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

FORM 10-Q

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

For the quarterly period ended March 31, 2021

or

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

Commission File Number: 000-50768

ACADIA PHARMACEUTICALS INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**06-1376651**
(State of Incorporation)	**(I.R.S. Employer Identification No.)**
12830 El Camino Real, Suite 400 **San Diego, California**	**92130**
(Address of Principal Executive Offices)	**(Zip Code)**

(858) 558-2871
(Registrant's Telephone Number, Including Area Code)

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

Title of Each Class	Trading Symbol	Name of Each Exchange on Which Registered
Common Stock, par value $0.0001 per share	**ACAD**	**The Nasdaq Stock Market LLC**

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

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

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

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

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

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

Total shares of common stock outstanding as of the close of business on April 27, 2021:

Class	Number of Shares Outstanding
Common Stock, $0.0001 par value	160,179,036

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PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

ACADIA PHARMACEUTICALS INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)

	March 31, 2021 (unaudited)	December 31, 2020
Assets		
Cash and cash equivalents	$ 304,487	$ 326,028
Investment securities, available-for-sale	273,281	305,930
Accounts receivable, net	56,832	48,247
Interest and other receivables	558	2,035
Inventory	10,311	9,682
Prepaid expenses	28,515	25,694
Total current assets	673,984	717,616
Property and equipment, net	9,757	9,161
Operating lease right-of-use assets	63,111	47,283
Intangible assets, net	738	1,108
Restricted cash	5,770	5,770
Other assets	1,813	1,678
Total assets	$ 755,173	$ 782,616
Liabilities and stockholders' equity		
Accounts payable	$ 8,849	$ 8,493
Accrued liabilities	100,524	97,474
Total current liabilities	109,373	105,967
Operating lease liabilities	60,581	44,460
Other long-term liabilities	3,613	5,180
Total liabilities	173,567	155,607
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized at March 31, 2021 and December 31, 2020; no shares issued and outstanding at March 31, 2021 and December 31, 2020	—	—
Common stock, $0.0001 par value; 225,000,000 shares authorized at March 31, 2021 and December 31, 2020; 160,172,235 shares and 159,637,771 shares issued and outstanding at March 31, 2021 and December 31, 2020, respectively	16	16
Additional paid-in capital	2,633,710	2,612,663
Accumulated deficit	(2,052,154)	(1,985,706)
Accumulated other comprehensive income	34	36
Total stockholders' equity	581,606	627,009
Total liabilities and stockholders' equity	$ 755,173	$ 782,616

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

ACADIA PHARMACEUTICALS INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except per share amounts)
(Unaudited)

	Three Months Ended March 31,	
	2021	2020
Revenues		
Product sales, net	$ 106,554	$ 90,068
Total revenues	106,554	90,068
Operating expenses		
Cost of product sales	2,185	2,799
License fees and royalties	2,507	2,175
Research and development	56,973	72,636
Selling, general and administrative	111,661	101,973
Total operating expenses	173,326	179,583
Loss from operations	(66,772)	(89,515)
Interest income, net	200	2,989
Other income (expense)	145	(1,497)
Loss before income taxes	(66,427)	(88,023)
Income tax expense	21	—
Net loss	$ (66,448)	$ (88,023)
Net loss per common share, basic and diluted	$ (0.42)	$ (0.57)
Weighted average common shares outstanding, basic and diluted	160,011	155,368

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

ACADIA PHARMACEUTICALS INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)
(Unaudited)

	Three Months Ended March 31,	
	2021	2020
Net loss	$ (66,448)	$ (88,023)
Other comprehensive income:		
Unrealized (loss) gain on investment securities	(6)	1,226
Foreign currency translation adjustments	4	2
Comprehensive loss	$ (66,450)	$ (86,795)

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

ACADIA PHARMACEUTICALS INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)
(Unaudited)

	Three Months Ended March 31,	
	2021	2020
Cash flows from operating activities		
Net loss	$ (66,448)	$ (88,023)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	13,184	22,348
Amortization of premiums and accretion of discounts on investment securities	689	87
Amortization of intangible assets	370	370
(Gain) loss on strategic investment	(145)	1,497
Depreciation	525	294
Changes in operating assets and liabilities:		
Accounts receivable, net	(8,585)	(5,855)
Interest and other receivables	1,477	(842)
Inventory	(492)	(37)
Prepaid expenses	(2,821)	(3,520)
Operating lease right-of-use assets	1,589	1,187
Other assets	10	18
Accounts payable	356	(599)
Accrued liabilities	2,761	24,057
Operating lease liabilities	(1,052)	(360)
Long-term liabilities	(1,567)	376
Net cash used in operating activities	(60,149)	(49,002)
Cash flows from investing activities		
Purchases of investment securities	(127,864)	(100,773)
Maturities of investment securities	159,817	131,315
Purchases of property and equipment	(1,076)	(934)
Net cash provided by investing activities	30,877	29,608
Cash flows from financing activities		
Proceeds from issuance of common stock, net of issuance costs	7,726	3,754
Net cash provided by financing activities	7,726	3,754
Effect of exchange rate changes on cash	5	2
Net decrease in cash, cash equivalents and restricted cash	(21,541)	(15,638)
Cash, cash equivalents and restricted cash		
Beginning of period	331,798	194,467
End of period	$ 310,257	$ 178,829
Supplemental disclosure of noncash information:		
Property and equipment purchases in accounts payable and accrued liabilities	$ 45	$ 1,269

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

ACADIA PHARMACEUTICALS INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)
(Unaudited)

	Three Months Ended March 31,	
	2021	**2020**
Total stockholders' equity, beginning balances	$ 627,009	$ 699,135
Common stock:		
Beginning balance	16	15
Ending balance	16	15
Additional paid-in capital:		
Beginning balance	2,612,663	2,402,945
Issuance of common stock from exercise of stock options and units	7,726	3,754
Stock-based compensation	13,321	22,288
Ending balance	2,633,710	2,428,987
Accumulated deficit:		
Beginning balance	(1,985,706)	(1,704,122)
Net loss	(66,448)	(88,023)
Ending balance	(2,052,154)	(1,792,145)
Other comprehensive income (loss):		
Beginning balance	36	297
Other comprehensive (loss) income	(2)	1,228
Ending balance	34	1,525
Total stockholders' equity, ending balances	$ 581,606	$ 638,382

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

1. Organization and Business

Acadia Pharmaceuticals Inc. (the Company), based in San Diego, California, is a biopharmaceutical company focused on the development and commercialization of innovative medicines to address unmet medical needs in central nervous system disorders. The Company was originally incorporated in Vermont in 1993 as Receptor Technologies, Inc. and reincorporated in Delaware in 1997.

