, or have fewer severe effects, than existing treatments or, if it is ultimately approved, neflamapimod. Competitors may also obtain FDA or other regulatory approval for their product candidates more rapidly than the Company may obtain approval for neflamapimod, which could result in their establishing or strengthening a commercial position before the Company is able to enter the market. The highly competitive nature of the biotechnology and pharmaceutical industries, as well as the rapid technological changes in those fields, could limit The Company's ability to advance neflamapimod commercially. If the Company is unable to compete effectively, this could have a material adverse effect on its business and results of operations.

The successful commercialization of neflamapimod, or any other product candidate the Company may develop or acquire, will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels, and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for the Company's product candidates, if approved, could limit its ability to market those products and decrease its ability to generate revenue.

In the United States, the availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers, and other third-party payors are essential for most patients to be able to afford prescription medications such as neflamapimod, if it is approved. The Company's ability to achieve acceptable levels of coverage, payment, and reimbursement for products by governmental authorities, private health insurers and other organizations will have an effect on the Company's ability to successfully commercialize neflamapimod and any other potential future product candidates. Assuming the Company obtains coverage for neflamapimod by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. the Company cannot be sure that coverage, payment, and reimbursement in the United States or elsewhere will be available for or any drug product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Further, if neflamapimod is approved in any jurisdictions outside of the United States, the Company may also be subject to extensive governmental price controls and other market regulations in those countries. Governments outside of the United States, particularly the countries of the European Union, tend to impose strict price controls on prescription pharmaceutical products. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, the Company may be required to conduct a clinical trial that compares the cost-effectiveness of its product candidate to other available therapies. If reimbursement of the Company's products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, the Company's business could be harmed, possibly materially. As a result, the Company might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay its commercial launch of the product and negatively impact the revenue the Company is able to generate from the sale of the product in that country. Adverse pricing limitations may hinder the Company's ability to recoup its investment in its product candidates, even after obtaining regulatory approval.

The market for any products for which the Company may receive regulatory approval will depend significantly on access to third-party payors' drug formularies, which are the lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. No uniform policy of coverage and reimbursement for drug products exists among third-party payors in the United States, and coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often time-consuming and costly. It will require the Company to provide scientific and clinical support for the use of its product candidates to each payor separately, with no assurance that coverage will be obtained.

In addition, efforts by governmental and third-party payors in the United States to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products. As a result, those payors may not cover or provide adequate payment for neflamapimod, if it is approved. Third-party payors are also increasingly challenging the prices charged for pharmaceutical products and services. Those payors may consider a product as substitutable, and only offer to reimburse patients for the less expensive product. Even if the Company shows improved efficacy or improved convenience of administration compared to existing treatments for its target indications, pricing of existing drugs may limit the amount the Company will be able to charge for neflamapimod.

If the Company is unable to obtain adequate coverage and payment levels for its products from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them, and patients may decline to purchase them. This in turn would affect the Company's ability to successfully commercialize any approved products and thereby adversely impact its profitability, results of operations, and financial condition.

Enacted and future healthcare legislation may increase the difficulty and cost for the Company to obtain marketing approval of and commercialize its product candidates, if approved, and also affect the prices it may set.

There have been, and the Company expects will continue to be, a number of legislative and regulatory proposals and changes to the healthcare systems in the United States and other jurisdictions that could affect the Company's future results of operations. In particular, a number of initiatives at the U.S. federal and state levels have aimed to reduce healthcare costs and improve the quality of healthcare. Existing regulatory policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of neflamapimod or any future product candidates the Company may develop or acquire. The Company cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If the Company is slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if it is not able to maintain regulatory compliance, the Company may lose any marketing approval that it may have obtained, and it may not achieve or sustain profitability.

In the United States, there have been and continue to be a number of significant legislative initiatives to contain healthcare costs. Federal and state governments continue to propose and pass legislation designed to reform delivery of, or payment for, healthcare, which include initiatives to reduce the cost of healthcare. For example, in March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act and the Healthcare and Education Reconciliation Act ("ACA"), which expanded healthcare coverage through Medicaid expansion and the implementation of the individual mandate for health insurance coverage and which included changes to the coverage and reimbursement of drug products under federal healthcare programs. The ACA contained a number of provisions that affect coverage and reimbursement of drug products or that could potentially reduce the demand for pharmaceutical products such as increasing drug rebates under state Medicaid programs for brand name prescription drugs and extending those rebates to Medicaid managed care and assessing a fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid. Since its enactment, there have been numerous judicial, administrative, executive and legislative challenges to certain aspects of the ACA. In June 2021 the U.S. Supreme Court dismissed a judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form.

The Company's industry continues to face potential changes in the legal and regulatory landscape on the federal, state and international levels. Additional legislative actions to control U.S. healthcare or other costs have passed. The Budget Control Act, as amended, resulted in the imposition of 2% reductions in Medicare (but not Medicaid) payments to providers in 2013 and will remain in effect through 2027 unless additional Congressional action is taken. There has also been increasing public and government interest in the United States with respect to specialty drug pricing practices, including proposed federal and state legislation designed to bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, put in place limits and caps on pharmaceutical prices, request rebates for certain pharmaceutical products, and reform government program reimbursement methodologies for drugs. For example, in March 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price ("AMP"), for single source and innovator multiple source drugs, beginning January 1, 2024. Payment methodologies may also be subject to changes in health care legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, President Biden signed the Inflation Reduction Act of 2022 ("IRA") into law in August 2022. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated, or the impact of the IRA on our business.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmacy benefit managers ("PBMs") and other members of the health care and pharmaceutical supply chain, an important decision that may lead to appears to be leading to further and more aggressive efforts by states in this area. The Federal Trade Commission in mid-2022 also launched sweeping investigations into the practices of the PBM industry, and members of Congress continue to propose reforms for the PBM industry, all or each of which could lead to additional federal and state legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements. Significant efforts to change the PBM industry as it currently exists in the U.S. may affect the entire pharmaceutical supply chain and the business of other stakeholders, including pharmaceutical product developers like the Company.

In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. In markets outside of the United States, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement, and to control the prices of medicinal products for human use.

The Company cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction. In the United States, future laws and regulation may result in more rigorous coverage criteria and increased downward pressure on the price pharmaceutical companies may receive for any approved product. Reductions in reimbursement from Medicare or other government programs may result in similar reductions in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent the Company from being able to generate revenue, attain profitability or commercialize its product candidates. Further, if the Company or any third parties with whom it engages in the future are slow or unable to adapt to changes in existing requirements or policies, or if the Company is not able to maintain regulatory compliance, its ability to generate revenue, attain profitability, or commercialize neflamapimod or any other products for which it receives regulatory approval may be materially and adversely affected.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of the Company's business may rely, which could negatively impact the Company's business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC, the NIA and other government agencies on which the Company's operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for clinical trial applications and/or marketing applications for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect the Company's business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government or slowdown shutdown occurs, it could significantly impact the ability of the NIA to disburse funds for our clinical trial and for the FDA to timely review and process the Company's regulatory submissions, which could have a material adverse effect on the Company's business. Further, in the Company's operations as a public company, future government shutdowns or slowdowns could impact its ability to access the public markets and obtain necessary capital in order to properly capitalize and continue its operations.

Regulatory authorities, including the FDA, may not accept data from clinical trials conducted outside of their jurisdiction.

The Company has in the past and may in the future conduct additional clinical trials evaluating its product candidates outside the U.S. The acceptance of trial data from clinical trials conducted outside the U.S. by the FDA may be subject to certain conditions or may not be accepted at all, and other comparable non-U.S. regulatory authorities may have similar restrictions and conditions with respect to clinical trials conducted outside of their jurisdiction. In cases where data from non-U.S. clinical trials are intended to serve as the basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of non-U.S. data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many comparable non-U.S. regulatory authorities have similar approval requirements.

There can be no assurance that the FDA will accept data from trials conducted outside of the U.S. or that any comparable non-U.S. regulatory authority will accept data form trials conducted outside of the applicable jurisdiction. If the FDA or any comparable non-U.S. regulatory authority does not accept such data or believes that additional data is necessary to supplement such data, it would result in the need for additional trials, which would be costly and time-consuming, could delay a product candidate's development plan, and which may result in product candidates not receiving approval for commercialization in the applicable jurisdiction.

Conducting clinical trials outside the U.S. may also expose us to additional risks, including risks associated with the following: additional foreign regulatory requirements; foreign exchange fluctuations; compliance with foreign manufacturing, customs, shipment and storage requirements; the failure of enrolled subjects in foreign countries to adhere to clinical protocol as a result of differences in standard-of-care; cultural differences in medical practice and clinical research; diminished protection of intellectual property rights; and compliance with general local legal requirements.

The Company's business activities may be subject to the Foreign Corrupt Practices Act "(FCPA") and similar anti-bribery and anti-corruption laws.

The Company's business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which the Company operates, including the U.K. Bribery Act. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. The Company's business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, the Company's dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the Securities and Exchange Commission ("SEC") and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of the Company's employees, agents, contractors, or collaborators, or those of the Company's affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against the Company, its officers, or its employees, the closing down of the Company's facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of its business. Any such violations could include prohibitions on the Company's ability to offer its products in one or more countries and could materially damage the Company's reputation, its brand, its international expansion efforts, its ability to attract and retain employees, and its business, prospects, operating results, and financial condition.

Risks Related to the Company's Intellectual Property

If the Company does not adequately protect its proprietary rights, the Company may not be able to compete effectively.

The Company relies upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to its neflamapimod drug development program. The Company's commercial success depends on obtaining and maintaining proprietary rights in the United States and in international jurisdictions, and successfully defending these rights against third-party challenges. The Company seeks to protect its proprietary position by filing patent applications related to its neflamapimod drug development programs in the United States and in other countries.

The Company acquired an exclusive license from Vertex in 2014 to develop and commercialize neflamapimod for the treatment of AD and other CNS disorders. This license covers know-how, preclinical and clinical data, and certain specified Vertex patent rights, including a composition of matter patent for neflamapimod that expired in 2017. The Company has thus focused its efforts on discoveries related to neflamapimod that are reflected in issued patents and patent applications covering a range of subjects, including: methods of treating patients suffering from DLB or AD, as well as methods of reducing amyloid plaque burden; methods of improving cognition and treating neurologic disorders; methods for promoting recovery of function in patients who have suffered acute neurologic injuries, including those resulting from various forms of stroke; and methods of treating patients suffering from dementia. In addition, the Company has filed patents related to formulations of neflamapimod, including pharmaceutical compositions for oral administration exhibiting desirable pharmacokinetics and processes for the manufacture thereof. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Although various extensions may be available, the life of a patent is limited.

The Company's issued patents and patent applications remain subject to uncertainty and continued monitoring. The Company's patent applications may fail to result in issued patents with claims that provide further coverage for neflamapimod in the United States or in foreign countries. The patent prosecution process is expensive and time-consuming, and the Company may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. The Company may also fail to identify further patentable aspects of its research and development output before it is too late to obtain patent protection. There is no assurance that all potentially relevant prior art relating to the Company's patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application.

Although the Company has already obtained several issued patents and are working to expand its estate with additional patent applications, third parties may challenge its patents' validity, enforceability, or scope, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful opposition to these patents or any other patents owned by or licensed to the Company could deprive it of rights necessary for the successful commercialization of neflamapimod, or any other product candidates it may develop. Further, if the Company encounters delays in regulatory approvals, the period of time during which it could market a product candidate under patent protection could be reduced.

The patent position of life sciences companies can often involve complex legal and factual questions and in recent years has been the subject of significant litigation. Publications of discoveries in 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 filing, or in some cases not at all. Therefore, the Company cannot know with certainty whether it was the first to make the inventions claimed in its owned or licensed patents or pending patent applications, or that it was the first to file for patent protection of such inventions. Further, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and the Company's patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in patent claims being narrowed, invalidated, held unenforceable, in whole or in part, or reduced in term. Such a result could limit the Company's ability to prevent others from using or commercializing similar or identical technology and products.

The Company also intends to rely on regulatory exclusivity for protection of its product candidates, if approved for commercial sale. Implementation and enforcement of regulatory exclusivity, which may consist of regulatory data protection and market protection, varies widely from country to country. Failure to qualify for regulatory exclusivity, or failure to obtain or to maintain the extent or duration of such protections that we expect for the Company's product candidates, if approved, could affect the Company's decision on whether to market the products in a particular country or countries or could otherwise have an adverse impact on its revenue or results of operations.

Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of the Company's patents, requiring it to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may also develop, seek approval for and launch generic versions of the Company's products.

There is no composition matter patent protection that covers neflamapimod. Rather, the Company's patents provide protection around either the use of neflamapimod for specific or medical indication (so called "use patents") or the administration of neflamapimod in specific manner (e.g., at a specific dose or in a specific formulation). Patents that are not around composition of matter are narrower in scope (i.e., they do not protect against development of neflamapimod in an indication other than that the patent defines), more difficult to defend against challenges against validity, and more difficult to enforce against infringement. For these reasons, some pharmaceutical companies choose not to develop and/or license compounds that are not covered by a composition of matter patent. The Company owns a patent that is issued in the US around co-crystals of neflamapimod, any of which if they were successfully developed would be afforded composition of matter patent protection under this patent.

Without patent protection for the Company's current or future product candidates, these candidates may be open to competition from other products. As a result, the Company's patent portfolio may not provide the Company with sufficient rights to exclude others from commercializing products similar or identical to the Company's.

If the Company fails to comply with its obligations under its existing license agreement with Vertex, or with any future intellectual property licenses with third parties, the Company could lose license rights that are important to its business.

The Company is party to an Option and License Agreement with Vertex, pursuant to which the Company acquired an exclusive license to develop and commercialize neflamapimod for the diagnosis, treatment, and prevention of AD and other CNS disorders. Under the terms of the Vertex Agreement, the Company must use commercially reasonable efforts during the license term to develop and obtain regulatory approval for a licensed product in specified major markets, and to promptly and effectively commercialize the licensed product once such approval is obtained. The Vertex Agreement also contains certain specified minimum diligence requirements, including making annual expenditures set forth in a development plan, and commencing a Phase 2 clinical trial of the licensed product within a specified time period.

The Vertex Agreement provides that either party may terminate the agreement if the other party is in material breach of its obligations thereunder, following a 60-day notice and cure period, or if the other party files for bankruptcy, reorganization, liquidation, receivership, or an assignment of a substantial portion of assets to creditors. The Vertex Agreement also provides that in the event the Company materially breaches any of certain specified diligence obligations as to a specific major market, Vertex's sole remedy for such breach, following the applicable notice and cure period, will be to terminate the license as to such specific major market country.

Accordingly, the Company must be diligent in meeting its obligations under the Vertex Agreement. Any uncured, material breach under the Vertex Agreement could result in the loss of certain of its rights to neflamapimod and could compromise the Company's development and commercialization efforts. This in turn would have an adverse effect on the Company's business, which could be material.

The Company may become subject to third parties' claims alleging infringement of their patents and proprietary rights, or the Company may need to become involved in lawsuits to protect or enforce its patents, which could be costly and time consuming, as well as potentially delay or prevent the development and commercialization of its product candidates or put its patents and other proprietary rights at risk

The Company's commercial success depends, in part, upon the Company's ability to develop, manufacture, market and sell its lead product candidate, neflamapimod, without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. While the Company is not currently subject to any pending intellectual property litigation, and is not aware of any such threatened litigation, the Company may be exposed to future litigation by third parties based on claims that its product candidates, technologies or activities infringe the intellectual property rights of others. Some claimants may have substantially greater resources than the Company does and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than it could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target the Company. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that the Company's product candidates may be subject to claims of infringement of the intellectual property rights of third parties.

The Company may be subject to third-party claims including infringement, interference or derivation proceedings, reexamination proceedings, post-grant review and *inter partes* review before the U.S. Patent and Trademark Office ("USPTO") or similar adversarial proceedings or litigation in other jurisdictions. Even if the Company believes such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block the Company's ability to commercialize the applicable product candidate unless the Company obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. These proceedings may also result in the Company's patent claims being invalidated or narrowed in scope. In addition, a court may hold that a third-party is entitled to certain patent ownership rights instead of the Company.

As a result of patent infringement claims, or in order to avoid potential infringement claims, the Company may choose to seek, or be required to seek, a license from the third party, which may require it to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if a license can be obtained on acceptable terms, the rights may be nonexclusive, which could give the Company's competitors access to the same intellectual property rights. If the Company is unable to enter into a license on acceptable terms, it could be prevented from commercializing one or more of its product candidates, forced to modify such product candidates, or to cease some aspect of the Company's business operations, which could harm the Company's business significantly. In addition, if the breadth or strength of protection provided by the Company's patents and patent applications is threatened, it could dissuade companies from collaborating with the Company to license, develop or commercialize current or future product candidates.

If the Company were to initiate legal proceedings against a third party to enforce a patent covering one of its product candidates, the defendant could counterclaim that the Company's patent is invalid or unenforceable. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, the Company cannot be certain that there is no invalidating prior art of which the Company and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, the Company would lose at least part, and perhaps all, of the patent protection on its product candidates. Furthermore, the Company's patents and other intellectual property rights also will not protect its technology if competitors design around the Company's protected technology without infringing its patents or other intellectual property rights.

Finally, even if resolved in the Company's favor, litigation or other legal proceedings relating to intellectual property claims may cause the Company to incur significant expenses and could distract its technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, which could damage the Company's reputation, harm its business, and the price of its common stock could be adversely affected.

The Company may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might adversely affect the Company's ability to develop, manufacture and market its product candidates.

From time to time, the Company may identify patents or applications in the same general area as its products and product candidates. The Company may determine these third-party patents are irrelevant to its business based on various factors including its interpretation of the scope of the patent claims and its interpretation of when the patent expires. If the patents are asserted against the Company, however, a court may disagree with the Company's determinations. Further, while the Company may determine that the scope of claims that will issue from a patent application does not present a risk, it is difficult to accurately predict the scope of claims that will issue from a patent application, the Company's determination may be incorrect, and the issuing patent may be asserted against the Company. The Company cannot guarantee that it will be able to successfully settle or otherwise resolve such infringement claims. If the Company fails in any such dispute, in addition to being forced to pay monetary damages, it may be temporarily or permanently prohibited from commercializing its product candidates. The Company might also be forced to redesign its product candidates so that it no longer infringes the third-party intellectual property rights, if such redesign is even possible. Any of these events, even if the Company were ultimately to prevail, could require it to divert substantial financial and management resources that it would otherwise be able to devote to its business.

Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing the Company's ability to protect its product candidates.

The Company's success is heavily dependent on intellectual property, particularly patents, and obtaining and enforcing patents in its industry involves both technological complexity and legal complexity. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of the Company's patents or narrow the scope of its patent protection.

As an example, the America Invents Act ("AIA"), which was passed in September 2011, resulted in significant changes to the U.S. patent system. Pursuant to the MA, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before the Company could therefore be awarded a patent covering an invention of the Company's even if the Company made the invention before it was made by the third party. This requires the Company to be cognizant going forward of the time from invention to filing of a patent application.