In April 2016, the U.S. Food and Drug Administration (FDA) approved the Company's first drug, NUPLAZID® (pimavanserin), for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis (PDP). NUPLAZID became available for prescription in the United States in May 2016.

2. Basis of Presentation and Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements of the Company should be read in conjunction with the audited financial statements and notes thereto as of and for the year ended December 31, 2020 included in the Company's Annual Report on Form 10-K (Annual Report) filed with the Securities and Exchange Commission (the SEC). The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States (GAAP) for interim financial information and in accordance with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, since they are interim statements, the accompanying financial statements do not include all of the information and notes required by GAAP for complete financial statements. In the opinion of management, the accompanying financial statements reflect all adjustments (consisting of normal recurring adjustments) that are necessary for a fair statement of the financial position, results of operations, cash flows, and stockholders' equity for the interim periods presented. Interim results are not necessarily indicative of results for a full year. The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and the accompanying notes. Actual results could differ materially from those estimates.

Risk and Uncertainties

The global pandemic resulting from the disease known as COVID-19, caused by a novel strain of coronavirus, SARS-CoV-2, has caused national and global economic and financial market disruptions and has adversely impacted our business. Sales of NUPLAZID in the first quarter of 2021 were negatively impacted by ongoing conditions related to the COVID-19 pandemic. At this time the Company cannot predict the magnitude of the pandemic or the full impact that it may have on the Company's financial condition, operations, suppliers, and workforce.

Cash, Cash Equivalents and Restricted Cash

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the statement of cash flows that sum to the total of the same such amounts shown in the statement of cash flows (in thousands):

	March 31, 2021		March 31, 2020	
	Beginning of period	End of period	Beginning of period	End of period
Cash and cash equivalents	$ 326,028	$ 304,487	$ 189,680	$ 173,059
Restricted cash	5,770	5,770	4,787	5,770
Total cash, cash equivalents and restricted cash shown in the statement of cash flows	$ 331,798	$ 310,257	$ 194,467	$ 178,829

Accounts Receivable

Accounts receivable are recorded net of customer allowances for distribution fees, prompt payment discounts, chargebacks, and credit losses. Allowances for distribution fees, prompt payment discounts and chargebacks are based on contractual terms. The Company estimated the current expected credit losses of its accounts receivable by assessing the risk of loss and available relevant information about collectability, including historical credit losses, existing contractual payment terms, actual payment patterns of its customers, individual customer circumstances, and reasonable and supportable forecast of economic conditions expected to exist throughout the contractual life of the receivable. Based on its assessment, as of March 31, 2021 the Company determined that an allowance for credit loss was not required.

Although the Company has not historically experienced significant credit losses, the Company's exposure may increase due to uncertainties associated with the global economic recession and other disruptions resulting from the COVID-19 pandemic.

License Fees and Royalties

The Company expenses amounts paid to acquire licenses associated with products under development when the ultimate recoverability of the amounts paid is uncertain and the technology has no alternative future use when acquired. Acquisitions of technology licenses are charged to expense or capitalized based upon management's assessment regarding the ultimate recoverability of the amounts paid and the potential for alternative future use. The Company has determined that technological feasibility for its product candidates is reached when the requisite regulatory approvals are obtained to make the product available for sale.

In connection with the FDA approval of NUPLAZID in April 2016, the Company made a one-time milestone payment of $8.0 million pursuant to its 2006 license agreement with the Ipsen Group in which the Company licensed certain intellectual property rights that complement its patent portfolio for its serotonin platform, including NUPLAZID. The Company capitalized the $8.0 million payment as an intangible asset and is amortizing the asset on a straight-line basis over the estimated useful life of the licensed patents through the second half of 2021. The Company recorded amortization expense related to its intangible asset of $0.4 million for each of the three months ended March 31, 2021 and 2020, respectively. As of March 31, 2021, estimated future amortization expense related to the Company's intangible asset was $0.7 million for the remainder of 2021.

Royalties incurred in connection with the Company's license agreement with the Ipsen Group, as disclosed in Note 9, *Commitments and Contingencies*, are expensed to license fees and royalties as revenue from product sales is recognized.

3. Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common shares and common stock equivalents outstanding for the period determined using the treasury stock method. For purposes of this calculation, stock options, employee stock purchase plan rights, restricted stock units, and warrants are considered to be common stock equivalents but are not included in the calculations of diluted net loss per share for the periods presented as their effect would be anti-dilutive. The Company incurred net losses for all periods presented and there were no reconciling items for potentially dilutive securities. More specifically, at March 31, 2021 and 2020, stock options, employee stock purchase plan rights, restricted stock units, and warrants totaling approximately 20,297,000 shares and 21,064,000 shares, respectively, were excluded from the calculation of diluted net loss per share as their effect would have been anti-dilutive.

4. Stock-Based Compensation

The following table summarizes the total stock-based compensation expense included in the Company's statements of operations for the periods presented (in thousands):

	Three Months Ended March 31,	
	2021	2020
Cost of product sales	$ 163	$ 849
Research and development	4,830	8,457
Selling, general and administrative	8,191	13,042
	$ 13,184	$ 22,348

The fair value of each employee stock option and each employee stock purchase plan right granted is estimated on the grant date under the fair value method using the Black-Scholes valuation model, which requires the Company to make a number of assumptions including the estimated expected life of the award and related volatility. The fair value of restricted stock units is estimated based on the market price of our common stock on the date of grant. The estimated fair values of stock options, purchase plan rights, and restricted stock units are then expensed over the vesting period. Performance-based stock awards vest upon the achievement of certain pre-defined company-specific performance-based criteria. Expense related to these performance-based stock awards is generally recognized ratably over the expected performance period once the pre-defined performance-based criteria for vesting becomes probable. During the three months ended March 31, 2021, the Company had a change in estimate related to the achievement of certain performance-based criteria for performance-based stock awards which resulted in a reduction in stock-based compensation expenses by approximately $6.1 million.

5. Balance Sheet Details

Inventory consisted of the following (in thousands):

	March 31, 2021	December 31, 2020
Finished goods	$ 947	$ 1,453
Work in process	7,731	6,367
Raw material	1,633	1,862
	$ 10,311	$ 9,682

Accrued liabilities consisted of the following (in thousands):

	March 31, 2021	December 31, 2020
Accrued sales allowances	$ 23,886	$ 14,115
Accrued research and development services	22,177	28,380
Accrued compensation and benefits	21,767	25,811
Accrued consulting and professional fees	18,370	18,969
Current portion of lease liabilities	6,082	5,087
Current portion of accrued branded prescription drug fees	5,203	1,845
Other	3,039	3,267
	$ 100,524	$ 97,474

6. Investments

The carrying value and amortized cost of the Company’s investments, summarized by major security type, consisted of the following (in thousands):

	March 31, 2021			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
U.S. Treasury notes	$ 139,390	$ 25	$ —	* $ 139,415
Government sponsored enterprise securities	20,004	—	(3)	20,001
Corporate debt securities	2,999	2	—	3,001
Commercial paper	110,864	7	(7)	110,864
	$ 273,257	$ 34	$ (10)	$ 273,281

	December 31, 2020			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
U.S. Treasury notes	$ 205,111	$ 6	$ (27)	$ 205,090
Government sponsored enterprise securities	10,004	—	(5)	9,999
Corporate debt securities	52,341	47	— *	52,388
Commercial paper	38,443	21	(11)	38,453
	$ 305,899	$ 74	$ (43)	$ 305,930

* Unrealized loss was less than $500.

The Company has classified all of its available-for-sale investment securities as current assets on its consolidated balance sheets based on the highly liquid nature of the investment securities and because these investment securities are considered available for use in current operations. The Company has classified all equity securities as other assets on its consolidated balance sheets.

At March 31, 2021 and December 31, 2020, the Company had 15 and 24 available-for-sale investment securities, respectively, in an unrealized loss position. The following table presents gross unrealized losses and fair value for those available-for-sale investment securities that were in an unrealized loss position as of March 31, 2021 and December 31, 2020, aggregated by investment category and length of time that the individual securities have been in a continuous loss position (in thousands):

	Less Than 12 Months		12 Months or Greater		Total	
	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses
March 31, 2021:						
U.S. Treasury notes	$ 5,011	$ — *	$ —	$ —	$ 5,011	$ — *
Government sponsored enterprise securities	15,001	(3)	—	—	15,001	(3)
Commercial paper	77,410	(7)	—	—	77,410	(7)
Total	$ 97,422	$ (10)	$ —	$ —	$ 97,422	$ (10)

	Less Than 12 Months		12 Months or Greater		Total	
	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses
December 31, 2020:						
U.S. Treasury notes	$ 129,631	$ (27)	$ —	$ —	$ 129,631	$ (27)
Government sponsored enterprise securities	10,004	(5)	—	—	10,004	(5)
Corporate debt securities	6,252	— *	—	—	6,252	— *
Commercial paper	23,466	(11)	—	—	23,466	(11)
Total	$ 169,353	$ (43)	$ —	$ —	$ 169,353	$ (43)

* Unrealized loss was less than $500.

At each reporting date, the Company performs an evaluation of impairment to determine if any unrealized losses are the result of credit losses. Impairment is assessed at the individual security level. Factors considered in determining whether a loss resulted from a credit loss or other factors include the Company's intent and ability to hold the investment until the recovery of its amortized cost basis, the extent to which the fair value is less than the amortized cost basis, the length of time and extent to which fair value has been less than the cost basis, the financial condition of the issuer, any historical failure of the issuer to make scheduled interest or principal payments, any changes to the rating of the security by a rating agency, any adverse legal or regulatory events affecting the issuer or issuer's industry, any significant deterioration in economic conditions.

The Company does not intend to sell the investments in unrealized loss position and it is unlikely that the Company will be required to sell the investments before the recovery of their amortized cost basis. Based on its evaluation, the Company determined its year-to-date credit losses related to its available-for-sale securities were immaterial at March 31, 2021.

Although the Company has not historically experienced significant losses on its investments, the Company's exposure may increase due to uncertainties associated with the global economic recession and other disruptions resulting from the COVID-19 pandemic.

7. Fair Value Measurements

The Company's investments include cash equivalents, available-for-sale investment securities consisting of money market funds, U.S. Treasury notes, and high quality, marketable debt instruments of corporations and government sponsored enterprises in accordance with the Company's investment policy, and equity securities. The Company's investment policy defines allowable investment securities and establishes guidelines relating to credit quality, diversification, and maturities of its investments to preserve principal and maintain liquidity. All investment securities have a credit rating of at least Aa3/AA- or better, or P-1/A-1 or better, as determined by Moody's Investors Service or Standard & Poor's.

The Company's cash equivalents, available-for-sale investment securities and equity securities are classified within the fair value hierarchy as defined by authoritative guidance. The Company's investment securities and equity securities classified as Level 1 are valued using quoted market prices. The Company obtains the fair value of its Level 2 financial instruments from third-party pricing services. The pricing services utilize industry standard valuation models whereby all significant inputs, including benchmark yields, reported trades, broker/dealer quotes, issuer spreads, bids, offers, or other market-related data, are observable. The Company validates the prices provided by the third-party pricing services by reviewing their pricing methods and matrices, and obtaining market values from other pricing sources. After completing the validation procedures, the Company did not adjust or override any fair value measurements provided by these pricing services as of March 31, 2021 and December 31, 2020.

The Company does not hold any securities classified as Level 3, which are securities valued using unobservable inputs. The Company has not transferred any investment securities between the classification levels.

The recurring fair value measurements of the Company's cash equivalents, available-for-sale investment securities and equity securities at March 31, 2021 and December 31, 2020 consisted of the following (in thousands):

		Fair Value Measurements at Reporting Date Using		
	March 31, 2021	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market fund	$ 277,224	$ 277,224	$ —	$ —
U.S. Treasury notes	139,415	139,415	—	—
Equity securities	1,454	1,454	—	—
Government sponsored enterprise securities	20,001	—	20,001	—
Corporate debt securities	3,001	—	3,001	—
Commercial paper	135,856	—	135,856	—
	$ 576,951	$ 418,093	$ 158,858	$ —

		Fair Value Measurements at Reporting Date Using		
	December 31, 2020	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market fund	$ 300,339	$ 300,339	$ —	$ —
U.S. Treasury notes	230,088	230,088	—	—
Equity securities	1,309	1,309	—	—
Government sponsored enterprise securities	9,999	—	9,999	—
Corporate debt securities	52,388	—	52,388	—
Commercial paper	38,453	—	38,453	—
	$ 632,576	$ 531,736	$ 100,840	$ —

8. Stockholders' Equity

In August 2020, the Company entered into an Agreement and Plan of Merger (the Merger Agreement) with CerSci Therapeutics Incorporated (CerSci). Approximately 1.2 million shares of the Company's common stock with a value of $44.3 million were issued to CerSci's former equity holders.

9. Commitments and Contingencies

Royalty Payments

Pursuant to the terms of its 2006 license agreement with the Ipsen Group, the Company is required to make royalty payments of two percent of net sales of NUPLAZID. This obligation terminates in 2021.