The AIA also introduced changes that provide opportunities for third parties to challenge any issued patent with the USPTO. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Such changes could increase the uncertainties and costs surrounding the prosecution of the Company's patent applications and the enforcement or defense of its issued patents.

In addition, the laws of foreign countries may not protect the Company's rights to the same extent as the laws of the United States. The complexity and uncertainty of European patent laws has increased in recent years, and the European patent system is relatively stringent in the type of amendments that are allowed during prosecution. Complying with these laws and regulations could limit the Company's ability to obtain new patents in the future that may be important for its business.

The Company enjoys only limited geographical protection with respect to certain patents, and it may not be able to protect its intellectual property rights throughout the world.

Filing, prosecuting and defending patents covering the Company's product candidates in all countries throughout the world would be prohibitively expensive. Competitors may use the Company's technologies in jurisdictions where it has not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where the Company has patent protection, but enforcement is not as strong as that in the United States or the EU. These products may compete with the Company's product candidates, and its patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Although the Company intends to protect its intellectual property rights in its expected significant markets, the Company cannot ensure that it will be able to initiate or maintain similar efforts in all jurisdictions in which the Company may wish to market its product candidates. The Company may also decide to abandon national and regional patent applications before grant. The grant proceeding of each national or regional patent is an independent proceeding, which may lead to situations in which applications might in some jurisdictions be refused by the relevant patent offices, while granted by others.

The legal systems of certain countries do not favor the enforcement of patents, trade secrets and other intellectual property protection, which could make it difficult for the Company to stop the infringement of its patents or marketing of competing products in violation of the Company's proprietary rights generally. Proceedings to enforce its patent rights in other jurisdictions, whether or not successful, could result in substantial costs and divert its efforts and attention from other aspects of the Company's business, could put the Company's patents at risk of being invalidated or interpreted narrowly and its patent applications at risk of not issuing, and could provoke third parties to assert claims against the Company. The Company may not prevail in any lawsuits that it initiates, and the damages or other remedies awarded, if any, may not be commercially meaningful.

Some countries also have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If the Company is forced to grant a license to any third parties with respect to any patents relevant to the Company's business, its competitive position may be impaired.

The Company's reliance on third parties requires the Company to share its trade secrets, which increases the possibility that its trade secrets will be misappropriated or disclosed, and confidentiality agreements with employees and third parties may not adequately prevent disclosure of trade secrets and protect other proprietary information.

The Company may rely on trade secrets or confidential know-how to protect various aspects of its business, especially where patent protection is believed by the Company to be of limited value. Because it relies on third parties to manufacture neflamapimod and any future product candidates, and the Company may also collaborate with third parties on the development of neflamapimod and any future product candidates, the Company must, at times, share trade secrets with such parties. The Company may also conduct joint research and development programs that require it to share trade secrets under the terms of the Company's research and development partnerships or similar agreements. Such trade secrets or confidential know-how can be difficult to protect as confidential.

To protect this type of information against disclosure or appropriation by competitors, the Company's policy is to require its employees, consultants, contractors and advisors to enter into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with the Company prior to beginning research or disclosing proprietary information. However, current or former employees, consultants, contractors and advisers may unintentionally or willfully disclose the Company's confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Enforcing a claim that a third party obtained illegally and is using trade secrets or confidential know-how is expensive, time-consuming and unpredictable. In addition, the enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction.

Despite the Company's efforts to protect its trade secrets, the Company's competitors may discover the Company's trade secrets, either through breach of the Company's agreements with third parties, independent development or publication of information by any of its third-party collaborators. A competitor's discovery of the Company's trade secrets could impair its competitive position and have an adverse impact on its business.

Intellectual property discovered or developed through government funded programs may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a manufacturing preference for U.S.-based companies. Compliance with such regulations may limit the Company's exclusive rights and limit its ability to contract with non-U.S. manufacturers.

The Company received a grant from the NIA to support its recently initiated Phase 2b clinical trial for treatment in patients with DLB. Pursuant to the Bayh-Dole Act of 1980 ("Bayh-Dole Act"), the U.S. government may have certain rights in any invention developed or reduced to practice with this funding. In addition, in the future the Company may discover, develop, acquire, or license intellectual property that has been generated through the use of U.S. government funding or grants in which the U.S. government may have certain rights pursuant to the Bayh-Dole Act. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require the Company to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (1) adequate steps have not been taken to commercialize the invention; (2) government action is necessary to meet public health or safety needs; or (3) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). Such "march-in" rights would apply to new subject matter arising from the use of such government funding or grants and would not extend to pre-existing subject matter or subject matter arising from funds unrelated to the government funding or grants. If the U.S. government exercises its march-in rights in the Company's intellectual property rights that are generated through the use of U.S. government funding or grants, the Company could be required to license or sublicense intellectual property discovered or developed by it or that it licenses on terms unfavorable to the Company, and there can be no assurance that the Company would receive compensation from the U.S. government for the exercise of such rights. The U.S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require the Company to expend substantial resources. Should any of these events occur, it could significantly harm the Company's business, results of operations and prospects. In addition, the U.S. government requires that, in certain circumstances, any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit the Company's ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

General Risk Factors

The Company's stock price may be volatile, there may be limited liquidity in the trading market for the Company's common stock, and the market price of its common stock may drop following the merger (the "Merger") between the Company (formerly known as Diffusion Pharmaceuticals Inc.) and EIP.

The market price of the Company's common stock may be subject to significant fluctuations. Market prices for securities of early-stage pharmaceutical, biotechnology and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of the Company's common stock to fluctuate include among others:

- the ability of the Company or its partners to develop product candidates and conduct clinical trials that demonstrate such product candidates are safe and effective;
- the ability of the Company or its partners to obtain regulatory approvals for product candidates, and delays or failures to obtain such approvals;
- failure of any of the Company's product candidates to demonstrate safety and efficacy, receive regulatory approval and achieve commercial success;
- failure by the Company to maintain its existing third-party license, manufacturing and supply agreements;
- failure by the Company or its licensors to prosecute, maintain, or enforce its intellectual property rights;
- changes in laws or regulations applicable to the Company's product candidates;
- any inability to obtain adequate supply of product candidates or the inability to do so at acceptable prices;
- adverse regulatory authority decisions;
- introduction of new or competing products by its competitors;
- failure to meet or exceed financial and development projections the Company may provide to the public;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by the Company or its competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and the Company's ability to obtain intellectual property protection for its technologies;
- additions or departures of key personnel;
- significant lawsuits, including intellectual property or stockholder litigation;
- if securities or industry analysts do not publish research or reports about the Company, or if they issue an adverse or misleading opinions regarding its business and stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions;
- sales of its common stock by the Company or its stockholders in the future;
- trading volume of the Company's common stock;
- adverse publicity relating to the Company's markets generally, including with respect to other products and potential products in such markets;
- changes in the structure of health care payment systems; and
- period-to-period fluctuations in the Company's financial results.

After completion of the Merger, the market price of Company's common stock is likely to be highly volatile and could fluctuate widely in price in response to various factors. First, the Company has relatively few shares of common stock outstanding in the "public float" since most of the shares are held by a small number of shareholders. In addition, the shares of common stock may be sporadically or thinly traded. As a consequence of this lack of liquidity, the trading of relatively small quantities of shares by shareholders may disproportionately influence the price of those shares in either direction. The price for such shares could, for example, decline precipitously in the event that a large number of the shares are sold on the market without commensurate demand, as compared to a seasoned issuer which could better absorb those sales without a material reduction in share price. An active trading market for the Company's shares of common stock may never develop or be sustained. If an active market for its common stock does not develop or is not sustained, it may be difficult for its stockholders to sell their shares at an attractive price or at all.

Second, the Company may be a speculative or "risky" investment due to its lack of profits to date. As a consequence of this enhanced risk, more risk-adverse investors may, under the fear of losing all or most of their investment in the event of negative news or lack of progress, be more inclined to sell their shares on the market more quickly and at greater discounts than would be the case with the stock of a seasoned issuer.

Additionally, in the past, plaintiffs have often initiated securities class action litigation against a company following periods of volatility in the market price of its securities. The Company may in the future be the target of similar litigation. Securities litigation could result in substantial costs and liabilities and could divert management's attention and resources.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about the Company, its business, or its market, its stock price and trading volume could decline.

The trading market for the Company's common stock will be influenced by the research and reports that equity research analysts publish about it and its business. Equity research analysts may elect not to provide research coverage of the Company's common stock after the completion of the Merger, and such lack of research coverage may adversely affect the market price of its common stock. In the event it does have equity research analyst coverage, the Company will not have any control over the analysts, or the content and opinions included in their reports. The price of the Company's common stock could decline if one or more equity research analysts downgrade its stock or issue other unfavorable commentary or research. If one or more equity research analysts cease coverage of the Company or fails to publish reports on it regularly, demand for its common stock could decrease, which in turn could cause its stock price or trading volume to decline.

Future sales of shares by existing stockholders could cause the Company's stock price to decline.

If existing stockholders of the Company sell, or indicate an intention to sell, substantial amounts of the Company's common stock in the public market after certain legal and contractual restrictions on resale lapse, the trading price of the common stock of the Company could decline. Based on shares outstanding immediately after the closing of the Merger, the Company had a total of approximately 5.7 million shares of common stock outstanding. Approximately 2.9 million of such shares of outstanding common stock are freely tradable, without restriction, in the public market. Approximately 1.1 million of such shares of outstanding common stock are held by directors, executive officers of the Company and other affiliates and are subject to volume limitations under Rule 144 promulgated under the Securities Act and various vesting agreements.

The Company may choose to waive certain of its rights under the lock-up agreements signed by certain equityholders.

In connection wither Merger, certain directors, executive officers and principal stockholders of the Company and EIP entered into lock-up agreements, pursuant to which such parties have agreed not to, except in limited circumstances, transfer, grant an option with respect to, sell, exchange, pledge or otherwise dispose of, or encumber any shares of the Company's common stock for up to 180 days following the closing of the Merger. However, in certain circumstances, the Company may choose to waive its rights under any or all of such lock-up agreements, either in whole or in part. In such an event, the holders of those shares may be permitted to sell or transfer the shares of common stock received in the Merger sooner than they otherwise would, which could result in a decrease to the Company's stock price. For example, in July 2023, the Company waived certain obligations under the lock-up agreement of AI EIPP Holdings LLC and its affiliates.

After completion of the Merger, the ownership of the Company common stock is highly concentrated, which may prevent you and other stockholders from influencing significant corporate decisions and may result in conflicts of interest that could cause the Company stock price to decline.

Executive officers and directors of the Company and their affiliates own or control approximately 32.6% of the outstanding shares of the Company common stock immediately following the closing of the Merger. Certain other former stockholders of EIP own or control approximately 64.2% of the outstanding shares of the Company common stock immediately following the closing of the Merger. Additionally, Dr. Alam and Dr. Sylvie Grégoire, our Chair, who are married, hold a significant interest in the Company's common stock on a fully diluted basis. For as long as Dr. Alam and Dr. Grégoire maintain a significant interest in the Company, they may be in a position to affect the Company's governance and operations. Accordingly, these stockholders, in the aggregate, may exercise substantial influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of the Company assets or any other significant corporate transactions. These stockholders may also delay or prevent a change of control of the Company, even if such a change of control would benefit the other stockholders of the Company. The significant concentration of stock ownership may adversely affect the trading price of the Company's common stock due to investors' perception that conflicts of interest may exist or arise.

The Company does not anticipate that it will pay any cash dividends in the foreseeable future.

The current expectation is that the Company will retain its future earnings, if any, to fund the development and growth of the Company's business. As a result, capital appreciation, if any, of the common stock of the Company will be your sole source of gain, if any, for the foreseeable future.

Changes in tax law could adversely affect the Company's business.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by Internal Revenue Service, the U.S. Treasury Department, and other governmental bodies. Changes to tax laws (which changes may have retroactive application) could adversely affect the Company or holders of its common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on the Company's business, cash flow, financial condition, or results of operations.

The Merger may have adverse tax consequences for former holders of EIP securities.

Subject to certain limitations and qualifications described in the section titled "*The Merger — Material U.S. Federal Income Tax Consequences of the Merger*" beginning on page 140 of our proxy statement/prospectus/information statement, dated July 13, 2023 and previously filed with the SEC, the Merger is believed to qualify as a reorganization within the meaning of Section 368(a) of the Code. This opinion is based on certain facts and representations on customary factual assumptions. If the Merger were to fail to so qualify, then each pre-Merger U.S. holder of EIP common stock generally would recognize gain or loss, as applicable, equal to the difference between (1) the sum of the fair market value of the shares of the Company's common stock received by such U.S. holder in the Merger and the amount of cash received for fractional shares by such U.S. holder in the Merger, if any, and (2) its adjusted tax basis in the shares of EIP common stock surrendered in exchange therefor.

Due to the Merger resulting in an ownership change under Section 382 of the Code for the Company, the Company's pre-merger net operating loss ("NOL") carryforwards and certain other tax attributes will be subject to limitation. In addition, the NOL carryforwards and other tax attributes of EIP may also be subject to limitation as a result of ownership changes.

As of December 31, 2022, the Company and EIP had U.S. federal NOL carryforwards of approximately $34.2 million and $38.2 million, respectively. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, (the "Code") and corresponding provisions of state law, if a corporation undergoes an "ownership change" (within the meaning of Section 382 of the Code ("Section 382")), the corporation's NOL carryforwards and certain other tax attributes (such as research tax credits) arising before the ownership change are subject to limitation on use after the ownership change. In general, an ownership change occurs if there is a cumulative change in the corporation's equity ownership by certain stockholders that exceeds fifty percentage points (by value) over a rolling three-year period. Similar rules may apply under state tax laws. The Merger resulted in an ownership change for the Company and, accordingly, the Company's NOL carryforwards and certain other tax attributes will be subject to limitations (or disallowance) on their use after the Merger. The Company's NOL carryforwards may also be subject to limitation as a result of prior or future shifts in equity ownership, as well. Consequently, even if the Company achieves profitability, it may not be able to utilize a material portion of its NOL carryforwards and other tax attributes, which could have a material adverse effect on cash flow and results of operations. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs or other unforeseen reasons, the Company's existing NOLs could expire or otherwise be unavailable to offset future income tax liabilities.

Now that the Merger has closed, there can be no further recourse by either party or its stockholders for a breach of representation or warranty.

The representations and warranties of the Company, EIP and Merger Sub contained in the Merger Agreement or any certificate or instrument delivered pursuant to the Merger Agreement terminated at the effective time of the Merger. To the extent that any such party's breach of any representations and warranties is discovered or occurs following the closing of the Merger, there is no mechanism pursuant to which the other parties can pursue recourse or remedy.

The Company's business may be affected from time-to-time by government investigations and litigation with third parties, including our ongoing matter with Paul Feller.

The Company may from time to time receive inquiries and subpoenas and other types of information requests from government authorities and other third parties and may become subject to claims and other actions related to its business activities. While the ultimate outcome of investigations, inquiries, information requests and legal proceedings is difficult to predict, defense of litigation claims (even if ultimately successful) can be expensive, time-consuming and distracting, and adverse resolutions or settlements of those matters may result in, among other things, modifications to business practices, costs and significant payments, any of which could have a material adverse effect on the Company's business, financial condition, results of operations and prospects.

For example, in August 2014, Paul Feller, the former Chief Executive Officer of the Company's legal predecessor, filed a complaint asserting various causes of action related to his past affiliations with the Company's legal predecessor. While the Company believes the claims in this matter are without merit and is defending itself vigorously, the Company is unable to predict the outcome and possible loss or range of loss, if any, associated with its resolution or any potential effect the matter may have on the Company's financial position. Depending on the outcome or resolution of this matter, it could have a material effect on the Company's consolidated financial position, results of operations and cash flows.

In addition, the Company's stockholders may serve demands and/or file lawsuits challenging the Merger, which may name the Company, EIP, members of the Company's former or current board of directors, members of the EIP board of directors and/or others as defendants. No assurance can be made as to the outcome of such demand or lawsuits, including the amount of costs associated with defending, settling, or any other liabilities that may be incurred in connection with the litigation or settlement of such claims, if any.

If the Company fails to maintain proper and effective internal controls, its ability to produce accurate financial statements on a timely basis could be impaired.

The Company will be subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of Nasdaq. The Sarbanes-Oxley Act requires, among other things, that the Company maintain effective disclosure controls and procedures and internal control over financial reporting. The Company must perform system and process evaluation and testing of its internal control over financial reporting to allow management to report on the effectiveness of its internal controls over financial reporting in its Annual Report on Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that the Company incur substantial professional fees and internal costs to expand its accounting and finance functions and that it expends significant management efforts. The Company may experience difficulty in meeting these reporting requirements in a timely manner.

The Company may discover weaknesses in its system of internal financial and accounting controls and procedures that could result in a material misstatement of its financial statements. The Company's internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If the Company is not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act, or if it is unable to maintain proper and effective internal controls, the Company may not be able to produce timely and accurate financial statements. If that were to happen, the market price of its common stock could decline and it could be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities.

Provisions in the Company's corporate charter documents and under Delaware law could make an acquisition of the Company, which may be beneficial to the Company's stockholders, more difficult and may prevent attempts by the Company's stockholders to replace or remove its current directors and members of management.

Provisions in the Company's certificate of incorporation, as amended, and its amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of the Company that stockholders may consider favorable, including transactions in which the Company's stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of the Company's common stock, thereby depressing the market price of its common stock. In addition, because the Company's board of directors is responsible for appointing the members of its management team, these provisions may frustrate or prevent any attempts by the Company's stockholders to replace or remove its current management by making it more difficult for stockholders to replace members of the Company's board of directors. Among other things, these provisions:

- allow the authorized number of the Company's directors to be changed only by resolution of its board of directors;
- limit the manner in which stockholders can remove directors from the Company's board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to the Company's board of directors;
- limit who may call stockholder meetings and the Company stockholders' ability to act by written consent;
- authorize the Company's board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by the Company's board of directors; and
- require the approval of the holders of at least 2/3 of the votes that all the Company's stockholders would be entitled to cast to amend or repeal specified provisions of the Company's certificate of incorporation, as amended, or for stockholders to amend or repeal the Company's amended and restated bylaws.

Moreover, because the Company is incorporated in Delaware, it is governed by the provisions of Section 203 of the Delaware General Corporation Law (the "DGCL"), which generally prohibits a person who, together with their affiliates and associates, owns 15% or more of a company's outstanding voting stock from, among other things, merging or combining with the company for a period of three years after the date of the transaction in which the person acquired ownership of 15% or more of the company's outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

The Company's certificate of incorporation designates the state courts in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by its stockholders, which could discourage lawsuits against the company and its directors, officers and employees.