License and Merger Agreements

The Company has entered into various collaboration, licensing and merger agreements which provide the Company with rights to certain know-how, technology and patent rights. The agreements generally include upfront license fees, development and commercial milestone payments upon achievement of certain clinical and commercial development and annual net sales milestones, as well as royalties calculated as a percentage of product revenues, with rates that vary by agreement. The Company did not incur any costs in upfront and license payments for the three months ended March 31, 2021 and incurred $10.0 million in upfront and license payments for the three months ended March 31, 2020. As of March 31, 2021, the Company may be required to make milestone payments up to $2.2 billion in the aggregate.

In August 2018, the Company entered into a license agreement with Neuren and obtained exclusive North American rights to develop and commercialize trofinetide for Rett syndrome and other indications. Under the terms of the agreement, the Company paid Neuren an upfront license fee of $10.0 million and it may be required to pay up to an additional $455.0 million in milestone payments based on the achievement of certain development and annual net sales milestones. In addition, the Company may be required to pay Neuren tiered, escalating, double-digit percentage royalties based on net sales. The license agreement was accounted for as an asset acquisition and the upfront cash payment of $10.0 million was expensed to research and development in the third quarter of 2018 as there is no alternative use for the asset.

In March 2020, the Company entered into a license agreement and research collaboration with Vanderbilt University and obtained exclusive worldwide rights to develop and commercialize novel drug candidates targeting positive allosteric modulators of the muscarinic M1 receptor (the M1 PAM program) with the potential to treat a range of central nervous system disorders. Under the terms of the agreement, the Company paid Vanderbilt University an upfront license fee of $10.0 million and may be required to pay up to $515.0 million in milestone payments based on the achievement of certain clinical and commercial development and annual net sales milestones. In addition, the Company may be required to pay Vanderbilt University tiered royalties based on net sales. Furthermore, the Company is required to spend a minimum annual amount in development and the pursuit of regulatory approval for the M1 PAM compounds over the first three years of the license agreement. Such amounts are not material to the Company. The license agreement was accounted for as an asset acquisition and the upfront cash payment of $10.0 million was expensed to research and development in the first quarter of 2020 as there is no future alternative use for the assets.

In August 2020, the Company entered into the Merger Agreement with CerSci. The lead development program is a unique Reactive Species Decomposition Accelerant, a non-opioid, mechanism focused on interrupting pathways that sensitize neurons to pain. The portfolio contains additional preclinical stage programs, including brain penetrant compounds, with potential for symptomatic and disease modifying treatment utility in neurodegenerative diseases. The Company incurred an aggregate of $52.8 million in upfront consideration and transaction costs, of which, $44.3 million was paid through the issuance of approximately 1.2 million shares of the Company's common stock. In addition, under the terms of the Merger Agreement, the Company may be required to pay CerSci's former equity holders up to $887.0 million in cash upon the achievement of certain development, commercialization and sales milestones, in addition to tiered cash royalties in the mid-single digits based on annual net sales. As substantially all of the fair value of the gross assets acquired was concentrated in the in-process research and development intangible assets acquired, the Company concluded that this transaction did not meet the definition of a business combination pursuant to FASB Accounting Standard Codification Topic 805, Business Combinations. As such, the transaction was accounted for as an asset acquisition and the upfront consideration of $45.7 million was expensed to research and development in the third quarter of 2020 as there is no future alternative use for the assets.

Corporate Credit Card Program

In connection with the Company's credit card program, the Company established a letter of credit for $2.0 million, which has automatic annual extensions and is fully secured by restricted cash.

Fleet Program

In connection with the Company's fleet program, the Company established a letter of credit for $0.4 million, which has automatic annual extensions and is fully secured by restricted cash.

Legal Proceedings

Between July 19 and August 3, 2018, following negative publicity about NUPLAZID, three purported company stockholders filed putative securities class action complaints (captioned Staublein v. Acadia Pharmaceuticals, Inc., Case No. 18-cv-01647, Stone v. Acadia Pharmaceuticals Inc., Case No. 18-cv-01672, and Barglow v. Acadia Pharmaceuticals Inc., Case No. 18-cv-01812) in the U.S. District Court for the Southern District of California against the Company and certain of its current and former executive officers. Thereafter, several putative lead plaintiffs filed motions to consolidate the cases and to appoint a lead plaintiff. On January 3, 2019, the Court consolidated the cases under the caption In re Acadia Pharmaceuticals Inc. Securities Litigation, Case No. 18-cv-01647, and took the lead plaintiff motions under submission. On February 26, 2019, the Court appointed a lead plaintiff and lead counsel. Lead plaintiff filed a consolidated complaint on April 15, 2019. The consolidated complaint generally alleges that defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 by making materially false and misleading statements regarding the Company's business, operations, and prospects by failing to disclose that adverse events and safety concerns regarding NUPLAZID threatened initial and continuing FDA approval, and by failing to disclose that the Company engaged in business practices likely to attract regulatory scrutiny. The consolidated complaint seeks unspecified monetary damages and other relief. Defendants filed a motion to dismiss the consolidated complaint on June 7, 2019. On June 1, 2020, the Court granted the motion in part and gave lead plaintiff leave to file an amended complaint. On July 16, 2020, lead plaintiff filed the amended complaint. Defendants filed a motion to dismiss the amended complaint on August 28, 2020. Lead plaintiff opposed the motion on September 15, 2020. Defendants' reply in support of the motion to dismiss was filed on November 11, 2020. On March 29, 2021, the Court granted the defendants' motion to dismiss with leave to amend. On April 16, 2021, lead plaintiff filed a third amended complaint. On April 20, 2021, the Court entered a schedule for filing and briefing a motion to dismiss the third amended complaint. The defendants' motion to dismiss the third amended complaint is due on May 31, 2021. The plaintiff's opposition to the motion is due on July 12, 2021. The defendants' reply in support of the motion is due on August 11, 2021. The motion is set to be heard on October 1, 2021.