The Company's certificate of incorporation provides that, unless the Company consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for certain proceedings, including: (1) any derivative action or proceeding brought on the Company's behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of the Company's directors, officers, employees or stockholders to the company or its stockholders, (3) any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware or (4) any action asserting a claim arising pursuant to any provision of the Company's certificate of incorporation or amended and restated bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Securities Act, the Exchange Act or any other claim for which federal courts have exclusive jurisdiction.

These exclusive-forum provisions may make it more expensive for stockholders to bring a claim than if the stockholders were permitted to select another jurisdiction and may limit the ability of the Company's stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with the Company or its directors, officers or employees, which may discourage such lawsuits against the Company and its directors, officers and employees. Alternatively, if a court were to find the choice of forum provisions contained in the Company's certificate of incorporation to be inapplicable or unenforceable in an action, the Company may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect its business, financial condition and operating results.

Certain stockholders could attempt to influence changes within the Company which could adversely affect the Company's operations, financial condition and the value of the Company Common Stock.

One or more of the Company's stockholders may from time to time seek to acquire a significant or controlling stake in the Company, engage in proxy solicitations, advance stockholder proposals or otherwise attempt to effect changes to the Company's board of directors or corporate governance policies. Campaigns by stockholders to effect changes at publicly traded companies are sometimes led by investors seeking to increase short-term stockholder value through actions such as financial restructuring, increased debt, special dividends, stock repurchases or sales of assets or the entire company. Responding to proxy contests and other actions by activist stockholders can be costly and time-consuming, could disrupt the Company's operations and divert the attention of the Company board of directors and senior management, and could adversely affect the Company's operations, financial condition, and the value of the Company Common Stock. For example, in November 2022, LifeSci Special Opportunities Master Fund Ltd. (the "LifeSci Fund"), a the Company stockholder, informed the Company of its intent to nominate an alternative slate of directors for election at the Company's 2022 annual meeting of stockholders, which was subsequently withdrawn following the Company and the LifeSci Fund entering into a settlement agreement on December 11, 2022.

The Company holds its cash and cash equivalents that it uses to meet its working capital needs in deposit accounts that could be adversely affected if the financial institutions holding such funds fail.

The Company holds its cash and cash equivalents that we use to meet our working capital needs in deposit accounts at multiple financial institutions. The balance held in these accounts may exceed the Federal Deposit Insurance Corporation ("FDIC"), standard deposit insurance limit or similar government guarantee schemes. If a financial institution in which the Company holds such funds fails or is subject to significant adverse conditions in the financial or credit markets, the Company could be subject to a risk of loss of all or a portion of such uninsured funds or be subject to a delay in accessing all or a portion of such uninsured funds. Any such loss or lack of access to these funds could adversely impact the Company's short-term liquidity and ability to meet its obligations.

For example, on March 10, 2023, Silicon Valley Bank ("SVB"), and on March 12, 2023, Signature Bank, were closed by state regulators and the FDIC was appointed receiver for each bank. The FDIC created successor bridge banks and all deposits of SVB and Signature Bank were transferred to the bridge banks under a systemic risk exception approved by the United States Department of the Treasury, the Federal Reserve and the FDIC. While the Company did not hold any of its funds in accounts with either of these institutions, if financial institutions in which the Company holds funds for working capital were to fail, the Company cannot provide any assurances that such governmental agencies would take action to protect its uninsured deposits in a similar manner.

The Company also maintains investment accounts with other financial institutions in which it holds its investments and, if access to the funds the Company uses for working capital is impaired, the Company may not be able to sell investments or transfer funds from its investment accounts to new accounts on a timely basis sufficient to meet its working capital needs.

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

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

The Company may not be able to enter into a transaction with a suitable acquiror or licensee for its product candidate trans sodium crocetinate ("TSC") or any transaction entered into may not be on terms that are favorable to the Company.

As previously announced, in connection with the Company's strategic review process during 2022-23, the Company made the strategic decision to voluntarily pause significant portions of the TSC development program. Currently, the Company believes the primary path available to derive value from its TSC-related assets would be to find a suitable acquiror or licensee for the asset. Although the Company's management has contacted numerous parties to assess their potential interest in such a transaction, to date, the Company has been unable to identify an interested counterparty. Furthermore, even if the Company is able to identify such a counterparty, supporting diligence activities conducted by potential acquirors or licensees and negotiating the financial and other terms of an agreement or license are typically long and complex processes, and the results of such processes cannot be predicted. There can be no assurance that the Company will enter into any transaction as a result of these effort or that any transaction involving the Company's TSC-related assets will be entered into or, if entered into, will be on terms that are favorable to the Company. Furthermore, the Company cannot predict the impact that such a transaction or, alternatively, a failure to monetize the TSC assets in any material way, might have on its stock price.

Exhibit 99.3

CERVOMED INC. BUSINESS

Unless the context otherwise requires, all references in this Exhibit 99.3 to "we," "our," "us," or "CervoMed" refer to the business of CervoMed Inc.

Overview

We are a clinical stage therapeutics company that is developing treatments for acute and chronic neurodegenerative diseases of the brain and the Central Nervous System ("CNS"), such as Dementia with Lewy Bodies ("DLB"), and other neurologic indications. In DLB, for which there are currently no approved therapies and no disease-modifying drugs in Phase 3 clinical trials, we believe that we are one of the leaders in the industry, as we are the only company of which we are aware with an asset that, in that disease, has shown statistically significant positive effects compared to placebo in a Phase 2a clinical trial and has initiated a Phase 2b clinical evaluation. Our novel approach focuses on reducing the impact of inflammation in the brain, or neuroinflammation, which we believe is a key factor in the manifestation of neurodegenerative disease. Chronic activation of the enzyme, p38 mitogen-activated protein kinase ("MAPK") alpha ("p38α") in the neurons (nerve cells) within the brains of people with neurodegenerative diseases is believed to impair how neurons communicate through synapses (the connections between neurons). This impairment, termed synaptic dysfunction, leads to deterioration of cognitive and motor abilities. Left untreated, synaptic dysfunction can result in neuronal loss that leads to devastating disabilities, institutionalization and, ultimately, death. We believe that inhibiting p38α activity in the brain, by interfering with key pathogenic drivers of disease, has the potential to improve cognitive and motor function observed in early-stage neurodegenerative diseases. We also believe it is possible to modify the course of these diseases by delaying permanent synaptic dysfunction and neuron death.

We are developing an oral therapy, neflamapimod, that penetrates the blood-brain barrier and inhibits activity of p38a in the neuron. Based on preclinical and clinical work to date, we believe if neflamapimod is given in the early stages of neurodegenerative diseases, it may reverse synaptic dysfunction and improve neuron health. In preclinical studies, neflamapimod has been shown to reverse the neurodegenerative process in the basal forebrain cholinergic ("BFC") system, the specific region of the brain that is the site of the major pathology in DLB. We have obtained positive Phase 2a clinical data in DLB, specifically, statistically significant improvement compared to placebo on measures of dementia severity and functional mobility (walking ability). In addition, we previously obtained Phase 2 clinical data in Alzheimer's Disease ("AD") that provides support by demonstrating blood-brain-barrier penetration, target engagement, and identification of dose-response.

There are an estimated 700,000 individuals with DLB in each of the United States ("U.S.") and the European Union ("EU"). The disease in afflicted persons progresses and severely impacts not only their daily lives but that of their caregivers. To date, the management of DLB, involves treating certain cognitive and motor symptoms, with modest albeit transient improvement. No approaches have been shown to clinically slow neuronal loss or prevent cognitive decline, and there are no approved therapies for treating the underlying disease's process. Our approach is based on understanding the mechanism by which neuroinflammation leads to the initiation of the neurodegenerative process through synaptic dysfunction. In major neurodegenerative diseases, the end result of the process is neuronal loss. Before neuronal loss commences, disease progression in major neurodegenerative disorders, including DLB, initially involves a protracted period of functional loss, particularly with respect to the synapses. We seek to target the molecular mechanisms within neurons that lead to synaptic dysfunction. We believe that successful treatment of synaptic dysfunction will provide patients with an improvement in cognition and motor function in the first few weeks or months after treatment initiation, followed by a slowing of neuronal loss and associated disease progression (i.e., further cognitive and motor function decline). Importantly, the clinical symptoms in DLB are most directly linked to synaptic dysfunction in cholinergic neurons (neurons producing the neurotransmitter acetylcholine) in a part of the brain named the basal forebrain, while scientific and preclinical data with neflamapimod support the notion that neflamapimod treats the molecular mechanisms underlying dysfunction and degeneration of such basal forebrain cholinergic neurons.

Neflamapimod has been evaluated in more than 300 healthy volunteers and patients, including in 149 subjects in Phase 2 clinical trials in either DLB or AD. We have obtained positive Phase 2a clinical data in DLB. Specifically, in a 91-subject, 16-week placebo-controlled Phase 2a clinical trial in DLB, in the all-subject analysis neflamapimod demonstrated improvement vs. placebo in dementia severity (evaluated by the Clinical Dementia Rating Sum of Boxes ("CDR-SB") test, p=0.023 vs. placebo) and motor function (evaluated by the Timed Up and Go ("TUG") test, TUG p=0.044 vs. placebo). In secondary analysis, at highest dose (40m three times daily, ("TID")), significant improvement vs. placebo was also seen on a cognitive test battery. The Phase 2 clinical data in AD provides support through demonstrating blood-brain-barrier penetration, target engagement in the brain, and understanding of dose-response.

Our next step in the clinical development of neflamapimod is the conduct of a Phase 2b placebo-controlled clinical trial intended to confirm the Phase 2a results and provide the data necessary to finalize design of a Phase 3 clinical trial, the general framework of which has been agreed upon with the U.S. Food and Drug Administration ("FDA"). The Phase 2b trial will be fully funded by an awarded grant from the National Institute of Health's National Institute on Aging ("NIA") and was initiated in the second quarter of 2023, with anticipated data-readout in the second half of 2024.

Building on what we learned in our Phase 2a trial, the Phase 2b trial, known as RewinD-LB, is a double-blind, 16-week study in 160 patients with early stage DLB randomized 1:1 to 40mg neflamapimod or placebo TID. Patients in both the neflamapimod and placebo groups who complete the main, randomized, double-blinded, 16-week phase of the study will receive neflamapimod on an open label basis for an additional 32 weeks. Key distinctions from Phase 2a trial include (1) the use of a single daily dose regimen of neflamapimod (40mg TID), (2) use of the CDR-SB, a measure of dementia severity, as a primary endpoint, and (3) the exclusion of patients with AD co-pathology, assessed by ptau181 levels in the blood). Clinical trial simulations indicate with the incorporation of these changes from our Phase 2a trial, the RewinD-LB study is designed to have >95%, approaching 100%, statistical power to detect significant improvement over placebo on the CDR-SB.

In addition to its potential to treat DLB, we believe the benefit of targeting neuroinflammation-induced synaptic dysfunction in the basal forebrain cholinergic system can be applied to other neurologic indications including as treatment promoting recovery in the three months after ischemic stroke and as a disease-modifying treatment for Early Onset Alzheimer's Disease ("EOAD"). The scientific rationale for evaluating neflamapimod to promote recovery after stroke is predicated on the BFC system playing a critical role in recovery, particularly motor function, after ischemic stroke. Impaired activity of that system by residual inflammation limits the extent of recovery that otherwise occurs in the weeks and months after an acute stroke event. Through the same mechanisms as in DLB, neflamapimod would be predicted to reverse suppression of basal forebrain cholinergic function, leading to improved recovery of motor activities. As there are overlapping disease mechanisms, the scientific rationale for EOAD is the same as that for DLB.

In 2012, we entered into an Option and License Agreement (including all subsequent amendments, the "Vertex Agreement") with Vertex Pharmaceuticals Inc. ("Vertex") and subsequently acquired an exclusive license from Vertex in 2014 to develop and commercialize neflamapimod for the treatment of AD and other neurodegenerative diseases. We have made a number of discoveries related to our lead product candidate, neflamapimod, which have enabled us to build a wholly owned intellectual property ("IP") portfolio, which provides protection to 2032 (methods of treating patients suffering from AD) and 2035 (uses of neflamapimod for improving cognition). In addition, we have a patent on the formulation of neflamapimod that is protected through 2039. For more information about the Vertex Agreement, see "*—Vertex Agreement*" below.

On August 16, 2023, we completed a merger transaction (the "Merger") in accordance with the terms and conditions of the Agreement and Plan of Merger, dated as of March 30, 2023 (the "Merger Agreement"), by and among the Company, Dawn Merger Sub Inc., a wholly owned subsidiary of the Company ("Merger Sub"), and EIP, pursuant to which Merger Sub merged with and into EIP, with EIP surviving the merger as a wholly owned subsidiary of the Company (the "Merger"). Immediately following the Merger, also on August 16, 2023, the Company changed its name from "Diffusion Pharmaceuticals Inc." to "CervoMed Inc."

Our Strengths

We believe that the following competitive strengths will allow us to execute on our mission to develop and commercialize disease modifying innovative drug treatments for patients who suffer from DLB and other neurodegenerative diseases:

- *Our approach to neurodegenerative diseases is highly differentiated and has the potential to be the first to market specific drug therapy for DLB.* Our approach focuses on reducing the impact of neuroinflammation, which is directly linked with the initiation of the neurodegenerative process through synaptic dysfunction. Our technology targets the molecular mechanisms within neurons that lead to synaptic dysfunction, thereby both improving cognitive function and slowing down the process that leads to neuronal loss. Currently, there are no approved therapies for DLB and there is limited drug development in this area, with neflamapimod being, to our knowledge, the only disease-modifying approach that has demonstrated significant positive effects on clinically outcome measures in a clinical trial in DLB.

- *Our drug has the potential to meet a significant unmet medical need and achieve substantial commercial return.* We believe that neflamapimod can address the high unmet medical need with respect to both the cognitive and motor aspects of DLB. DLB is the second most common neurodegenerative dementia, with an estimated 700,000 individuals with the disease in each of the United States and EU. Further, the commercialization model focuses on a neurologist call point, and high pricing leverage due to the high caregiver burden and health care costs associated with DLB.

- *The path to approval in DLB does not depend on having to demonstrate an effect on disease progression.* A major challenge in developing effective drug treatments for chronic neurodegenerative diseases, particularly AD, has been that approaches to date do not show improvement in disease outcomes in Phase 2 clinical trials (i.e., trials of less than six-month duration). As a result, demonstration of clinical efficacy depends on clinical trial duration of at least 12 to 18 months and large subject numbers (~1,000 or more), effectively requiring Phase 3 trials designed to show an effect of slowing disease progression relative to placebo treatment. In early-stage DLB, because there is less extensive neuronal loss and fixed deficits compared to AD, there is the potential to reverse disease progression and improve disease outcomes in Phase 2 clinical trials. Moreover, neflamapimod has shown the ability to reverse disease progression and restore function in preclinical studies and has shown improvement vs. placebo on clinically meaningful outcomes in a 16-week Phase 2a clinical trial. If the Phase 2a results are confirmed in the recently initiated Phase 2b trial (the placebo-controlled portion, of which will also be of 16 weeks duration) with a statistically significant difference between placebo and neflamapimod treatment on the primary endpoint, based on discussions we have had with the FDA, and pending confirmation in an end-of-phase 2 meeting with the FDA that we plan to have after Phase 2b, approval for neflamapimod could be obtained with the conduct of a single 24-week treatment duration Phase 3 study involving a few hundred subjects, although there can be no assurances. See section in Exhibit 99.2 titled "*Risk Factors-Risks Related to the Company's Product Development and Regulatory Approval*" for a further description of these factors and uncertainties.

- *Neflamapimod has been extensively tested in animals and humans.* The safety and tolerability profile has been extensively evaluated and is well understood. Specifically, long-term toxicology studies of neflamapimod have been completed and the drug has been administered to over 300 volunteers and subjects to date, some of whom have received up to 30 times the dose we will be using in our recently initiated Phase 2b clinical trial and plan to utilize in Phase 3.

- *We have assembled a highly experienced executive management team.* Our Chief Executive Officer, John Alam, MD, is a biotech industry veteran with 30 years' experience and is an industry leader in translational medicine. He has a proven track record of creating value through clinical development success, including having played major roles during the clinical development of five innovative drugs that are now on the market, and is an emerging drug development leader in neurodegenerative diseases, including having been the global head of all R&D activities directed towards neurodegenerative diseases at Sanofi, a top ten global pharmaceutical company. Dr. Alam also has direct experience with neflamapimod from his time at Vertex, where he was Executive Vice President, Medicines Development and Chief Medical Officer. Dr. Alam also led the clinical development of Biogen's first approved drug for the treatment of multiple sclerosis, Avonex. Our Chair of the Board of Directors, Dr. Sylvie Grégoire, is also an industry veteran with 30 years' experience who previously held executive leadership posts in several multinational life sciences firms. Dr. Grégoire has extensive experience with corporate governance and board operations and is currently also on the board of directors at of two public life sciences companies, Novo Nordisk A/S (NYSE: NVO) and PerkinElmer, Inc. (NYSE: PKI), and one private company, F2G; and she previously was chair of Corvidia Therapeutics (acquired by Novo Nordisk), and member of the board of directors of ViFor Pharma (acquired by CSL) and Cubist Pharmaceuticals (acquired by Merck). Our Chief Financial Officer, William Tanner, through his more than 20 years' experience as a healthcare research analyst at well recognized investment banks, has expertise and relevant industry experience. Our Chief Operating Officer, Robert J. Cobuzzi, Jr., Ph.D., has over 25 years of cross-functional leadership experience in the pharmaceutical and biotechnology industries across the areas of corporate development, research & development, and operations, including senior leadership positions at Endo International Plc, Adolor Corporation, Diffusion Pharmaceuticals and AstraMerck. Dr. Cobuzzi also currently serves as a Venture Partner for Sunstone Life Science Ventures and also is Chairman of Sunstone's Business Development Board. Moreover, we benefit from the significant pharmaceutical development experience of our management team members, several of whom have worked on neflamapimod in the past at Vertex and are well acquainted with the unique properties of the compound for application in our target indications.

- *To provide a strong scientific underpinning for the neflamapimod program, we have surrounded ourselves with thought leaders in the fields of cell biology, intracellular signal transduction, neurotherapeutics, and translational neuroscience.* Our Scientific Advisory Board ("SAB") is chaired by Dr. Ole Isacson, who serves as Professor of Neurology at Harvard Medical School and is a Founding Director of Neuroregeneration Research Institute at McLean Hospital. Other members of our SAB include Dr. Lewis Cantley, who serves as the Director of the Sandra and Edward Meyer Cancer Center and as Professor of Cancer Biology in Medicine at Weill Cornell Medical College; Dr. Jeffrey Cummings, Director of the Center for Neurodegeneration and Translational Neuroscience at the Cleveland Clinic, Director Emeritus of the Cleveland Clinic Lou Ruvo Center for Brain Health and Professor at the Cleveland Clinic Lerner College of Medicine; and Dr. Heidi McBride, Canada Research Chair in Mitochondrial Cell Biology and as Professor in the Department of Neurology and Neurosurgery at McGill University.