On February 7, 2020, a purported company stockholder filed a derivative complaint (captioned Barney v. Davis et al., Case No. 20-cv-0238) in the U.S. District Court for the Southern District of California against the Company's directors and certain of its current and former executive officers. The complaint asserts claims for breach of fiduciary duty, waste of corporate assets, and unjust enrichment arising from allegations similar to those in the federal securities class action described above. On September 9, 2020, the Court substituted plaintiffs and re-captioned the case Shumacher v. Davis et al., Case No. 20-cv-0238. On June 23, 2020, a second derivative complaint (captioned Lazarus v. Davis et al., Case No. 20-cv-0843) was filed in the U.S. District Court for the District of Delaware. On September 9, 2020, the Court transferred the Lazarus case to the U.S. District Court for the Southern District of California and re-captioned the case Lazarus v. Davis et al., Case No. 20-cv-1774. On January 15, 2021, the Court consolidated the cases under the name In re ACADIA Pharmaceuticals Inc. Stockholder Derivative Litigation, Case No. 20-cv-0238, appointed lead counsel for the plaintiffs, and designated the complaint in the Shumacher case as the operative complaint. The consolidated case is stayed until the defendants in the federal securities class action answer, or the federal securities class action is dismissed with prejudice and all appeals are exhausted, or any party to the stipulation to stay gives 15 days' written notice that it no longer consents to the voluntary stay.

On July 24, 2020, the Company filed complaints against (i) Aurobindo Pharma Limited and its affiliate Aurobindo Pharma USA, Inc. and (ii) Teva Pharmaceuticals USA, Inc. and its affiliate Teva Pharmaceutical Industries Ltd., and on July 30, 2020, the Company filed complaints against (i) Hetero Labs Limited and its affiliates Hetero Labs Limited Unit-V and Hetero USA Inc., (ii) MSN Laboratories Private Ltd. and its affiliate MSN Pharmaceuticals, Inc., and (iii) Zydus Pharmaceuticals (USA) Inc. and its affiliate Cadila Healthcare Limited. These complaints, which were filed in the United States District Court for the District of Delaware, allege infringement of certain of the Company's Orange Book-listed patents covering NUPLAZID. The cases have been assigned to the Honorable Richard G. Andrews. On September 1, 2020, Aurobindo filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On September 22, 2020, the Company filed its answer to Aurobindo's counterclaims. On August 31, 2020, Teva filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On September 21, 2020, the Company filed its answer to Teva's counterclaims. On October 5, 2020, Hetero filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On October 26, 2020, the Company filed its answer to Hetero's counterclaims. On September 30, 2020, MSN filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity regarding certain of the Company's Orange Book-listed patents covering NUPLAZID. On November 5, 2020, the Company filed its first amended complaint against MSN in the United States District Court for the District of Delaware, alleging infringement of certain of the Company's Orange Book-listed patents covering NUPLAZID. On November 19, 2020, MSN filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity regarding certain of the Company's Orange Book-listed patents covering NUPLAZID. On December 10, 2020, the Company filed its answer to MSN's counterclaims. On November 2, 2020, Zydus filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On November 23, 2020, the Company filed its answer to Zydus's counterclaims. On December 8, 2020, the parties' joint proposed scheduling order was entered by Judge Andrews. On April 7, 2021, the Company filed its first amended complaints against Hetero and Teva and its second amended complaint against Hetero, to include an additional Orange Book-listed patent covering NUPLAZID. On April 8, 2021, the Company filed its first amended complaint against Zydus and on April 9, 2021, the Company filed its first amended complaint against Aurobindo. On April 20, 2021, MSN filed its answer, affirmative defenses, and counterclaims to the Company's second amended complaint, seeking declaratory judgments of noninfringement and invalidity regarding certain of the Company's Orange Book-listed patents covering NUPLAZID. On April 21, 2021, Teva filed its answer, affirmative defenses, and counterclaims to the Company's first amended complaint, seeking declaratory judgments of noninfringement and invalidity. On April 22, 2021, Zydus filed its answer, affirmative defenses, and counterclaims to the Company's first amended complaint, seeking declaratory judgments of noninfringement and invalidity. A joint trial in the matters is scheduled for May 15, 2023.

The Company entered into an agreement effective April 22, 2021 with Hetero settling all claims and counterclaims in the litigation. The agreement allows Hetero to launch its generic pimavanserin product on July 27, 2038, subject to certain triggers for earlier launch. The Hetero case was dismissed by joint agreement on May 3, 2021.

On April 19, 2021, a purported Company stockholder filed a putative securities class action complaint (captioned Marechal v. Acadia Pharmaceuticals, Inc., Case No. 21-cv-0762) in the U.S. District Court for the Southern District of California against the Company and certain of its current executive officers. The complaint generally alleges that defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 by making materially false and misleading statements regarding the Company's business, operations, and prospects by failing to disclose that the materials submitted in support of its sNDA seeking approval of pimavanserin for the treatment of hallucinations and delusions associated with dementia-related psychosis contained statistical and design deficiencies and that the FDA unlikely to approve the sNDA in its current form. The complaint seeks unspecified monetary damages and other relief.

Management currently believes that none of the foregoing claims or actions pending against the Company as of March 31, 2021 is likely to have, individually or in the aggregate, a material adverse effect on the Company's business, liquidity, financial position, or results of operations. Given the unpredictability inherent in litigation, however, the Company cannot predict the outcome of these matters. The Company is unable to estimate possible losses or ranges of losses that may result from these matters, and therefore it has not accrued any amounts in connection with these matters other than attorneys' fees incurred to date.

10. Leases

The Company leases facilities and certain equipment under noncancelable operating leases with remaining lease terms of 0.8 years to 10.2 years, some of which include options to extend for up to two five-year terms. These optional periods were not considered in the determination of the right-of-use asset or the lease liability as the Company did not consider it reasonably certain that it would exercise such options.

The operating lease costs were as follows (in thousands):

	Three Months Ended March 31,	
	2021	2020
Operating lease cost	$ 2,378	$ 1,487

Supplemental cash flow information related to the Company's leases were as follows (in thousands):

	Three Months Ended March 31,	
	2021	2020
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flows from operating leases	$ 1,014	$ 1,291
Right-of-use assets obtained in exchange for operating lease obligations:	17,417	276

The balance sheet classification of the Company's lease liabilities was as follows (in thousands):

	March 31, 2021	December 31, 2020
Operating lease liabilities		
Current portion included in accrued liabilities	$ 6,082	$ 5,087
Operating lease liabilities	60,581	44,460
Total operating lease liabilities	$ 66,663	$ 49,547

Maturities of lease liabilities were as follows (in thousands):

	Operating Leases
Remainder of 2021	$ 4,071
Years ending December 31,	
2022	8,739
2023	8,506
2024	8,275
2025	8,355
Thereafter	44,276
Total lease payments	82,222
Less:	
Imputed interest	(15,559)
Total operating lease liabilities	$ 66,663

Operating lease liabilities are based on the net present value of the remaining lease payments over the remaining lease term. In determining the present value of lease payments, the Company uses its incremental borrowing rate based on the information available at the lease commencement date. As of March 31, 2021, the weighted average remaining lease term was 9.6 years and the weighted average discount rate used to determine the operating lease liability was 4.4%.

In the fourth quarter of 2018, the Company entered into an agreement to lease the 4th and 5th floors of corporate office space in San Diego, California with total minimum lease payments of $50.4 million over an initial term of 10 years and 9 months. In February 2020, the Company entered into the first amendment to the lease agreement to lease the 2nd floor of corporate office space in San Diego, California with total minimum lease payments of $25.3 million over an initial term of approximately 10 years and 7 months. In March 2020, the Company entered into the second amendment to the lease agreement which increased the total minimum lease payments of the original corporate office space to $51.4 million. In the third quarter of 2020, the lease for the 4th and 5th floors of corporate office space commenced and the Company capitalized a right of use asset and related lease liability of $40.3 million. During the three months ended March 31, 2021, the lease for the 2nd floor of corporate office space commenced and the Company capitalized a right of use asset and related lease liability of $19.2 million. In connection with this lease and the amendment, the Company established a letter of credit for $3.1 million, which has automatic annual extensions and is fully secured by restricted cash.

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

The following discussion and analysis of our consolidated financial condition and results of operations should be read in conjunction with our unaudited condensed consolidated financial statements and related notes included in this quarterly report on Form 10-Q, or this Quarterly Report, and the audited financial statements and notes thereto as of and for the year ended December 31, 2020 included with our Annual Report on Form 10-K, or our Annual Report, filed with the Securities and Exchange Commission, or SEC. Past operating results are not necessarily indicative of results that may occur in future periods.

This Quarterly Report contains forward-looking statements. These forward-looking statements involve a number of risks and uncertainties. Such forward-looking statements include statements about the benefits to be derived from NUPLAZID® (pimavanserin), trofinetide and other drug candidates, the potential market opportunities for pimavanserin and other drug candidates, our strategy for the commercialization of NUPLAZID, our plans for exploring and developing pimavanserin for indications other than in Parkinson's disease psychosis, our plans and timing with respect to seeking regulatory approvals, the potential commercialization of any of our drug candidates that receive regulatory approval, the progress, timing, results or implications of clinical trials and other development activities involving NUPLAZID and other drug candidates, our strategy for discovering, developing and, if approved, commercializing drug candidates, our existing and potential future collaborations, our estimates of future payments, revenues and profitability, our estimates regarding our capital requirements, future expenses and need for additional financing, the potential or expected impact of the global COVID-19 pandemic on our business, possible changes in legislation, and other statements that are not historical facts, including statements which may be preceded by the words "believes," "expects," "hopes," "may," "will," "plans," "intends," "estimates," "could," "should," "would," "continues," "seeks," "aims," "projects," "predicts," "pro forma," "anticipates," "potential" or similar words. For forward-looking statements, we claim the protection of the Private Securities Litigation Reform Act of 1995. Readers of this Quarterly Report are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date on which they are made. We undertake no obligation to update or revise publicly any forward-looking statements. Actual events or results may differ materially from our expectations. Important factors that could cause actual results to differ materially from those stated or implied by our forward-looking statements include, but are not limited to, the risk factors set forth under the section captioned "Risk Factors" in this Quarterly Report.

Overview

Impact of COVID-19 on our Business

On March 11, 2020, the World Health Organization declared a pandemic resulting from the disease known as COVID-19 caused by a novel strain of coronavirus, SARS-CoV-2. As a result of the pandemic, there have been changes in the practice of medical care and medical education. For example, many health care providers initially expanded their utilization of telemedicine to conduct patient visits, and in many regions within the United States the ability of our commercial and medical field teams to call upon medical clinics, hospitals, long-term care facilities and skilled nursing facilities was restricted or converted to virtual access. Currently, health care providers are conducting patient visits in-person and through telemedicine and our sales force has been able to call upon medical clinics, hospitals, long-term care facilities and skilled nursing facilities either in person in accordance with applicable regulatory guidance and local policies or virtually. Most medical congresses, an important means for medical education are continuing to be conducted virtually and enrollment in clinical trials is being assessed based on local COVID-19 conditions and regional regulation and public health guidance.

In an effort to protect the health and safety of our employees and our stakeholders, we adopted recommended policies applicable to office-based employees such as working from home, limiting the number of employees on site, and limiting business travel. For our field-based commercial and medical affairs personnel, we have instituted a protocol to assess the safety of employees to conduct in-person interactions on a localized basis in accordance with applicable regulatory guidance and local policies.

Since the beginning of the pandemic, we have been able to provide an uninterrupted supply of NUPLAZID to patients. We are monitoring our supply chain closely and do not anticipate disruptions in our ability to continue delivering NUPLAZID to patients.

In addition, our business could be adversely affected by the effects of public health threats, including the COVID-19 pandemic. During the first quarter of 2021, sales of NUPLAZID were negatively impacted by ongoing conditions related to the pandemic, including a reduction in patient office visits and a further decline in census at long-term care facilities. The impacts and pace of recovery resulting from the pandemic are difficult to predict at this time, and no assurances can be given that the pandemic will not have significant additional impacts on our business, results of operations, financial condition and prospects.

Background

We are a biopharmaceutical company focused on the development and commercialization of innovative medicines that address unmet medical needs in central nervous system (CNS) disorders. We have a portfolio of product opportunities led by our novel drug, NUPLAZID (pimavanserin), which was approved by the U.S. Food and Drug Administration (FDA) in April 2016 for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis (PDP). We hold worldwide commercialization rights to pimavanserin. NUPLAZID is available in 34 mg capsule and 10 mg tablet dosage forms.