Our Strategy

Our mission is to develop and commercialize innovative medicines that change the course of the disease of patients who suffer from neurodegenerative diseases.

The key elements of our strategy are:

- Advance clinical development of neflamapimod for treatment of DLB with a focus on moving the program through to Phase 3 initiation in the first half of 2025. We initiated a Phase 2b clinical trial with neflamapimod in DLB in the second quarter of 2023 and anticipate completing enrollment in the first half of 2024. The efficacy data, which would come at the end of the four-month placebo-controlled portion of the trial, are expected in the second half of 2024. With those results in hand, we plan to meet with the FDA in an end-of-phase 2 meeting to finalize the design of a single Phase 3 clinical trial, which we are targeting to initiate in the first half of 2025.

- Advance clinical development of neflamapimod for other disease indications. Neflamapimod's mechanism of action with respect to treating cholinergic dysfunction and degeneration provides opportunities to advance our drug in a range of neurologic disorders in addition to DLB. Our anticipated second indication is as a three-month treatment following ischemic stroke to promote neurologic recovery, particularly of motor function. A potential third indication is as disease-modifying treatment for EOAD. In addition, we believe there is strong scientific basis for evaluating neflamapimod in combination with anti-amyloid beta directed approaches in Late Onset AD ("LOAD").

- Commercialize neflamapimod ourselves and/or in collaboration with one or more partners. If neflamapimod receives regulatory approval, we intend to retain significant commercial rights in North America and Europe. In the future, we may seek partners to commercialize our products in other regions.

- Expand our pipeline through in-licensing and acquisitions. We intend to leverage our expertise in drug development and business development, as well as our understanding of translational neuroscience with respect to synaptic dysfunction, to evaluate product candidates that are complementary to neflamapimod in our pursuit of novel therapies for DLB, AD and other neurodegenerative diseases.

Our Approach

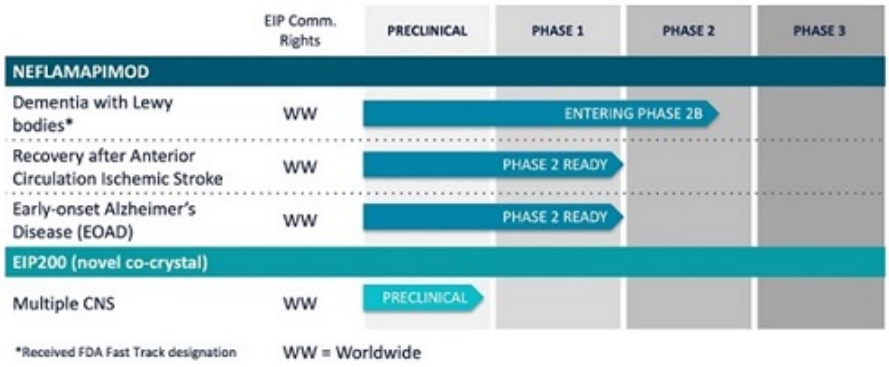
Our approach is based on an understanding of the mechanism by which neuroinflammation leads to the initiation and establishment of the neurodegenerative process through dysfunction of synapses (the interconnections between neurons), i.e., synaptic dysfunction. Treating synaptic dysfunction has emerged as a major therapeutic objective to address progression of neurodegenerative diseases, particularly in the early stages prior to the onset of significant cell death. Importantly, in animal models, while neurodegeneration is irreversible, synaptic dysfunction is reversible. In addition, even in animal models of rapidly progressive neurodegeneration, interventions that reverse synaptic dysfunction both improve function and "arrest" the neurodegenerative process. Thus, therapeutic interventions that target synaptic dysfunction have the potential to both reverse and slow disease progression in the early stages of neurodegenerative dementias.

The basal forebrain, and specifically nerve cells producing the neurotransmitter acetylcholine (i.e., "cholinergic neurons"), play critical roles in controlling and optimizing a wide range of cognitive, motor, and visual tasks. Synaptic dysfunction in the basal forebrain cholinergic system is the primary pathogenic driver of disease expression and progression DLB. Basal forebrain cholinergic dysfunction also plays a major role in disease progression in the early stages of AD, and basal forebrain cholinergic function is rate limiting for optimal recovery after ischemic stroke.

In collaborative work conducted with the New York University Langone Medical Center, we have demonstrated that neflamapimod specifically targets the specific molecular mechanisms underlying basal forebrain cholinergic dysfunction, and eventually degeneration, and, as discussed in subsequent sections, can successfully reverse disease progression in animals with basal forebrain cholinergic degeneration.

Our Pipeline

Set forth below is a table presenting our clinical pipeline:



Neflamapimod in Dementia with Lewy Bodies (DLB)

Unmet Medical Need

DLB is the second most common neurodegenerative dementia (after AD), representing 10-20% of the dementia population. The Lewy Body Dementia Association estimates that there are 1.4 million individuals in the United States affected with Lewy body dementia, which includes both Parkinson's disease dementia ("PDD") and non-Parkinson's DLB. As non-Parkinson's DLB and PDD are prevalent in the United States at a 1:1 ratio, there are approximately 700,000 individuals with DLB in the United States. Furthermore, the prevalence in European countries is similar to that in the United States, and so we believe there are also approximately 700,000 individuals with DLB in the EU.

DLB is characterized by progressive dementia and fluctuating cognition (particularly deficits in attention), visual hallucination, motor dysfunction (disturbances in gait and balance) and sleep disturbances. With respect to life expectancy, in a large cohort of DLB and AD cases (251 DLB, 222 AD), after controlling for age at diagnosis, comorbidity, and antipsychotic prescribing, the survival for DLB was shorter compared to AD, with a median (average) survival of less than four years with DLB (3.3 years for males and 4.0 for females), while that for AD was nearly seven years (6.7 years for males and 7.0 years for females). Antecedent to death, the time progression to severe dementia is also shorter by nearly two years with DLB compared to AD.

Separate from survival and progression to severe disease, even in the mild-to-moderate stages, with deficits occurring in both cognitive and motor function, the disease burden with respect to quality of life and caregiver burden, is greater in DLB than in AD.

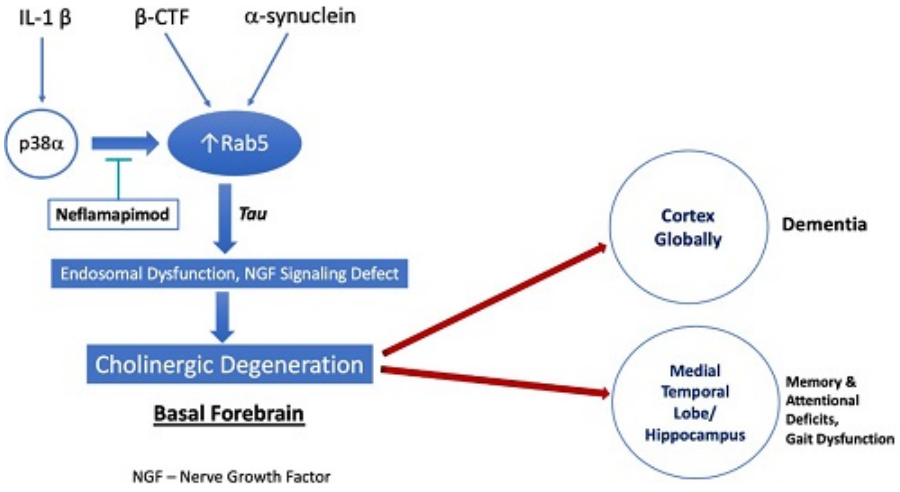
Furthermore, patients with DLB are more frequently admitted to general hospitals and utilize inpatient care to a substantially higher degree than do those with AD or the general elderly population. Most importantly, in a large prospective study, mild dementia patients with DLB were admitted to a nursing home after only a median of 1.8 years from presentation and diagnosis, nearly two years shorter than the 3.7 years in the AD group.

There are no disease-modifying treatments available for DLB, so management of DLB currently focuses on relief of symptoms, including its cognitive and parkinsonian (e.g., tremor) manifestations. Though not approved for DLB, cholinesterase inhibitors are used in its management, with some limited, though transient, improvement in cognition and a reduction in the frequency and severity of visual hallucinations. However, despite treatment with cholinesterase inhibitors, the cognitive and functional impairments progress rapidly, caregiver burden remains high, and new treatments are needed for these patients. With respect to the motor component of DLB, dopaminergic medications (e.g., carbidopa/levodopa) work less well in DLB compared to in Parkinson's disease ("PD") and patients with DLB generally have a limited response to these medications, which are in any case poorly tolerated in this patient population; a reason for the poor response is that DLB is primarily a disease of the cholinergic system, rather than the dopaminergic system.

Scientific Rationale

Recent evidence indicates that the primary pathology in DLB is in the basal forebrain cholinergic system, degeneration and dysfunction of which drives neurodegeneration in other regions of the brain. A series of publications from the laboratories of William Mobley at UCSD and Ralph A. Nixon at NYU Langone have defined the molecular mechanisms that lead to neurodegeneration of cholinergic neurons. As shown in figure below, the cholinergic degeneration is believed to result from inflammation and various aggregated proteins that lead to aberrant activation of the protein Rab5, a master regulator of endocytosis and endosomal trafficking, further leading to impaired retrograde axonal transport and a block in nerve growth factor ("NGF") signaling from the synapses back to the neuronal cell body. The resulting loss of trophic support is then believed to lead to dysfunction, and, eventually, degeneration of cholinergic neurons, which are particularly vulnerable to this pathogenic process because of their very long axonal processes. In this pathogenic model for cholinergic degeneration in DLB, a key therapeutic target is Rab5. Neflamapimod was hypothesized to act on Rab5 because of scientific literature showing that the immediate target of neflamapimod, p38α kinase, is the major activator of Rab5. Based on that hypothesis, neflamapimod was evaluated in a preclinical study in an animal model of basal forebrain cholinergic degeneration and in a clinical trial in patients with DLB, a disease in which, basal forebrain cholinergic degeneration is also prominent. The results of those studies were recently published, and the clinical and preclinical findings are summarized in the following sections.

Molecular Mechanisms Underlying Cholinergic Neurodegeneration in DLB and Point of Intervention for Neflamapimod



In distinction to AD, pure DLB (DLB in the absence of concomitant AD) has relatively limited neurodegeneration and neuronal loss in the cortical regions of the brains. Moreover, based on a range of animal and human pathology studies, the cholinergic degenerative process in the basal forebrain is believed to be reversible. The cholinergic neurons in that region of the brain do not die, rather they stop functioning and atrophy (shrink in size). However, as those neurons are still present, they can be rescued and the disease process reversed with successful pharmacological treatment, a possibility that we believe our product candidate, neflamapimod, has demonstrated in preclinical studies involving animal models (see results below). Moreover, we believe that the positive Phase 2a results in DLB described reflect a similar effect on the basal forebrain cholinergic system, with the magnitude of the treatment effect being most prominent in patients with low levels of plasma phosphorylated tau at position 181("ptaul81"), a plasma biomarker that is associated with both AD co-pathology and neuronal loss in the cortex.

AscenD-LB: Our Phase 2a Clinical Trial in Dementia with Lewy Bodies (DLB)

AscenD-LB was a Phase 2a double-blind, placebo-controlled, 16-week treatment, exploratory clinical trial of neflamapimod in mild-to-moderate DLB conducted at 22 centers in the United States and two centers in the Netherlands. 91 subjects were enrolled between October 2019 and March 2020 and randomized to receive 40 mg neflamapimod capsules or matching placebo capsules (randomized 1:1) for 16 weeks. The dosing regimen was based on weight, with trial participants weighing less than 80 kg receiving capsules twice daily ("BID") and those weighing greater than or equal to 80 kg receiving capsules TID. All subjects had to have already been receiving oral cholinesterase inhibitor therapy for at least three months (stable dose for greater than six weeks) and continued such therapy without dose modification during the trial.

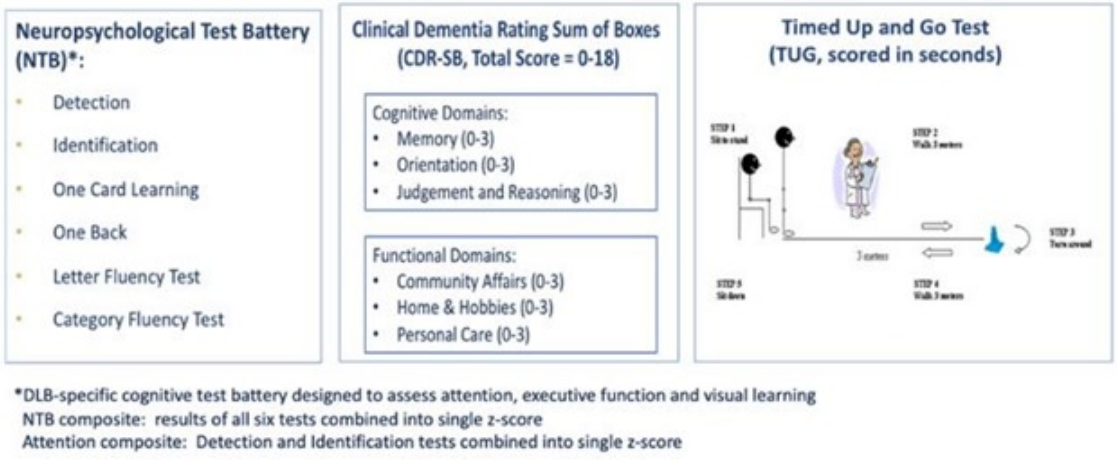
The major clinical outcome measures were as follows:

- A six test Neuropsychological Test Battery ("NTB"). The NTB is a cognitive test battery designed to evaluate attention, executive function, and visual learning, i.e., the cognitive domains most impacted in DLB. The NTB was analyzed using a standard statistical approach by which the individual test results are normalized by using "z-scores" and the combined using equal weights into a single composite z-score. The two tests within the NTB that evaluate information processing speed (Detection and Identification tests) were also combined into an Attention composite z-score.

- CDR-SB. The CDR-SB is obtained through a semi-structured questionnaire given to both the caregiver and subject and is scored from 0-3 in each of three cognitive (memory, orientation, judgement and reasoning) and three functional domains (community affairs, home & hobbies, personal care)

- TUG test. The TUG test, measuring functional mobility, monitors the time in seconds that a subject takes to rise from a chair, walk three meters, turn around 180 degrees, walk back to the chair, and sit down while turning 180 degrees.

Outcome Measures in AscenD-LB Phase 2a Clinical Trial of Neflamapimod in DLB



*DLB-specific cognitive test battery designed to assess attention, executive function and visual learning
NTB composite: results of all six tests combined into single z-score
Attention composite: Detection and Identification tests combined into single z-score

The Phase 2a trial results were analyzed by calculating the mean difference between neflamapimod and placebo treatment for each endpoint over the course of the study, and the "p-value" for that difference. The p-value is a statistical term that refers to the probability that the difference between neflamapimod and placebo is due to chance (i.e., that is the difference was a random error), rather than being due to a true treatment effect. For example, a p-value of 0.05 means that there is a 5% probability that the effect is due to chance. By convention, a p-value lower than 0.05 is taken to mean that there is a true drug treatment effect. As the Phase 2a study was an exploratory (i.e., not designed to definitively demonstrate efficacy), any p-value less than 0.05, should be taken as evidence of efficacy, and not definitive demonstration of efficacy. Definitive demonstration of efficacy requires confirmatory trials, such as our Phase 2b trial, in which there is a single prospectively defined primary efficacy endpoint, on which the results show a p-value of less than 0.05.

In the modified intention-to-treat population (all subjects with at least one on-treatment efficacy evaluation) analysis of the AscenD-LB trial, neflamapimod demonstrated improvement vs. placebo in dementia severity (evaluated by the gold standard CDR-SB, p=0.023) and functional mobility (gait or walking ability, as assessed by the TUG test p=0.044). In additional analyses, at highest dose (40mg TID) vs. placebo, significant improvement on NTB was evident (p=0.049). In addition, encouraging positive trends on the 10-item Neuropsychiatric Inventory ("NPI-10") were seen; particularly with respect to visual hallucinations, where a significant reduction in frequency relative to placebo was seen. We believe, if the effects on multiple aspects of DLB, including on both cognition and gait, are confirmed in Phase 2b and 3, neflamapimod would be a transformative treatment for this serious disease.

Efficacy Results in Phase 2a Trial of Neflamapimod in DLB

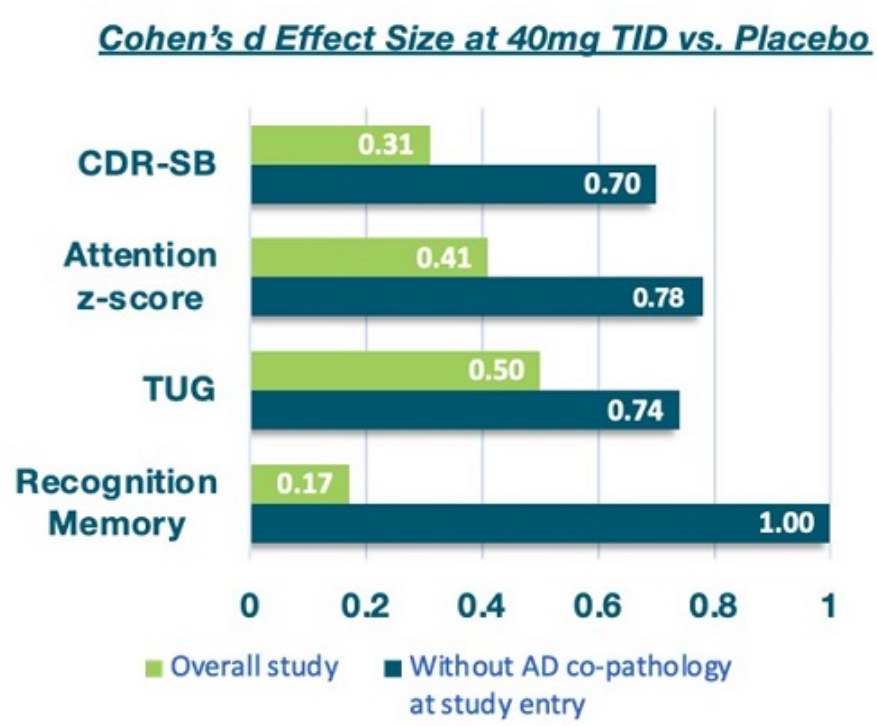
		40mg BID + 40mg TID			40mg TID		
Outcome	**Measure**	**Mean vs. placebo (95% CI)**	**p-value**		**Mean vs. placebo (95% CI)**	**p-value**	
Dementia Severity	Clinical Dementia Rating Sum of Boxes (CDR-SB)	-0.45 (-0.83, -0.06)	0.023	+	-0.56 (-0.96, -0.16)	0.007	+
Cognition	Neuropsychological Test Battery (NTB) Composite z-score	0.04 (-0.11, 0.19)	>0.2		0.17 (0.00, 0.35)	0.049	+
	Attention Composite z-score	0.14 (-0.06, 0.35)	0.17		0.28 (0.04, 0.51)	0.023	+
Motor Function	Timed and Go Test (TUG)	-1.4 (-2.7, -0.1)	0.044	+	-1.4 (-2.6, -0.2)	0.024	+

Improvement is reflected as decrease in CDR-SB and TUG and increase in NTB and Attention composites

Number of participants: 41 for placebo, 20 each for 40mg BID and 40mg TID

Post-hoc analyses of the AscenD-LB data stratified by baseline plasma ptau181 (tau protein phosphorylated at residue 181) have identified this biomarker as an enrichment strategy to further improve treatment response in subjects with DLB. These analyses were conducted because recent scientific literature has demonstrated that DLB subjects with abnormally elevated plasma ptau181 have AD associated co-pathology (specifically amyloid plaque and/or tau pathology by PET scan or cerebrospinal fluid ("CSF") analysis). Further, compared to subjects with DLB without elevated plasma ptau181, subjects with DLB with elevated plasma ptau181 have more extensive neuronal loss (neurodegeneration) and, therefore, would be expected to be less responsive to treatment. Within the AscenD-LB trial, the subjects without elevated plasma ptaul81 had an average higher treatment response (evaluated by Cohen's *d* effect size), compared to the average response in the overall study, and demonstrated significant improvement in cognitive tests of Attention, the CDR-SB, the TUG test, and in a rest of recognition memory (International Shopping List Test recognition index) with Cohen's *d* treatment effect size that was greater than 0.7 for each of these endpoints, indicating clinical effects that are moderate-to-large in magnitude. For comparison, in published studies in the scientific literature, the cholinesterase inhibitors have Cohen's *d* effect size of approximately 0.3 in the treatment of AD or DLB.