We believe that pimavanserin has the potential to address important unmet medical needs in neurological and psychiatric disorders in addition to PDP and we plan to continue to study the use of pimavanserin in multiple disease states. For example, we believe dementia-related psychosis (DRP), represents one of our most important opportunities for further development. In September 2019, we announced that our Phase 3 HARMONY study, a double-blind, placebo-controlled relapse prevention trial evaluating pimavanserin for the treatment of DRP, would be stopped early as part of a planned interim efficacy analysis for positive efficacy as it met the primary endpoint, demonstrating a highly statistically significant longer time to relapse of psychosis with pimavanserin compared to placebo. In December 2019, we announced top-line results from the HARMONY study in connection with a presentation at the 12th Clinical Trials on Alzheimer's Disease (CTAD) Meeting. Pimavanserin met the primary endpoint of the study by significantly reducing the risk of relapse of psychosis by 2.8 fold compared to placebo (HR = 0.353; one-sided p=0.0023). In addition, pimavanserin met the key secondary endpoint in the study by significantly reducing the risk of discontinuation of any reason by 2.2 fold (HR = 0.452; one-sided p=0.0024). Pimavanserin was well-tolerated over the entire nine-month study duration. Patients receiving pimavanserin treatment had no worsening in cognition or motor symptoms from baseline. In June 2020, we submitted to the FDA a supplemental New Drug Application (sNDA) for NUPLAZID for the treatment of hallucinations and delusions associated with DRP. In July 2020 the FDA notified us of their filing of our sNDA with a Prescription Drug User Fee Act (PDUFA) target action date of April 3, 2021. In April, 2021 the FDA issued a complete response letter (CRL) indicating that it had completed its review of the sNDA and determined that the application could not be approved in its present form. Despite prior agreements with the FDA's Division of Psychiatry regarding the pivotal Phase 3 HARMONY study design targeting a broad DRP patient population analyzed as a single group, the Division, in the CRL, cited a lack of statistical significance in some of the subgroups of dementia, and insufficient numbers of patients with certain less common dementia subtypes as lack of substantial evidence of effectiveness to support approval. We plan to meet with the FDA to address the CRL and determine potential next steps toward approval of pimavanserin in DRP. An estimated 8.0 million people in the United States are living with dementia, and studies suggest that approximately 30% of dementia patients, or 2.4 million people, have psychosis, commonly consisting of delusions and hallucinations. Approximately 1.2 million patients in the United States are currently treated for DRP. In the fourth quarter of 2017, the FDA granted Breakthrough Therapy Designation for pimavanserin for the treatment of DRP.

Schizophrenia remains a disease area with high unmet need and we are currently exploring the utility of pimavanserin in this area. Specifically, we are evaluating pimavanserin as an adjunctive treatment for negative symptoms of schizophrenia, for which there are currently no FDA-approved therapies. Negative symptoms of schizophrenia have been associated with poor long-term outcomes and disability even when the positive symptoms are well controlled, representing a high unmet need. In November 2019, we announced positive top-line results from our Phase 2 ADVANCE study that evaluated the efficacy of adjunctive pimavaserin compared to placebo in 403 patients with predominantly negative symptoms of schizophrenia who have achieved adequate control of positive symptoms with their existing antipsychotic treatment. Pimavanserin demonstrated a statistically significant improvement on the study's primary endpoint, the change from baseline to week 26 on the Negative Symptom Assessment-16 (NSA-16) total score compared to placebo (p=0.043). A greater improvement in the NSA-16 total score compared to placebo was observed in patients who received the highest pimavanserin dose of 34 mg (n=107; unadjusted p=0.0065). 53.8% of patients who were randomized to receive pimavanserin completed the trial on 34 mg, 44.7% on 20 mg, and 1.5% on 10 mg. In the study, pimavanserin did not separate from placebo on the key secondary endpoint, the Personal and Social Performance (PSP), scale. In the third quarter of 2020, we initiated a second pivotal study, ADVANCE-2. The Phase 3 study is evaluating the efficacy of pimavanserin 34 mg once daily compared to placebo in approximately 386 patients with predominantly negative symptoms of schizophrenia who have achieved adequate control of positive symptoms with their existing antipsychotic treatment.

In August 2018, we acquired an exclusive North American license to develop and commercialize trofinetide for Rett syndrome and other indications from Neuren. Rett syndrome is a debilitating neurological disorder that occurs predominantly in females following apparently normal development for the first six months of life. Typically, between six to eighteen months of age, patients experience a period of rapid decline with loss of purposeful hand use and spoken communication and inability to independently conduct activities of daily living. Symptoms also include seizures, disorganized breathing patterns, scoliosis and sleep disturbances. Trofinetide is a novel synthetic analog of the amino-terminal tripeptide of insulin-like growth factor 1 (IGF-1), designed to treat the core symptoms of Rett syndrome by reducing neuroinflammation and supporting synaptic function. Trofinetide has been granted FDA Fast Track Status and an Orphan Drug Designation in the U.S. and an Orphan Designation in Europe, as well as Rare Pediatric Disease designation in the U.S. Currently, there are no approved medicines for the treatment of Rett syndrome. In October 2019, we initiated the Phase 3 LAVENDER randomized, double-blind placebo-controlled study evaluating trofinetide in girls and young women 5-20 years of age with Rett syndrome. Based on current enrollment projections, we expect results from our LAVENDER study in the fourth quarter of 2021.

In August 2020, we entered into a Merger Agreement with CerSci. The lead product candidate, ACP-044, is a novel, potentially first-in-class, orally administered, peripherally-restricted, non-opioid analgesic being evaluated for the treatment of pain. The mechanism of action is designed to interrupt multiple pain pathways and sensitization of neurons to pain, by accelerating the decomposition of peroxynitrite, a nitroxidative agent elevated following tissue injury. In addition, through the acquisition, we obtained a portfolio of preclinical stage molecules, including brain penetrant compounds, with potential for symptomatic and disease modifying utility in neurodegenerative diseases. ACP-044 has shown promising results in animal models evaluating incisional, inflammatory, and neuropathic pain, as well as favorable tolerability and pharmacokinetic properties in Phase 1 trials. In March, 2021 we initiated a Phase 2 study evaluating ACP-044 for the treatment of postoperative pain following bunionectomy surgery. In addition, we plan to initiate a Phase 2 study evaluating ACP-044 for the treatment of pain associated with osteoarthritis in the second quarter of 2021.

In March 2020, we acquired an exclusive worldwide license to develop and commercialize novel drug candidates targeting positive allosteric modulators (PAMs) of the muscarinic M1 receptor with the potential to treat cognition in dementia and psychotic symptoms in schizophrenia, from Vanderbilt University. Under the agreement, we obtained exclusive worldwide rights to certain highly selective M1 PAMs, which represent a promising approach for improving cognitive function and other neuropsychiatric symptoms in patients suffering from CNS disorders. The agreement includes a portfolio of candidates, with molecules at various stages of testing, including the lead compound, ACP-319, which is in Phase 1 testing, and several additional compounds in pre-clinical development as well as any additional compounds generated in an ongoing discovery program.

We have incurred substantial operating losses since our inception due in large part to expenditures for our research and development activities and more recently for our sales and marketing activities related to the commercialization of NUPLAZID. As of March 31, 2021, we had an accumulated deficit of $2.1 billion. We expect to continue to incur operating losses for the next few years as we advance our programs and incur significant development and commercialization costs.

We maintain a website at www.acadia-pharm.com to which we regularly post copies of our press releases as well as additional information about us. Our filings with the SEC are available free of charge through our website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Interested persons can subscribe on our website to email alerts that are sent automatically when we issue press releases, file our reports with the SEC or post certain other information to our website. Information contained in our website does not constitute a part of this Quarterly Report or our other filings with the SEC.