Magnitude of Neflamapimod Treatment Effect vs. Placebo in Subjects with Baseline Plasma ptau181 less than 2.2 pg/mL (i.e., without biomarker evidence of AD co-pathology)*



*By convention the magnitude of a treatment is considered small when the Cohen's *d* effect size between 0.2 and, moderate when it is 0.4 to 0.8 and large when it is 0.8 or greater.

The initial results of the AscenD-LB trial were published in the major scientific journal Nature Communications in September 2022 and, more recently in September 2023, Neurology, the medical journal of the American Academy of Neurology, published additional pre-specified analyses of the AscenD-LB Phase 2a clinical trial showing the association between plasma ptau181 levels at study entry and patient's response to neflamapimod in the treatment of DLB.

RewinD-LB: Our Ongoing Phase 2b Clinical Trial in DLB

We initiated a Phase 2b clinical trial of neflamapimod in subjects with DLB in the second quarter of 2023 and, on August 14, 2023, we announced dosing of the first patient in the trial. The design of this study trial is based on the findings and the learnings from the Phase 2a DLB trial. The learnings from Phase 2a that we believe position the Phase 2b trial for success are as follows:

- The optimal dose is 40mg TID.
- Clinical endpoints that can detect effects on both cognitive and motor function (specifically, CDR-SB and TUG) perform better to distinguish drug treatment from placebo than endpoints that are purely focused on evaluating cognition. Moreover, in AD, CDR-SB is accepted by regulatory authorities as an approval endpoint. Accordingly, we have chosen CDR-SB as the primary endpoint in the Phase 2b trial.
- Subjects with pure DLB (i.e., those without AD co-pathology as evidenced by increased concentrations of plasma ptaul81) appear to have a greater response to treatment. Therefore, we have chosen to exclude subjects with elevated (i.e., abnormal) levels of plasma ptau181, in the Phase 2b trial. We believe that excluding subjects with abnormal plasma ptaul81 substantially increases the statistical power to demonstrate treatment effects in clinical trials of neflamapimod in DLB.

Considering the above, the Phase 2b clinical trial was designed as a randomized double-blind, placebo-controlled clinical trial of neflamapimod 40 mg administered TID in subjects with DLB. Success in the Phase 2b clinical trial will confirm and expand upon the results from Phase 2a (Study 501) ahead of any future Phase 3 trial.

Neflamapimod will be administered orally, 40 mg TID, with a second group receiving matching placebo. Each group will have at least 80 subjects (enrolling a total of 160 subjects) diagnosed with DLB by consensus criteria, including having abnormal dopamine transporter scan. Subjects with elevated plasma ptau181 (i.e., having evidence of AD co-pathology) will be excluded. Treatments (neflamapimod or placebo) will be administered for 16 weeks in the main trial (i.e., placebo-controlled portion of the study), with a 36-week open label treatment extension for subjects completing the initial 16-weeks of the trial. Following completion of informed consent procedures, subjects will enter the Screening phase of the trial. Once eligibility is confirmed and before the first dose of study drug, subjects will be randomly assigned on 1:1 basis to placebo or neflamapimod treatment. Dosing will start on Day 1 following completion of all Baseline procedures. During the placebo-controlled portion of the trial, subjects will return to the clinic at the end of weeks 2, 4, 8, 12 and 16.

The primary objective of the trial is to demonstrate that neflamapimod, compared with placebo, improves dementia severity, as assessed by change from baseline to week 16 in CDR-SB score. Secondary objectives include studying safety of neflamapimod and treatment effects on (1) cognition, assessed by a DLB-specific cognitive test battery, (2) motor function, as assessed by the TUG test, and (3) global rating of treatment effect, assessed by the ADCS-Clinician Global Impression of Change (“CGIC”). Tertiary endpoints will examine whether neflamapimod affects neuropsychiatric outcomes as assessed by the NPI-12, effect on fluctuations in cognition as assessed by the Dementia Cognitive Fluctuations Scale, impact on resting-state EEG (as well alpha-reactivity evaluated by EEG) and in a sub-set of subjects, basal forebrain atrophy assessed by structural MRI.

Sample size was evaluated by power analysis via simulations, conducted by utilizing the data in the Phase 2a study for the major clinical endpoints in the neflamapimod 40mg TID and placebo groups, to generate for each patient a change from baseline for each endpoint at individual visits over the course of the simulated clinical study, and then analyzing the result of each clinical trial utilizing the linear mixed effects model for repeated measures that will be utilized to analyze the Phase 2b study. Based on the simulation of 100 clinical trials with 80 patients per treatment group, and assuming a 10% dropout rate, there is ~85% power with the NTB, 95% power with TUG, and >95% power with CDR-SB (approaching 100%) to detect a treatment effect at an alpha level of 0.05.

In January 2023, we were awarded a $21.0 million grant from the MA that is estimated to fully fund development costs associated with the Phase 2b trial. The NIA grant funds will be disbursed over the course of the trial as costs are incurred. In February 2023, an initial $6.9 million was disbursed to a dedicated account at the NIH’s Payment Management System (“PMS”), from which we draw from time to time to pay expenses associated with the clinical study and of which, as of June 30, 2023, total cash funding of approximately $4.3 million had been received by us. Consistent with the anticipated timeline for conducting the full study, including the 32-week extension period for patients completing the 16-week placebo-controlled portion of the study, we expect an additional $8.1 million disbursement to the PMS in February 2024 and the remainder of the grant to be disbursed in February 2025. Future disbursements are dependent on Congress authorizing the overall NIH budget for the respective fiscal years and CervoMed demonstrating progress on the project that is “satisfactory” to the NIA.

Phase 3 Development in DLB Based on Success in Phase 2b Clinical Trial

We met with the FDA in January 2020, after completion of the AscenD-LB Phase 2a trial, in an end-of-phase 2 (“EOP2”) meeting to discuss potential Phase 3 clinical designs that may support approval of neflamapimod for the treatment of DLB. In that meeting, the FDA stated that a single Phase 3 clinical trial of six months’ treatment duration may be sufficient to support approval of neflamapimod if the trial demonstrated robust, clinically meaningful effects on cognition and on either function or a global measure (e.g., clinical global measure impression of change, CGIC). Based on those discussions, we believe that if the Phase 2b trial demonstrates significant effects on the primary endpoint CDR-SB (a clinically meaningful measure of cognition and function), the result would be highly predictive of success in Phase 3, as the Phase 3 clinical trial must replicate the Phase 2b findings over six months (vs. four months in Phase 2b). Further, the number of subjects to be enrolled in a Phase 3 trial, which at the time of the EOP2 meeting was proposed to be 250 subjects, would be adjusted based on treatment effect size observed in the Phase 2b results to provide >95% statistical power for the primary efficacy endpoint. We are also evaluating CGIC in our planned Phase 2b trial for incorporation as an endpoint in the Phase 3 clinical trial. The size of a Phase 3 clinical trial, and certain other aspects of the Phase 3 trial (e.g., choice of secondary endpoints) would be discussed with the FDA in a second EOP2 meeting that we would expect to schedule after the primary efficacy data are available from the recently initiated Phase 2b clinical trial.

Neflamapimod in Alzheimer's Disease (AD)

Ahead of our most recent work in DLB, our clinical trials in AD provided us data around blood-barrier penetration target engagement (biological activity in the brain), and an understanding of dose-response, i.e., the completion of the steps in early clinical studies to successful CNS drug development.

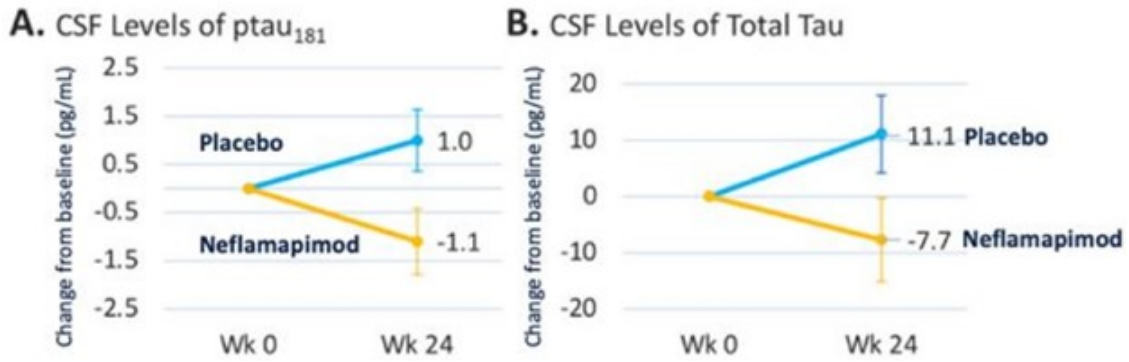
Two Phase 2a studies in AD were completed in early 2017. Results from these studies demonstrated that neflamapimod is well tolerated, crosses the blood brain barrier and is pharmacologically active in the brain.

Reverse-SD was a Phase 2b clinical trial in subjects with AD. 161 subjects were enrolled at 38 sites in the Czech Republic (5 sites), Denmark (3 sites), Netherlands (3 sites), United Kingdom (11 sites) and United States (16 sites) and were randomized 1:1 to receive neflamapimod 40 mg capsules or matching placebo capsules twice daily with food for 24 weeks. Inclusion criteria were as follows: men and women aged 55 to 85 years, with CDR-Global score of 0.5 or 1.0 (i.e., with mild AD); CDR memory sub-score of at least 0.5; MMSE score of 20 to 28, inclusive; positive biomarker for AD, as defined by CSF Aβ1-42 <1000 pg/mL and phospho-tau/Aβ1-42 >0.024 in the Roche Eclesys® immunoassay; receiving either no AD-specific therapy or on a stable dose monotherapy (either cholinesterase inhibitor or memantine; dual therapy excluded).

Including all subjects in the analysis, there was no evident difference between the neflamapimod and placebo groups in the primary clinical efficacy endpoint, the combined change from baseline to week 24 in the z-scores of Hopkins Verbal Learning Test ("HVLT") Total Recall and Delayed Recall. In the analysis of CSF biomarkers, there were statistically significant effects of neflamapimod treatment, with a reduction relative to placebo, in the change from baseline to week 24 in CSF protein levels of phosphorylated tau (p-tau181, p=0.01 vs. placebo) and total tau (p=0.03 vs. placebo), and a trend on CSF neurogranin (p=0.07 vs. placebo).

Because in the scientific literature tau pathology has been shown to be downstream (is a consequence) of p38α kinase activity, the effect of neflamapimod on CSF levels of ptau181 and total tau demonstrates target engagement, i.e., these CSF results is consistent with "target engagement" within the brains of subjects. Target engagement is the industry term for the drug having the intended pharmacological effect in humans that would be expected based on its mechanism of action; in this case, that neflamapimod is inhibiting p38α activity. Furthermore, as CSF ptau181 and CSF total tau are considered to reflect neurodegeneration and synaptic dysfunction, respectively, we believe the results also provide objective evidence of neflamapimod impacting the neurodegenerative process in patients, including specifically on synaptic dysfunction.

Effects of Neflamapimod on the Change from Baseline to Week 24 on CSF Levels of Phosphorylated Tau and Total Tau



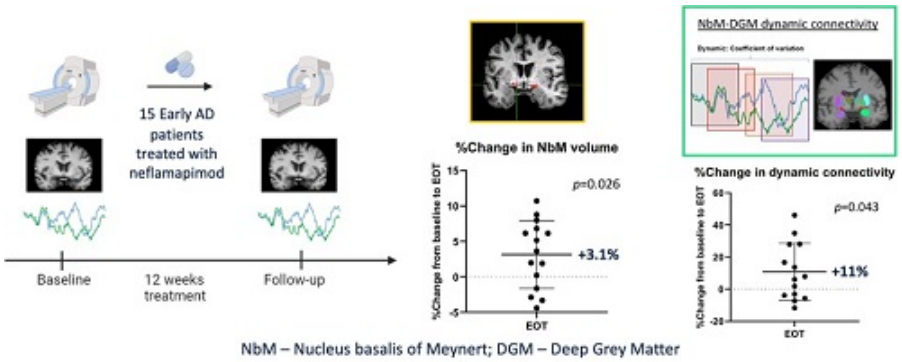
As a single dose of neflamapimod was utilized in the trial, pre-specified pharmacokinetic pharmacodynamic analyses were conducted to evaluate the results for potential dose-dependency. These analyses showed improvement, relative to the placebo group, in tests of episodic memory in neflamapimod-treated subjects with the highest (top quartile) trough plasma drug concentrations; with positive trends evident both for the primary endpoint (combined change in z-scores of HVLT total recall and delayed recall) and the major secondary endpoint of change in Wechsler Memory Scale Combined Immediate and Delayed Recall composites. This analysis provided critical dose-response information as it indicated that 40mg BID was too low a dose, but that a dose of 40mg TID would achieve therapeutically effective drug concentration levels in the blood. Moreover, combined with the CSF biomarker findings, the results suggested that neflamapimod had potential to slow disease progression in AD, and that clinical trials of longer clinical duration to evaluate that potential were warranted.

An investigator-initiated study (i.e., not sponsored and conducted by us) in subjects with mild AD was initiated in late 2018 at the CHU in Toulouse, France. The primary objective of this study was to assess the effects of neflamapimod on neuroinflammation compared to placebo after 12 weeks of treatment using a novel PET radiotracer, 18FDPA-714. This novel PET radiotracer targets binding of the translocator protein that has been suggested to be specific for microglial activation. The study was originally intended to enroll 40 subjects, 20 receiving placebo and 20 receiving neflamapimod 40mg BID for 12 weeks. However, the study was interrupted by the COVID-19 pandemic, and eventually completed in early 2022, having enrolled 26 subjects. While the results have not been reported publicly or published, our understanding is that, with the enrollment numbers and greater than expected variability in the PET data, the data was inconclusive.

Results of Imaging of Basal Forebrain by MRI after Treatment with Neflamapimod

With the development and availability of analytic MRI-based techniques to evaluate potential treatment effects on the basal forebrain, the MM images from one of the two Phase 2a studies in mild AD were reanalyzed by specialized neuroimaging group at the Amsterdam Medical Center. The goal of this exploratory analysis, which was presented at the AD/PD meeting in Gothenburg, Sweden in April 2023, was to assess the treatment effects of neflamapimod on the Nucleus basalis of Meynert (“NbM”), the largest cluster of cholinergic neurons in the basal forebrain, assessed by MRI (magnetic resonance imaging), in a previously completed Phase 2a trial in subjects with mild AD (n=15). Structural and MM assessments had been conducted at baseline and following 12 weeks of treatment with neflamapimod. The analysis demonstrated that the NbM volume was statistically significantly higher at the end of treatment (“EOT”, mean 3.1% higher vs. baseline, p=0.026); with eight of 15 subjects having greater than 3% NbM higher volume at EOT, compared to baseline. Treatment with neflamapimod was also associated with a statistically significantly higher functional dynamic connectivity between the NbM and deep grey matter (“DGM”) at EOT (mean 11% higher vs. baseline, p=0.043); with six of 13 subjects showing a greater than 10% higher dynamic NbM-DGM connectivity at EOT, compared to baseline. We believe, the potential regression of atrophy and recovery of function in neflamapimod-treated subjects in this trial suggests a restoration of cholinergic neurons in the NbM in line with the data generated in previous preclinical studies that demonstrated neflamapimod reversed the neurodegenerative process in the basal forebrain cholinergic system.

Neflamapimod treatment was associated with increased basal forebrain volume and functional connectivity



NbM – Nucleus basalis of Meynert; DGM – Deep Grey Matter

Neflamapimod Clinical Safety Results

Adverse events seen in all Phase 2 clinical trials in both CNS and non-CNS disorders are shown in the table below. Regarding more specifically clinical trials in CNS disease, 149 subjects with either AD or DLB have received neflamapimod for up to 24 weeks at either 40 mg BID or TID or 125 mg BID, the most commonly reported adverse events were headache (15 events, 10%), respiratory infection (11 events, 7%), diarrhea (11 events, 7%), fall, (11 events, 7%), and somnolence (seven events, 5%), all mild to moderate in severity. Headache, diarrhea, and somnolence appear to have the strongest association with neflamapimod.

There were five Serious Adverse Events reported in the 149 subjects with AD and DLB treated with neflamapimod (vs. eight who were administered placebo), involving hypokalemia, myeloma, head injury, brain tumor, and brain lesion, none of which were considered related to neflamapimod.

Adverse Events in Phase 2 Clinical Trials of Neflamapimod (CNS and non-CNS disease)

	Number (%) of Adverse Events Reported	
Adverse Event	Neflamapimod (N=217)	Placebo (N=151)
Headache	22 (10%)	7 (5%)
Diarrhea	21 (10%)	8 (5%)
Abdominal Pain	13 (6%)	8 (5%)
Respiratory infection	11 (5%)	8 (5%)
Fall	11 (5%)	7 (5%)
Dizziness	10 (5%)	4 (3%)
Back pain	10 (5%)	2 (1%)
Common cold	10 (5%)	1 (1%)

With respect to liver enzyme abnormalities, during 12 weeks of dosing at 250mg BID (i.e., four-fold higher daily dosing than in the recently initiated Phase 2b trial) in 44 subjects with rheumatoid arthritis, elevations in liver transaminase levels were noted in six subjects (14%). Additionally, in one subject (1%) participating in the Reverse-SD 24-week trial in mild AD, ALT and AST levels increased to three times the upper limit of normal. Subjects were asymptomatic, there were no associated increases in bilirubin, and the elevations resolved with treatment discontinuation.

In the most recently completed AscenD-LB trial involving 91 subjects with DLB, neflamapimod was well tolerated with no treatment discontinuations due to study drug-related adverse events. There were four SAEs reported in the placebo group (haematochezia, internal bleeding, intraparenchymal hemorrhage, asthma exacerbation) and two in neflamapimod BID recipients (brain lesions, head injury), all of which were considered unrelated to treatment. In addition, one SAE (brain tumor diagnosis) was reported 34 days after the last dose in a neflamapimod BID recipient. There were no SAEs or early treatment discontinuations in the neflamapimod TID recipients. Liver enzyme abnormalities were not observed in the AscenD-LB trial.

Neflamapimod Preclinical Results

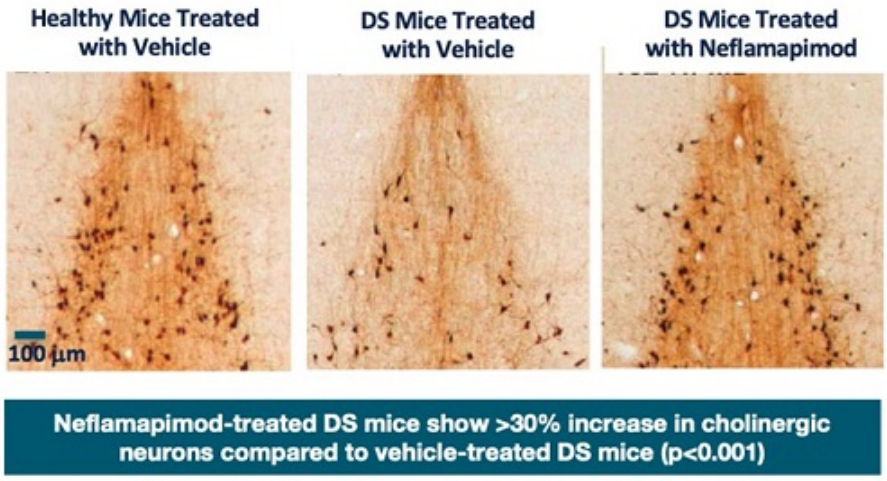
Ts2 Transgenic Mice

Nearly all individuals who have Down Syndrome, characterized by trisomic chromosome 21, develop AD by their fourth decade of life, and have typical AD pathology when autopsied at death. This may be explained by chromosome 21 containing the gene for amyloid-precursor-protein, which is the gene linked to familial or genetic early onset AD in humans. Ts2 transgenic mice is a mouse model of Down Syndrome, as it is partially trisomic at chromosome 16, which is the mouse equivalent of chromosome 21. Along with developmental behavioral abnormalities, the Ts2 mice develop typical early onset dementia pathology, including endosomal abnormalities and cholinergic neurodegeneration in the basal forebrain cholinergic system. Accordingly, Ts2 mice provide an ideal opportunity to evaluate the effects of drug treatment on basal forebrain cholinergic dysfunction and degeneration.

To evaluate the potential of neflamapimod on the neurodegenerative process, the effects of neflamapimod were evaluated in Ts2 mice. Wild-type mice, referred to as either WT or 2N, and Ts2 mice were treated over 28 days, twice daily, with either vehicle or 3 mg/kg of neflamapimod in vehicle, with nine mice in each group. Treatment was initiated at 6-7 months of age, representing a time point at which endosomal pathology and cholinergic neuronal loss is developing. To assess for effects on cholinergic neurodegeneration, neurons staining positively for choline acetyl transferase (“ChAT+” neurons), were quantitated in the region of the forebrain that is enriched for cholinergic neurons, which is known as the medial septal nucleus (“MSN”).

At the end of treatment, consistent with current scientific literature, the number of cholinergic neurons in the MSN region was significantly decreased in vehicle-treated TS2 mice compared to vehicle-treated WT mice ($p<0.001$). This effect was reversed with neflamapimod treatment, with the number cholinergic neurons in the MSN increased in neflamapimod-treated TS2 mice compared to vehicle-treated TS2 mice, and the number of ChAT+ neurons were similar to those seen in WT mice ($p<0.001$).

Neflamapimod restores numbers of cholinergic neurons in basal forebrain (i.e., reverses disease progression) in Ts2 transgenic mouse.



Cholinergic neurons, as assessed by staining positive for ChAT+ in the MSN of the basal forebrain, in healthy or Ts2 transgenic mice after treatment for four weeks with either vehicle or neflamapimod.

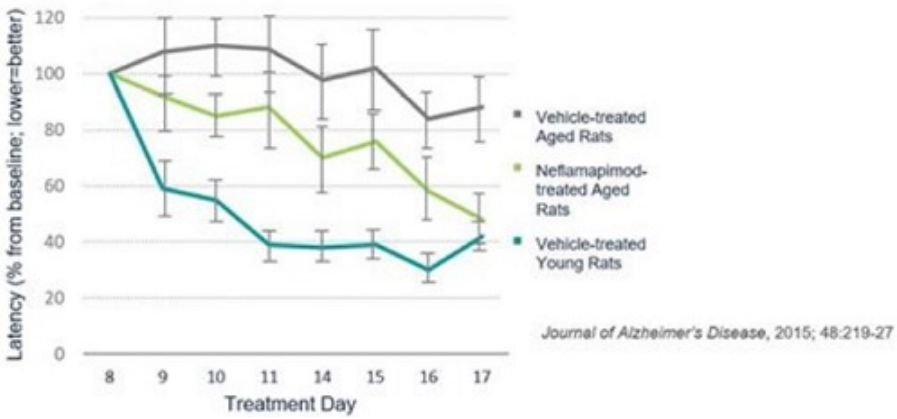
The finding of reversal of disease progression is consistent with studies in the scientific literature that suggest that "loss" of cholinergic neurons in the basal forebrain cholinergic system is not due to cell death. Rather, the "degeneration" and loss of such basal forebrain cholinergic neurons appears to be due to a loss of cholinergic phenotype and functional properties, and neuronal shrinkage, all of which in animal studies can be reversed. That is, the effect of reversing disease progression, evidenced by increased number of cholinergic neurons, is not a regenerative effect. Rather, we believe it reflects that treatment with neflamapimod is restoring the functional status of diseased neurons that don't express ChAT, allowing them to express ChAT. There is also evidence from studies in early AD, that cholinergic phenotype loss, rather than frank neuronal death and loss, occurs in the basal forebrain of humans as well.

Aged Rat Model

To obtain preclinical proof-of-principle and confirm the role of p38α in the development of synaptic dysfunction, we tested neflamapimod in a rat model of age-related cognitive decline. When evaluated in the Morris-Water-Maze test, rats show cognitive deficits starting at 20 to 22 months of age, which is equivalent to approximately 60 years of age in humans. Of note, because the deficits in Morris-Water-Maze performance can be fully reversed by implanting healthy cholinergic neurons in the basal forebrain, those deficits are believed to be due to basal forebrain cholinergic dysfunction and degeneration.

The published results of these tests showed that treatment with neflamapimod fully reversed the learning deficits in the Morris-Water-Maze test in 20 to 22 month old rats with identified cognitive deficits, with the performance of aged rats on the last day of testing (day 17) treated with neflamapimod at the optimal dose being significantly better than vehicle—treated aged rats (p=0.007 for latency; p=0.01 for distance) and being similar to that of young rats (i.e., fully reversed cognitive deficits). The figure below further details the results of these tests, in which two groups of 15 rats each (aged rats with cognitive deficits and a control group of young rats) received vehicle or active drug treatment for 21 days. The Morris-Water-Maze test was conducted on days 4-8 and days 11-17. The figure below shows reduction in latency (note: decreased latency indicates better performance).

Neflamapimod Improved Morris-Water-Maze Performance in Aged Rats



Neflamapimod dosing reverses cognitive deficits as assessed by Morris-Water-Maze test. At Day 17, p=0.007 for neflamapimod-treated aged rats compared to vehicle-treated aged rats.

Neflamapimod in Potential Acute Indication: Recovery after Ischemic Stroke

We believe the therapeutic benefit of targeting neuroinflammation-induced synaptic dysfunction is not limited to chronic neurodegenerative diseases. A drug that improves synaptic function could also be considered for evaluation of the potential to improve brain function after acute neurological injury. In the future, we may investigate neflamapimod in the treatment of certain acute indications such as ischemia-induced stroke. To date, we have generated preclinical evidence suggesting that neflamapimod could improve recovery after ischemic stroke in an animal model.

Every year, more than 795,000 people in the United States suffer a stroke, and approximately 610,000 of these are first or new strokes. About 87% of all strokes are ischemic strokes, in which blood flow to the brain is blocked. The prognosis for recovery from stroke is influenced by a number of different factors, including stroke severity, type of stroke, location of infarct, co-morbidity with other disorders, and other clinical complications. The majority of survivors of an acute stroke demonstrate some level of neurological recovery during the three to six months after the initial event. Despite this initial period of recovery, 40 to 50% of patients exhibit persistent neurological deficits.

During the last 10 years, the medical and scientific communities have gained a better understanding of the mechanisms underlying neuronal recovery following a stroke. The major translational opportunity for therapeutics that target recovery after stroke is the time window in which intervention must be initiated. Rather than just the first few hours after the stroke (as is the case with neuroprotection, i.e., acute stroke therapy to reduce the size of stroke), the window for therapeutics that target recovery is days and even weeks after an acute stroke. Waiting to initiate therapy until 48 hours after the stroke allows inclusion of a homogenous patient population as the diagnosis and extent of the stroke can be definitively established by that time in most patients (the exception being the minority who have a “stuttering” stroke). As a result, a proof-of-concept (“POC”) study in stroke recovery is in the range 50-100 patients per treatment arm, compared to 500+ per treatment arm in neuroprotection trials.

The scientific rationale for evaluating neflamapimod to promote recovery after stroke is that the BFC system plays a critical in recovery, particularly motor function recovery, after ischemic stroke, and that system is suppressed by residual inflammation in the weeks and months after the acute stroke event. Neflamapimod, through the same mechanisms operating in DLB, would be expected to reverse the suppression of BFC function, leading to improved recovery of motor function. Supporting that concept is our preclinical data with neflamapimod demonstrating significant improvement in neurological recovery vs. vehicle treatment, and TUG results from the AscenD-LB clinical trial where positive effects of neflamapimod on basal forebrain mediated control of movement were observed in the clinic.

In the preclinical study of neflamapimod that evaluated effects on recovery after stroke, which has been published in a peer-reviewed scientific journal, transient ischemia of sufficient duration was induced such that significant neurologic disability developed without mortality, and the neurologic disability did not substantially reverse during follow-up without therapy. These rats were then treated with either vehicle or one of two different doses of neflamapimod. The three groups in the study were: vehicle control (n =18), 1.5 mg/kg neflamapimod (n = 21) and 4.5 mg/kg neflamapimod (n = 21). Six weeks of neflamapimod treatment, starting at 48-hours after stroke, led to substantial improvement on multiple parameters of neurologic function compared to vehicle controls ($p<0.001$ for each of global neurologic scores; motor and sensory specific tests).

We have no immediate plans to initiate a clinical trial evaluating neflamapimod for treatment of acute stroke. However, we have had extensive discussions with stroke experts and have designed a POC trial to improve recovery after ischemic trial. The potential clinical trial would be a 12-week placebo-controlled phase 2 POC trial that would enroll 120 subjects with uncomplicated acute moderate or moderate-to-severe ischemic stroke in the anterior circulation stroke (confirmed by MRI) and demonstrated motor deficits (hemiparesis or hemiplegia). Subjects would be randomized 1:1 to placebo or neflamapimod 40 mg TTD for 12 weeks, starting three to seven days after the acute stroke. The primary endpoint would be motor function by the Fugl-Meyer motor scale at the end of three months treatment. Secondary endpoints would include the Time Up and Go test, Montreal Cognitive Assessment, and the proportion of subjects with modified Rankin Scale score < 2 (no to slight disability).

Neflamapimod in Early Onset Alzheimer's Disease

EOAD is defined as AD dementia with onset of the dementia prior to age 65. It is the most common form of early-onset AD, representing between one-third and one-half of individuals with dementia onset before age 65. The Alzheimer's Association estimates the number of individuals in the United States with EOAD in 2023 to be approximately 200,000.

While the age cut-off is arbitrary, a variety of observations indicate that EOAD is a distinct biological and clinical entity from LOAD, onset > age 65, with substantial differences in clinical presentations, greater genetic predisposition for EOAD, differences in neuropathologic burden and topography, and differences in functional connectivity. For example, in EOAD patients, memory problems appear less frequently, but loss of visuo-spatial functioning, language, attention, and executive function are more prevalent. In addition, functional MRI and other studies indicate that, compared with LOAD, EOAD impacts fronto-parietal networks, with a relative sparing of the posterior default mode network and medial temporal lobe, i.e., the hippocampus. As well, the severity of neuropsychiatric symptoms (anxiety, night-time behaviors and motor disturbances) is higher in EOAD than in LOAD.

That EOAD and LOAD are distinct clinical entities was further demonstrated in a recently published cross-sectional study in a large cohort (n=1750) of subjects with autopsy-confirmed sporadic (i.e., non-familial) AD. Within the cohort, there was a clear binomial distribution for age of onset (i.e., two distinct patient populations), an early-onset population with a mean onset at age 57.2 (±3.8) years and a late-onset population with a mean age of onset of 76.7 (±7.5) years. As the point of intersection between the two distributions (the age at onset, which is equally likely to belong to both) was age 63.0 years, this age cutoff was utilized to categorize the subjects in the cohort as having EOAD or LOAD. By this definition, the subjects with EOAD in their cohort were more likely than those with LOAD to present with noncognitive behavioral or motor symptoms or nonmemory cognitive complaints, and had more executive dysfunction, but less language impairment, on objective cognitive testing. Subjects with EOAD also had faster cognitive and functional decline than those with LOAD. Moreover, at autopsy, subjects with EOAD were more likely than those with LOAD to have pure AD pathology, without concomitant non-AD pathology, while subjects with LOAD were more likely than those with EOAD to have cerebrovascular pathology, MTL/hippocampal sclerosis, and in a sub-analysis, hippocampal TDP-43.

While survival from diagnosis is similar between EOAD and LOAD, with an age of onset 20 years lower, the impact in terms of life-years lost for each individual impacted is significantly greater with EOAD compared to LOAD.

While the relative contribution of pathogenic mechanisms in the cholinergic system as compared to those in the hippocampus remains controversial for LOAD, the literature of the last five years indicates that the earliest, and primary pathology in EOAD is in the basal forebrain cholinergic system and the dysfunction and degeneration of these neurons drives neurodegeneration in other regions of the brain. As such, we believe, given our drug's specific activity against cholinergic degeneration, within the AD spectrum neflamapimod has the greatest potential as a single agent in EOAD.

We have no near-term plans to initiate a clinical trial evaluating neflamapimod for treatment of EOAD. Rather, if we are able to demonstrate, as we expect, proof-of-concept in DLB with data from the recently initiated Phase 2b clinical trial, we would pursue clinical development in EOAD. Because disease progression in early-stage disease is more consistent in EOAD compared to LOAD, we would expect a registrational clinical trial that was designed to show effects on disease progression would be substantially smaller than that required for LOAD (300-400 subjects vs. 800-1000 subjects) and of 12 months duration (vs. 18 months for LOAD).

Neflamapimod in LOAD

The defining clinical characteristics of LOAD are deficits in episodic memory (the recollection of everyday events) and the driving pathology is in the hippocampus, the part of the brain in which episodic memory is formed. Accordingly, the amyloid beta therapies have been developed as a treatment for LOAD based on preclinical data demonstrating that amyloid beta has deleterious effects on synaptic function in the hippocampus. However, scientific literature also indicates that degeneration of the basal forebrain cholinergic system also contributes to disease expression and progression in LOAD, and we believe that a reason for the limited success of amyloid beta directed therapies is that they do not impact disease progression in the basal forebrain. Moreover, in preclinical studies, p38α expression increased amyloid beta production, while reducing p38α activity decreased amyloid pathology; and neflamapimod treatment of transgenic AD mice reduced amyloid beta levels and in the Ts2 mice reduced the expression of the major enzyme (beta secretase) that produces amyloid beta. Based on this science, we believe there is a strong rationale for combining neflamapimod with amyloid beta directed therapies. However, given the costs associated with developing therapies for LOAD (costs that are further increased when developing combinations) we would expect only to conduct such combination trials in the context of a collaboration with a larger pharmaceutical company, ideally one that has either late-stage development or an approved amyloid beta directed therapy in its portfolio. However, we are not yet a party to any such agreement and have not yet identified any potential collaborators. Accordingly, at this time, we have not included LOAD in our pipeline chart.

EIP200 (Novel Co-Crystal of Neflamapimod)

We have an issued patent, set to expire in 2038, in the United States for novel co-crystals of neflamapimod with identified, specific, Generally Recognized as Safe compounds that have the potential to improve the solubility and other physical properties of neflamapimod. The development of one of these co-crystals as a product would be supported by composition of matter protection afforded by this patent, providing additional patent protection if we developed a such co-crystal product ourselves and/or the opportunity to license such a product to another pharmaceutical company while retaining the rights to neflamapimod. The ability to develop one or more of these co-crystal products requires a fuller evaluation of the potential manufacturing processes than has been performed to date.

Neflamapimod — History of Development

History

Neflamapimod was originally discovered at Vertex, which initiated clinical investigations in 1999 to determine the effects of the drug on rheumatoid arthritis. During its clinical investigations of neflamapimod, Vertex completed single and multi-dose Phase 1 studies and initiated Phase 2a development in rheumatoid arthritis. A total of approximately 150 healthy volunteers and patients received neflamapimod in Vertex-sponsored studies for up to one month at 750 mg twice daily and up to 3 months at a dose of 250 mg twice daily.

In a Phase 2a trial in active rheumatoid arthritis conducted by Vertex, a total of 59 healthy volunteers and patients (44 on active drug of 250 mg, and 15 on placebo, twice daily) were enrolled in a 12-week treatment. In this trial, a statistically significant effect of neflamapimod administration on American College of Rheumatology 20 (“ACR20”) response rate was demonstrated ($p = 0.027$ in the primary endpoint analysis: area-under-the-curve of ACR20 response over the 12-week trial period). In a pharmacokinetic/pharmacodynamic analysis, neflamapimod administration also reduced C-reactive protein and IL-6 levels with increasing cumulative drug exposure.

Neflamapimod was generally well tolerated in this rheumatoid arthritis (“RA”) Phase 2a trial. The most common adverse events associated with neflamapimod were abdominal pain (21% of the 44 healthy volunteers), diarrhea (18%), infection (16%), headache (14%), increased aspartate aminotransferase (14%) and increased alanine aminotransferase (11%). No treatment-emergent neurologic events were seen. Regarding liver function test abnormalities, transaminase levels returned to normal after treatment discontinuation and were not associated with bilirubin elevations. Liver enzyme elevations are a well-known dose-dependent clinical side effect of p38 MAPK inhibitors. In the case of neflamapimod however, we believe the threshold for inducing liver enzyme elevation is a dose level of 250 mg twice daily when administered for more than 4 weeks, which on a daily dose level is four-fold higher than the 40mg TID dose regiment we are moving forward in DLB and other CNS indications (500 mg per day in RA vs. 120 mg per day in DLB and other CNS indications).

Toxicology

A full chronic repeated dose toxicology program has been completed in rodents (rats) and non-rodents (dogs). In the rodent species, in the six-month toxicology study, no human relevant findings were evident at dose levels that provided plasma neflamapimod drug concentration levels approximately ten-fold higher than those achieved in the AD clinical trials. In shorter-term studies, the primary target organ was the liver, with findings commencing at plasma drug concentration levels 20-fold higher than the AD clinical trial exposures. In the non-rodent species, in 9- and 12-month toxicology studies, dose dependent findings were evident beginning at plasma neflamapimod drug concentrations more than ten-fold higher than achieved with 40 mg twice daily in AD clinical trials, with minimal to equivocal findings at that dose level in the liver, bone marrow and CNS. The CNS findings demonstrated damage to axons, or nerve fibers, primarily in the spinal cord. p38α and p38β have been reported to have a role in transport of proteins in axons, and therefore we believe these toxicity findings are related to the inhibition of both p38α and p38β at the very high doses administered in the non-rodent studies. The doses we are using in our clinical trials are at least ten-fold lower than the doses at which these effects were observed.

Acquisition from Vertex

Vertex ultimately discontinued its pursuit of neflamapimod in the early 2000s to focus on the clinical development of a therapy for rheumatoid arthritis with a different p38α inhibitor, which, unlike neflamapimod, does not enter the brain. Neflamapimod lay dormant with Vertex until we expressed our interest in exploring the drug for other indications. Based on our team's previous direct experience with this compound and our understanding of its profile and emerging science around p38α in the brain, EIP, our wholly-owned subsidiary, entered into an Option and License Agreement with Vertex in August 2012, and subsequently acquired an exclusive license from Vertex in 2014 to develop and commercialize neflamapimod for the treatment of AD and other neurodegenerative diseases.

Neflamapimod — Regulatory Status

We submitted an investigational new drug application ("IND") application to the Division of Neurology Products ("DNP") of the FDA in February 2015. The DNP cleared our application in March 2015, and the IND remains open and active.

The FDA granted neflamapimod Fast Track designation for the treatment of DLB in October 2019.

Following a review of the long-term animal toxicology studies discussed above, the DNP placed a partial clinical hold on our first Phase 2a in mild AD (Study 303) in August 2015, limiting administration of neflamapimod to doses that lead to plasma drug levels which provide at least a 10-fold safety margin to the plasma drug levels in animals that in long-term animal toxicity studies had previously led to minimal or equivocal findings in the liver, bone marrow and CNS. At the present time, this partial clinical hold effectively limits our clinical dosing in the United States to 40 mg of neflamapimod three times daily in patients with a weight of greater than or equal to 60 kg (132 pounds), based on agreements with the FDA and on our current understanding of plasma drug levels achieved with neflamapimod in humans. As our current plans across our indications do not envision surpassing this dose level, we do not expect this partial clinical hold to impact our ongoing and planned clinical trials.

In Europe, clinical trial applications in support of our clinical trials have been reviewed and approved by the national regulatory authorities in each of the Netherlands, United Kingdom, Czech Republic and Denmark. In addition, the Agence Nationale de Sécurité du Médicament et des Produits de Santé (the French national regulatory authority) has reviewed and approved a clinical trial application for an investigator-initiated study of neflamapimod in Toulouse, France.

Vertex Agreement

In August 2012, we entered into an Option and License Agreement with Vertex. The Vertex Agreement granted us an option to acquire an exclusive worldwide license to develop and commercialize neflamapimod for the diagnosis, treatment and prevention of AD and other neurodegenerative diseases. In August 2014, we exercised an option to acquire the license to neflamapimod.

The Vertex Agreement contains certain milestone events and the related payments that we would be obligated to make to Vertex if and when such events occur. Each milestone payment is payable only once for each distinct licensed product, upon the first occurrence of the applicable milestone event. The first expected milestone events concern filing of a new drug application ("NDA") with the FDA for marketing approval of neflamapimod, in the U.S., or a similar filing for a non-U.S. major market, as specified in the Vertex Agreement. The Vertex Agreement also provides that we will make royalty payments to Vertex in the event aggregate net sales, as defined in the agreement, for a commercialized licensed product meet specified thresholds. Such royalties will be on a sliding scale of percentages of net sales in the low-to mid-teens, depending on the amount of net sales in the applicable years. We are also obligated to make a milestone payment to Vertex upon net sales reaching a certain specified amount in any 12-month period. The Vertex Agreement states that royalties will be reduced by 50% during any portion of the royalty term when there is no valid claim of an issued patent within specified patent rights covering the licensed product. We also have the right to deduct, on a country by country basis, from royalties otherwise payable to Vertex under the terms of the Vertex Agreement, 50% of all royalties, upfront fees, milestones and other payments paid by us or any of our affiliates or sublicensees to third parties under licenses that are necessary for the development, manufacture, sale or use of a licensed product, provided that in no event will the royalty payable to Vertex be reduced to less than 50% of the rates specified in the Vertex Agreement, subject to certain adjustments specified therein. In the aggregate, our potential milestone payment obligations, all of which relate to development milestones, under the Vertex Agreement are up to $117 million. To date, we have made an aggregate of $100,000 in payments to Vertex. In connection with our obligations under the Vertex Agreement, there is no minimum annual expenditure requirement. Our diligence obligations under the Vertex Agreement have included the making of annual expenditures in connection with the development of neflamapimod, commencement of a Phase 2 clinical trial of neflamapimod, and the commercial sale of neflamapimod within six months of market approval.

The Vertex Agreement provides that we may sublicense the rights granted to us by Vertex, in whole or in part, to a third party (through multiple levels of sublicensing) (i) who is providing services to us in connection with the manufacture or development of the licensed product, solely for the purpose of providing such services, or (ii) with the prior written consent of Vertex, which shall not be unreasonably withheld.

The license term under the Vertex Agreement is deemed to have commenced on August 21, 2014, and continues until the expiration of the royalty term, unless sooner terminated in accordance with the terms of the Vertex Agreement. The royalty term commences on the first commercial sale of a licensed product and ends upon the later of (i) the date of expiration, unenforceability or invalidation of the last valid claim of certain specified underlying patent rights, or (ii) ten years after the date of such first commercial sale. Upon the expiration of the royalty term, the license will convert to a perpetual, fully paid-up non-royalty bearing license with the same scope.

The Vertex Agreement may be terminated by us for any reason upon 90 days' prior written notice to Vertex if such termination occurs before receipt of the first marketing approval of a licensed product, and otherwise upon twelve months' prior written notice to Vertex. Either party may terminate the Vertex Agreement if the other party is in material breach of its obligations thereunder, following a 60-day notice and cure period, or if the other party files for bankruptcy, reorganization, liquidation, receivership, or an assignment of a substantial portion of assets to creditors. The Vertex Agreement also provides that in the event we materially breach any of certain specified diligence obligations as to a specific major market, Vertex's sole remedy for such breach, following the applicable notice and cure period, will be to terminate the license as to such specific major market country.

Trans Sodium Crocetinate (TSC)

Prior to the Merger in August 2023, while operating as Diffusion Pharmaceuticals Inc., the Company focused on developing novel therapies that may enhance the body's ability to deliver oxygen to areas where it is needed most. The most advanced of these product candidates, TSC, has been investigated and developed to enhance the diffusion of oxygen to tissues with low oxygen levels, also known as hypoxia, most recently as an adjuvant treatment to standard of care therapy for glioblastoma multiforme brain cancer ("GBM") and other hypoxic solid tumors. Although we have paused all development activity related to TSC, including the initiation of Diffusion's previously announced Phase 2 study of TSC in newly diagnosed GBM patients which incorporated an innovative use of positron emission tomography ("PET") scans and hypoxia-specific radiotracers to evaluate the oxygenating enhancing effects of TSC on tumor hypoxia, we intend to continue to attempt to identify sale or out-licensing transactions for the Company's TSC-related assets.

Sales and Marketing

We do not currently have any infrastructure for the sales, marketing or distribution of an approved drug product. In order to market and successfully commercialize neflamapimod or any other future product candidate, to the extent it or they are approved, we must either develop these capabilities internally or make arrangements with third parties to perform these services. We may also collaborate with strategic partners that have experience in these fields. There are significant expenses and risks involved in establishing our own sales, marketing and distribution functions, including our ability to hire, retain and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Alternatively, to the extent that we depend on third parties for such services, any revenues we receive will depend upon the efforts of those third parties, and there can be no assurance that such efforts will be successful.

Manufacturing

We do not own or operate manufacturing facilities, nor do we have plans to develop our own manufacturing operations in the foreseeable future. Our lead product candidate, neflamapimod, is a small molecule drug that is manufactured using commercially available technologies.

The recently initiated Phase 2b clinical trial is being conducted with drug substance has already been manufactured. In addition, we have sufficient drug substance available to cover the anticipated needs for Phase 3 in DLB. This drug substance was manufactured at an established commercial contract manufacturing organization, that is approved for and manufactures drug both for investigational use and marketed products. We would anticipate utilizing the company for clinical trials beyond the Phase 3 clinical trial in DLB, as well potentially for commercial use. However, supplies of our neflamapimod drug substance could be interrupted from time to time, and we cannot be certain that alternative supplies could be obtained within a reasonable timeframe, at an acceptable cost, or at all. In addition, a disruption in the supply of drug substance could delay the commercial launch of our product candidates, if approved, or result in a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates. Growth in the costs and expenses of raw materials may also impair our ability to cost effectively manufacture our product candidates.

We also currently rely on a third-party contract manufacturing organization (different than that for drug substance) for the manufacture of our neflamapimod drug product. We have used the same manufacturer for our neflamapimod drug product in all our clinical trials to date. If neflamapimod is ultimately approved for commercial sale, we expect to continue to rely on third-party contractors for manufacturing the drug product. Although we intend to do so prior to any commercial launch, we have not yet entered into long-term agreements for the commercial supply of either drug substance or drug product with our current manufacturing providers, or with any alternate manufacturers.

Competition

Given the potential market opportunity for the treatment of DLB and other neurodegenerative diseases, an increasing number of established pharmaceutical firms and smaller biotechnology/biopharmaceutical companies are pursuing a range of potential therapies for these diseases in various stages of clinical development.

While there are numerous companies pursuing AD disease modifying approaches, there are a limited number of companies and disease modifying approaches for DLB.

With regard to public biopharmaceutical companies that we would consider competitive with our approach, and actively evaluating treatments in DLB, we are aware of Eisai Co. Ltd., or Eisai, Cognition Therapeutics, Inc. and Athira Pharma, Inc. All three companies are in Phase 2 clinical trials, and none have reported positive (statistically significant improvement over placebo) clinical trial results in DLB at this time.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize, including neflamapimod, may compete with existing therapies and new therapies that may become available in the future.

Our competitors may have significantly greater financial resources, an established presence in the market, and significantly greater expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific, sales, marketing and management personnel, establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of neflamapimod, and any other product candidates that we develop to address DLB and other CNS diseases, if approved, are likely to be their efficacy, safety, convenience, price, the level of competition, and the availability of reimbursement from government and other third-party payors. Our potential commercial opportunity could also be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

Intellectual Property

We strive to protect and enhance the proprietary technologies, inventions and improvements that we believe are important to our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements and our product candidates that are important to the development and implementation of our business.

We have made a number of discoveries related to our lead product candidate, neflamapimod, which are reflected in ten main patent families, each of which we wholly own (dates below are without consideration of potential patent term extension:

- The first patent family relates to methods of treating patients suffering from AD, as well as methods of reducing amyloid plaque burden. In this family, we hold issued patents in the United States, Europe, Japan, China, Canada, Australia, and Hong Kong. These patents are set to expire in 2032.

- The second patent family relates to the use of neflamapimod for improving cognition. In this family, we hold issued patents in the United States, Europe, Japan, and a pending application in China. These patents are set to expire in 2035.

- The third patent family relates to co-crystals of neflamapimod in this family, we hold an issued patent in the United States. This patent is set to expire in 2038.

- The fourth patent family relates to methods for promoting recovery of function in patients who have suffered acute neurologic injuries, including those resulting from various forms of stroke. In this family, we hold an issued patent in the United States, Europe, and Japan, and pending applications in Korea and Hong Kong. These patents are set to expire in 2035-2036.

- The fifth patent family relates to methods of treating patients suffering from dementia. In this family, we have an issued patent the United States for the treatment to patients with mild cognitive impairment to improve episodic memory and a pending application in Europe. Patents that issue in this family, if any, are expected to expire in 2037.

- The sixth patent family relates to formulations of neflamapimod, including pharmaceutical compositions for oral administration exhibiting desirable pharmacokinetics and processes for the manufacture thereof. In this family, we have an issued patent in the United States that is set to expire in 2039.

- The seventh patent family relates to the treatment of DLB. In this family we have pending applications in the United States, Europe, Japan, China, Canada, and Hong Kong. Patents that issue in this family, if any, are expected to expire in 2040.

- The eighth patent family is co-owned by Boston University and relates to methods of treating prion disease. In this family, we have a pending application in the United States. Patents that issue in this family, if any, are expected to expire in 2040.

- The ninth patent family relates to treatment of gait dysfunction related to neurodegenerative disease. An International Application is pending. Patents that issue in this family, if any, are expected to expire in 2041.

- The tenth patent family relates to treatment of a subpopulation of patients having DLB but no substantial Alzheimer's like tau pathology. Patents that issue in this family, if any, are expected to expire in 2042.

Pursuant to the terms and conditions of the Vertex Agreement, Vertex has granted us an exclusive license under specified Vertex patent rights, including U.S. patent No. 5,945,418, which relates to the composition of matter for neflamapimod. This patent expired in 2017.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for regularly filed applications in the United States are granted a term of 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, a patent term can be extended to recapture a portion of the U.S. Patent and Trademark Office delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

We also rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements and invention assignment agreements with our collaborators, employees and consultants, as we determine necessary. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our drugs or processes, obtain licenses from third parties or cease certain activities.

From time to time, we may find it necessary or prudent to obtain licenses from third party patent owners. Where licenses are available at reasonable cost, such licenses are considered a normal cost of doing business. In other instances, we may use the results of freedom-to-operate studies to guide our early-stage research away from areas where we are likely to encounter obstacles in the form of third-party intellectual property. We strive to identify potential third-party intellectual property issues in the early stages of research in our programs in order to minimize the cost and disruption of resolving such issues.

Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future drugs may have an adverse impact on us.

Government Regulation

The FDA and comparable regulatory authorities in other countries impose requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These requirements can, in some instances, be substantial and burdensome. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of pharmaceutical products. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

U.S. Government Regulation of Drug Products

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. Failure to comply with the applicable U.S. requirements at any time during the product development and approval process or after approval may subject an applicant to a variety of administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve a pending NDA, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters or other notices of violation, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on our business and results of operations.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- Completion of nonclinical laboratory tests, potentially animal studies and formulation studies in compliance with the FDA's good laboratory practice ("GLP") regulations;
- Submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- Approval by an institutional review board ("IRB") covering each clinical trial site before each trial may be initiated at that site;
- Performance of adequate and well-controlled human clinical trials in accordance with good clinical practice ("GCP") regulations and other clinical trial-related requirements to establish the safety and efficacy of the proposed drug product for each indication;
- Submission to the FDA of an NDA seeking marketing approval;
- A determination by the FDA within 60 days of its receipt of an NDA that the NDA is sufficiently complete to permit a substantial review, in which case the NDA is filed;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice ("cGMP") requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;

- Satisfactory completion of FDA audits of clinical trial sites that generated data in support of the NDA to assure compliance with GCP regulations and the integrity of the clinical data and/or FDA audits of the nonclinical studies submitted as part of the NDA; and

- FDA review and approval of the NDA, including consideration of the views of an FDA advisory committee, if one was involved, prior to any commercial marketing or sale of the drug in the United States.

Preclinical Studies and IND

Nonclinical studies generally include laboratory evaluation of product chemistry, toxicity and formulation, as well as in vitro and animal studies to assess the potential for adverse events and in some cases to establish a rationale for the investigational product's therapeutic use. The Consolidated Appropriations Act for 2023, signed into law on December 29, 2022, (P.L. 117-328) amended the FDCA to specify that nonclinical testing for drugs may, but is not required to, include in vivo animal testing. According to the amended language, a sponsor may fulfill nonclinical testing requirements by completing various in vitro assays (e.g., cell-based assays, organ chips, or microphysiological systems), in silico studies (i.e., computer modeling), other human or non-human biology-based tests (e.g., bioprinting), or in vivo animal tests. The conduct of nonclinical studies is subject to federal regulations and requirements, including GLP regulations.

An IND sponsor must submit the results of preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational new drug to humans, and it must become effective before human clinical trials may begin. Some long-term nonclinical testing may continue even after the IND is submitted and clinical trials have been initiated. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA issues a notice expressly authorizing the proposed trial to proceed or raises concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to initiate. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns or non-compliance. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators (generally physicians not employed by or under the trial sponsor's control) in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial, as well as review and approval of the trial by an IRB. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the trial procedures, subject selection and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB acting on behalf of each institution participating in the clinical trial must review and approve the trial plan, informed consent forms, and communications to trial subjects before the trial commences at that institution. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and are reasonable in relation to anticipated benefits, and whether the planned human subject protections are adequate. The IRB must continue to oversee the clinical trial while it is being conducted. An IRB must operate in compliance with FDA regulations.

Sponsors of certain clinical trials generally must register such trials and disclose certain trial information within specific timeframes to the National Institutes of Health ("NIH") for public dissemination on the clinicaltrials.gov data registry. Information related to the investigational product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Sponsors are also obligated to disclose the results of their clinical trials after completion, but such disclosures may be delayed in some cases for up to two years after the date of completion of the trial. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government. The NIH's Final Rule on ClinicalTrials.gov registration and reporting requirements became effective in 2017, and the government has brought enforcement actions against non-compliant clinical trial sponsors. Competitors may use the publicly available information about clinical trials to gain knowledge regarding the progress of development programs. Sponsors or distributors of investigational products for the diagnosis, monitoring, or treatment of one or more serious diseases or conditions must also have a publicly available policy on evaluating and responding to requests for expanded access requests.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug candidate is initially administered to healthy human volunteers and tested for safety, dosage tolerance, structure-activity relationships, mechanism of action, absorption, metabolism, distribution, and excretion. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to administer ethically to healthy volunteers, the initial human testing is often conducted in patients with the target disease or condition. If possible, Phase 1 trials may also be used to gain an initial indication of product effectiveness.

- Phase 2: The drug candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more extensive clinical trials.

- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to evaluate the efficacy and safety of the product for its intended use, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product as well as an adequate basis for marketing approval. Typically, two adequate, well-controlled Phase 3 trials are required by the FDA for drug product approval. Under some limited circumstances, however, the FDA may approve an NDA based upon a single Phase 3 clinical trial plus confirmatory evidence from a post-market trial or, alternatively, a single large, robust, well-controlled multicenter trial without confirmatory evidence.

- Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted to further assess the drug's safety and effectiveness after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the investigational drug, findings from animal or in vitro testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. It is possible that Phase 1, Phase 2 or Phase 3 trials may not be completed successfully within any specified period, or at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Sponsors may also choose to discontinue clinical trials as a result of risks to subjects, a lack of favorable results, or changing business priorities. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated checkpoints based on access to certain data from the trial.

Congress also recently amended the FDCA, as part of the Consolidated Appropriations Act for 2023, in order to require each sponsor of a Phase 3 clinical trial, or other "pivotal study" of a new drug to support marketing authorization, to design and submit a diversity action plan for such clinical trial. The action plan must include the sponsor's diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. A sponsor must submit a diversity action plan to the FDA by the time the sponsor submits the relevant clinical trial protocol to the agency for review. The FDA may grant a waiver for some or all of the requirements for a diversity action plan. It is unknown at this time how the diversity action plan may affect Phase 3 trial planning and timing or what specific information FDA will expect in such plans, but if the FDA objects to a sponsor's diversity action plan or otherwise requires significant changes to be made, it could delay initiation of the relevant clinical trial.

Concurrent with clinical trials, companies may perform additional nonclinical studies and develop additional information about a drug candidate's chemistry and physical characteristics as well as finalize a process for its manufacturing in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that a drug candidate does not undergo unacceptable deterioration over its proposed labeled shelf life.

Marketing Application Submission, Review by the FDA, and Marketing Approval

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical studies and clinical trials are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. The NDA must contain proof of the product candidate's safety and substantial evidence of effectiveness for its proposed indication or indications in the form of relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. In particular, a marketing application must demonstrate that the manufacturing methods and quality controls used to produce the drug product are adequate to preserve the drug's identity, strength, quality, and purity. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by investigators. FDA approval of an NDA must be obtained before the corresponding drug may be marketed in the United States.

Under the Prescription Drug User Fee Act, as amended ("PDUFA"), each NDA submission is subject to a substantial application user fee, and the sponsor of an approved NDA is also subject to an annual program fee. The FDA adjusts the PDUFA user fees on an annual basis. The application user fee must be paid at the time of the first submission of the application, even if the application is being submitted on a rolling basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business.

The FDA reviews all NDAs submitted to determine if they are substantially complete before it accepts them for filing and may request additional information rather than accepting a submission for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt and must inform the sponsor by the 74th day after the FDA's receipt of the submission whether the application is sufficiently complete to permit substantive review. The FDA may refuse to file any submission that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the marketing application must be resubmitted with the additional information requested by the agency. The resubmitted application is also subject to review before the FDA accepts it for filing.

Once an NDA is accepted for filing, the FDA's goal is to review the application within 10 months after it accepts the application for filing, or, if the application meets the criteria for "priority review," six months after the FDA accepts the application for filing. The review process is often significantly extended by FDA requests for additional information or clarification after the NDA has been accepted for filing. The review process may be extended by the FDA for three additional months to consider new information or in the case of a clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

During the review process, the FDA reviews the NDA to determine, among other things, whether the product is safe and effective and whether the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued strength, quality, and purity. The FDA may refer any NDA, including applications for novel drug candidates which present difficult questions of safety or efficacy to an advisory committee to provide clinical insight on application review questions. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it considers such recommendations carefully when making final decisions on approval.

Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent manufacture of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies as part of the review process and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

Under the Pediatric Research Equity Act ("PREA"), amendments to the FDCA, an NDA or supplement to an NDA must contain data that are adequate to assess the safety and efficacy of the product candidate for the claimed indications in all relevant pediatric populations and to support dosing and administration for each pediatric population for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. The PREA requires a sponsor that is planning to submit a marketing application for a product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration to submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 clinical trial. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including trial objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from pre-clinical studies, early-phase clinical trials or other clinical development programs.

The testing and approval process requires substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all, and we may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or preclude us from marketing its products. After the FDA evaluates an NDA and conducts inspections of the manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter ("CRL"). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL indicates that the review cycle of the application is complete and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing, information or clarification for FDA to reconsider the application. The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product. If a CRL is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. If and when the deficiencies have been addressed to the FDA's satisfaction in a resubmission of the marketing application, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

If regulatory approval of a product is granted, such approval is limited to the conditions of use (e.g., patient population, indication) described in the application and may entail further limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a Risk Evaluation and Mitigation Strategy ("REMS") plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS plan is needed, the sponsor of the NDA must submit a proposed REMS to obtain approval for the product. The FDA also may condition approval on, among other things, changes to proposed labeling (e.g., adding contraindications, warnings or precautions) or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization and may limit further marketing of the product based on the results of these post-marketing studies. Some types of changes to an approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and separate FDA review and approval. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Fast Track, Priority Review, and Breakthrough Therapy Designations

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of new drugs that meet certain criteria. Specifically, new drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept the sections and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application. A fast track designated product candidate may also qualify for accelerated approval (described below) or priority review, under which the FDA sets the target date for FDA action on the NDA or biologics license application at six months after the FDA accepts the application for filing.

Priority review is granted when there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. If criteria are not met for priority review, the application is subject to the standard FDA review period of 10 months after FDA accepts the application for filing.

In addition, a sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough therapy designation provides all the features of fast track designation in addition to intensive guidance on an efficient development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review and regulatory staff in a proactive, collaborative, cross-disciplinary review, where appropriate. A drug designated as breakthrough therapy is also eligible for accelerated approval if the relevant criteria are met.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Fast track, priority review and breakthrough therapy designations do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval but may expedite the development or approval process.

Accelerated Approval

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval from the FDA and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a drug or biologic when it has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality ("IMM"), and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform post-marketing clinical trials to verify and describe the predicted effect on IMM or other clinical endpoint, and the product may be subject to expedited withdrawal procedures. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug or biologic, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval when the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate long-term clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. For example, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large clinical trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product candidate's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm the predicted clinical benefit of the product during post-marketing studies, would allow the FDA to withdraw approval of the product. As part of the Consolidated Appropriations Act for 2023, Congress provided FDA additional statutory authority to mitigate potential risks to patients from continued marketing of ineffective drugs or biologics previously granted accelerated approval. Under the act's amendments to the FDCA, FDA may require the sponsor of a product granted accelerated approval to have a confirmatory trial underway prior to approval. The sponsor must also submit progress reports on a confirmatory trial every six months until the trial is complete, and such reports are published on FDA's website. The amendments also give FDA the option of using expedited procedures to withdraw product approval if the sponsor's confirmatory trial fails to verify the claimed clinical benefits of the product.

All promotional materials for product candidates being considered and approved under the accelerated approval program are subject to prior review by the FDA.

Patent term restoration

Depending upon the timing, duration and specifics of FDA approval of our product candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act, informally known as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product candidate's approval date. The patent term restoration period is generally one half of the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of the NDA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved product candidate is eligible for the extension and the application for extension must be made prior to expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Pediatric exclusivity

Pediatric exclusivity is a type of non-patent marketing exclusivity available in the United States and, if granted, it provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity or listed patents. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. The issuance of a written request does not require the sponsor to undertake the described studies.

Abbreviated new drug applications for generic drugs

In 1984, with passage of the Hatch-Waxman Act, which established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs based on an innovator or "reference" product, Congress also enacted Section 505(b)(2) of the FDCA, which provides a hybrid pathway combining features of a traditional NDA and a generic drug application. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application ("ANDA") to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug ("RLD").

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to an RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug."

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication Approved Drug Products with Therapeutic Equivalence Evaluations, also referred to as the Orange Book. Clinicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing clinicians or patient.

In contrast, Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. A Section 505(b)(2) applicant may eliminate the need to conduct certain preclinical or clinical studies, if it can establish that reliance on studies conducted for a previously-approved product is scientifically appropriate.

In addition, under the Hatch-Waxman Amendments, the FDA might not approve an ANDA or 505(b)(2) NDA until any applicable period of non-patent exclusivity for the RLD has expired. These market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity ("NCE"), is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA or 505(b)(2) NDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity for an NDA, 505(b)(2) NDA or supplement thereto if one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant are deemed by the FDA to be essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. The three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving follow-on applications for drugs containing the original active agent. Five-year and three-year exclusivity also will not delay the submission or approval of a traditional NDA filed under Section 505(b)(1) of the FDCA. However, an applicant submitting a traditional NDA would be required to either conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) NDA applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

I. the required patent information has not been filed by the original applicant;

II. the listed patent has expired;

III. the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or

IV. the listed patent is invalid, unenforceable or will not be infringed by the manufacture, use or sale of the new product.

If a Paragraph I or II certification is filed, the FDA may make approval of the application effective immediately upon completion of its review. If a Paragraph III certification is filed, the approval may be made effective on the patent expiration date specified in the application, although a tentative approval may be issued before that time. If an application contains a Paragraph IV certification, a series of events will be triggered, the outcome of which will determine the effective date of approval of the ANDA or 505(b)(2) application.

If the follow-on applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the follow-on application in question has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA or 505(b)(2) applicant. Alternatively, if the listed patent holder does not file a patent infringement lawsuit within the required 45-day period, the follow-on applicant's ANDA or 505(b)(2) NDA will not be subject to the 30-month stay.

Post-Approval Requirements

Following approval of a new product, the manufacturer and the approved product are subject to pervasive and continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting of adverse experiences with the product, product sampling and distribution restrictions, complying with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations (i.e., “off-label use”) and limitations on industry-sponsored scientific and educational activities. The manufacturer and its products are also subject to similar post-approval requirements by regulatory authorities comparable to FDA in jurisdictions outside of the United States where the products are approved. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. If there are any modifications to the product, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or a supplement to an NDA, which may require the applicant to develop additional data or conduct additional nonclinical studies and clinical trials. The FDA may also place other conditions on approvals including the requirement for a REMS to assure the safe use of the product. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. The manufacturing facilities for our product candidates must meet applicable cGMP requirements to the FDA's or comparable foreign regulatory authorities' satisfaction before any product is approved and our commercial products can be manufactured. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. These manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic prescheduled or unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Future inspections by the FDA and other regulatory agencies may identify compliance issues at the facilities of our contract manufacturing organizations that may disrupt production or distribution or require substantial resources to correct. In addition, the discovery of conditions that violate these rules, including failure to conform to cGMPs, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including voluntary recall and regulatory sanctions as described below.

Once an approval or clearance of a drug is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or other enforcement-related letters or clinical holds on post-approval clinical trials;
- refusal of the FDA to approve pending marketing applications or supplements to approved marketing authorizations, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal health care programs; or mandated modification of promotional materials and labeling and the issuance of corrective information.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act ("PDMA"), which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Most recently, the Drug Supply Chain Security Act ("DSCSA"), was enacted with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that is expected to culminate in November 2023. From time to time, new legislation and regulations may be implemented that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. It is impossible to predict whether further legislative or regulatory changes will be enacted, whether FDA regulations, guidance or interpretations will be changed or what the impact of such changes, if any, may be.

Other U.S. Health Care Laws and Regulations

If our product candidates are approved in the United States, we will have to comply with various U.S. federal and state laws, rules and regulations pertaining to health care fraud and abuse, including anti-kickback laws and physician self-referral laws, rules and regulations. Violations of the fraud and abuse laws are punishable by criminal and civil sanctions, including, in some instances, exclusion from participation in federal and state health care programs, including Medicare and Medicaid. These laws include:

- The federal anti-kickback statute ("AKS") prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the AKS or specific intent to violate it to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the FCA or federal civil money penalties statute;
- The federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal healthcare programs, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or an obligation to pay or transmit money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payers if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;

- The federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) imposes criminal and civil liability for executing a scheme to defraud any health care benefit program or making false statements relating to health care matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- The federal transparency requirements under the Physician Payments Sunshine Act require manufacturers of FDA-approved drugs, devices, biologics and medical supplies covered by Medicare or Medicaid to report, on an annual basis, to the Department of Health and Human Services (HHS) information related to payments and other transfers of value to physicians, certain advanced non-physician health care practitioners, and teaching hospitals or to entities or individuals at the request of, or designated on behalf of, such physicians, non-physician health care practitioners, and teaching hospitals as well as certain ownership and investment interests held by physicians and their immediate family members; and

- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving health care items or services reimbursed by nongovernmental third-party payors, including private insurers.

The majority of states also have statutes or regulations similar to the aforementioned federal laws, some of which are broader in scope and apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines, or the relevant compliance guidance promulgated by the federal government, in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures to the extent that those laws impose requirements that are more stringent than the Physician Payments Sunshine Act. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of their exceptions and safe harbors, it is possible that business activities can be subject to challenge under one or more of such laws. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry.

Ensuring that business arrangements with third parties comply with applicable healthcare laws and regulations is costly and time consuming. If business operations are found to be in violation of any of the laws described above or any other applicable governmental regulations a pharmaceutical manufacturer may be subject to penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from governmental funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings, additional reporting obligations and oversight if subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and curtailment or restructuring of operations, any of which could adversely affect a pharmaceutical manufacturer’s ability to operate its business and the results of its operations.

Pharmaceutical Coverage, Pricing, and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of our products, when and if approved for marketing in the United States, will depend, in part, on the extent to which our products will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. In addition, these third-party payors are increasingly reducing reimbursements for medical products, drugs and services. Furthermore, the U.S. government, state legislatures and foreign governments have continued implementing cost containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Limited third-party reimbursement for our product candidates or a decision by a third-party payor not to cover our product candidates could reduce physician usage of our products once approved and have a material adverse effect on our sales, results of operations and financial condition.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product and therapeutic candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell product and therapeutic candidates that obtain marketing approval. The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product and therapeutic candidates. 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 otherwise may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

As previously mentioned, the primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other healthcare funding and applying new payment methodologies. In recent years, the U.S. Congress has considered reductions in Medicare reimbursement levels for medicines and biologics administered by physicians. The U.S. Centers for Medicare and Medicaid Services ("CMS"), the agency that administers the Medicare and Medicaid programs, also has authority to revise reimbursement rates and to implement coverage restrictions for some drugs and biologics. Cost reduction initiatives and changes in coverage implemented through legislation or regulation could decrease utilization of and reimbursement for any approved products we may market in the future. While Medicare regulations apply only to pharmaceutical benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from federal legislation or regulation may result in a similar reduction in payments from private payors.

The Biden Administration has indicated that lowering prescription drug prices is a priority. For example, in July 2021, President Biden issued a sweeping executive order on promoting competition in the American economy that includes several mandates pertaining to the pharmaceutical and healthcare insurance industries and called on HHS to release a comprehensive plan to combat high prescription drug prices. The drug pricing plan released by HHS in September 2021 in response to the executive order makes clear that the Biden Administration supports aggressive action to address rising drug prices, including allowing HHS to negotiate the cost of Medicare Part B and D drugs. It is unclear how other healthcare reform measures of the Biden administration will impact healthcare laws and regulations or our business.

In addition, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Notably, the Creating and Restoring Equal Access to Equivalent Samples Act of 2019 (the "CREATES Act"), which became effective on December 20, 2019, addresses concerns articulated by both the FDA and others in the industry that some brand manufacturers have improperly restricted the distribution of their products, including by invoking the existence of a REMS for certain products, to deny generic and biosimilar product developers access to samples of brand products. Because generic and biosimilar product developers need samples to conduct certain comparative testing required by the FDA, some have attributed the inability to timely obtain samples as a cause of delay in the entry of generic and biosimilar products. To remedy this concern, the CREATES Act establishes a private cause of action that permits a generic or biosimilar product developer to sue the brand manufacturer to compel it to furnish the necessary samples on "commercially reasonable, market-based terms." Whether and how generic and biosimilar product developments will use this new pathway, as well as the likely outcome of any legal challenges to provisions of the CREATES Act, remain highly uncertain and its potential effects on our future commercial products are unknown.

More recently, in August 2022, President Biden signed into the law the Inflation Reduction Act of 2022 (the "IRA"). Among other things, the IRA has multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. Starting in 2023, a manufacturer of a drug or biological product covered by Medicare Parts B or D must pay a rebate to the federal government if the drug product's price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by Medicare Parts B or D. Additionally, starting in payment year 2026, CMS will negotiate drug prices annually for a select number of single-source Part D drugs without generic or biosimilar competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers ("PBMs") and other members of the healthcare and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area. The Federal Trade Commission in mid-2022 also launched sweeping investigations into the practices of the PBM industry that could lead to additional federal and state legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements. Significant efforts to change the PBM industry as it currently exists in the United States may affect the entire pharmaceutical supply chain and the business of other stakeholders, including pharmaceutical developers like us. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug, which could have an adverse effect on customers for our product candidates. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Human Capital

As of August 16, 2023, following the Merger, we had seven full-time employees and one part-time employee, three of whom have a Ph.D. or M.D. degree. We do not have any employees that are represented by a labor union or that have entered into a collective bargaining agreement with us.

Diversity and Inclusion

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

Compensation and Benefits

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

Safety and Wellness

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

Employee Development and Training

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

Facilities

Our current headquarters are comprised of leased office space in Boston Massachusetts. The lease term is currently month-to-month at a rate of $2,800 per month. We also have a short-term agreement to utilize membership-based co-working space in Charlottesville, Virginia. Rent expense related to this agreement was approximately $2,000 for the six months ended June 30, 2023.

We believe the space is adequate to meet our near-term needs.

Legal Proceedings

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

We believe we have meritorious defenses to the claims and intend to litigate those defenses. However, at this stage, we are unable to predict the outcome and possible loss or range of loss, if any, associated with its resolution or any potential effect the matter may have on our financial position. Depending on the outcome or resolution of this matter, it could have a material effect on our consolidated financial position, results of operations and cash flows.

In addition, from time to time, we are subject to various pending or threatened legal actions and proceedings, including those that arise in the ordinary course of its business, which may include employment matters, breach of contract disputes and stockholder litigation. Such actions and proceedings are subject to many uncertainties and to outcomes that are not predictable with assurance and that may not be known for extended periods of time.

Available Information

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