Financial Operations Overview

Product Revenues

Net product sales consist of sales of NUPLAZID, our first and only commercial product to date. The FDA approved NUPLAZID in April 2016 and we launched the product in the United States in May 2016.

Cost of Product Sales

Cost of product sales consists of third-party manufacturing costs, freight, and indirect overhead costs associated with sales of NUPLAZID. Cost of product sales may also include period costs related to certain inventory manufacturing services, excess or obsolete inventory adjustment charges, unabsorbed manufacturing and overhead costs, and manufacturing variances.

License Fees and Royalties

License fees and royalties consist of milestone payments expensed or capitalized and subsequently amortized under our 2006 license agreement with the Ipsen Group. License fees and royalties also include royalties of two percent due to the Ipsen Group based upon net sales of NUPLAZID.

Research and Development Expenses

Our research and development expenses have consisted primarily of fees paid to external service providers, salaries and related personnel expenses, facilities and equipment expenses, and other costs incurred related to pre-commercial product candidates. We charge all research and development expenses to operations as incurred. Our research and development activities have primarily focused on NUPLAZID (pimavanserin) which was approved by the FDA for the treatment of hallucinations and delusions associated with PDP in April 2016. We currently are responsible for all costs incurred in the ongoing development of pimavanserin and we expect to continue to make substantial investments in clinical studies of pimavanserin for indications other than PDP, including schizophrenia. In April 2021, the FDA issued a CRL in response to our sNDA seeking approval of pimavanserin for the treatment of hallucinations and delusions associated with DRP. At this time, due to the risks in the regulatory and approval processes, we are unable to estimate with any certainty the costs we will incur for the continued development of pimavanserin for DRP, including work necessary to support a resubmission of the sNDA. Additionally, in connection with the FDA approval of NUPLAZID, we committed to conduct post-marketing studies, including a randomized, placebo-controlled withdrawal study in patients treated with NUPLAZID and a randomized, placebo-controlled eight-week study or studies in predominantly frail and elderly patients that would add to the NUPLAZID safety database by exposing an aggregate of at least 500 patients to NUPLAZID. We will be responsible for all costs incurred for these post-marketing studies. We expect to incur increased research and development expenses as a result of our development of trofinetide under the exclusive North American license granted to us by Neuren, including the costs of the Phase 3 LAVENDER study and a long-term extension study. We also expect to incur increased research and development expenses as a result of our recently executed exclusive worldwide license agreement for the M1 PAM program, including ACP-319, and the research collaboration with Vanderbilt University, as well as our recent acquisition of CerSci and its ACP-044 product candidate and preclinical programs. We currently are responsible for all costs incurred in the development of trofinetide, ACP-044, ACP-319 and the M1 PAM program, as well as milestone payments subject to achievement of development milestones.

We use external service providers to manufacture our product candidates and for the majority of the services performed in connection with the preclinical and clinical development of pimavanserin, trofinetide, ACP-044 and ACP-319. Historically, we have used our internal research and development resources, including our employees and discovery infrastructure, across several projects and many of our costs have not been attributable to a specific project. Accordingly, we have not reported our internal research and development costs on a project basis. To the extent that external expenses are not attributable to a specific project, they are included in other early stage programs. The following table summarizes our research and development expenses for the three months ended March 31, 2021 and 2020 (in thousands):

	Three Months Ended March 31,	
	2021	2020
Costs of external service providers:		
NUPLAZID (pimavanserin)	$ 17,762	$ 28,994
Trofinetide	7,958	9,633
Early stage programs	4,668	1,620
Upfront and milestone payments*	5,000	10,000
Subtotal	35,388	50,247
Internal costs	16,755	13,932
Stock-based compensation	4,830	8,457
Total research and development	$ 56,973	$ 72,636

* Includes upfront and milestone consideration as well as transaction costs associated with acquired in-process research and development.

Although NUPLAZID was approved by the FDA for the treatment of hallucinations and delusions associated with PDP, at this time, due to the risks inherent in regulatory requirements and clinical development, we are unable to estimate with certainty the costs we will incur for the ongoing or additional development of pimavanserin in additional indications, including those within DRP and schizophrenia, and the development of trofinetide, ACP-044, ACP-319 and the M1 PAM program. Due to these same factors, we are unable to determine with any certainty the anticipated completion dates for our current research and development programs. Clinical development and regulatory approval timelines, probability of success, and development costs vary widely. While our current development efforts are primarily focused on advancing the development of pimavanserin in additional indications other than PDP, we anticipate that we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success of each product candidate, as well as an ongoing assessment of the commercial potential of each opportunity and our financial position. We cannot forecast with any degree of certainty which product opportunities will be subject to future collaborative or licensing arrangements, when such arrangements will be secured, if at all, and to what degree any such arrangements would affect our development plans and capital requirements. Similarly, we are unable to estimate with certainty the costs we will incur for post-marketing studies that we committed to conduct in connection with FDA approval of NUPLAZID.

We expect our research and development expenses to increase and continue to be substantial as we conduct studies pursuant to our post-marketing commitments and pursue the development of pimavanserin in additional indications other than PDP, including our studies within schizophrenia, and the development of trofinetide in Rett syndrome, the development of ACP-044 for pain management, and the development of ACP-319. The lengthy process of completing clinical trials and supporting development activities and seeking regulatory approval for our product opportunities requires the expenditure of substantial resources. Any failure by us or delay in completing clinical trials, or in obtaining regulatory approvals, could cause our research and development expenses to increase and, in turn, have a material adverse effect on our results of operations.

Selling, General and Administrative Expenses

Our selling, general and administrative expenses consist of salaries and other related costs, including stock-based compensation expense, for our commercial personnel, including our specialty sales force, our medical education professionals, and our personnel serving in executive, finance, business development, and business operations functions. Also included in selling, general and administrative expenses are fees paid to external service providers to support our commercial activities associated with NUPLAZID, professional fees associated with legal and accounting services, costs associated with patents and patent applications for our intellectual property and charitable donations to independent charitable foundations that support Parkinson’s disease patients generally. We expect our selling, general and administrative expenses to increase in future periods to support commercial activities associated with NUPLAZID and our further development of pimavanserin in additional indications other than PDP.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based on our condensed consolidated financial statements. We have identified the accounting policies that we believe require application of management’s most subjective judgments, often requiring the need to make estimates about the effect of matters that are inherently uncertain and may change in subsequent periods. Our actual results may differ substantially from these estimates under different assumptions or conditions. There have been no significant changes to our critical accounting policies and estimates since December 31, 2020. For a description of our critical accounting policies that affect our significant judgments and estimates used in the preparation of our consolidated financial statements, refer to our Annual Report.

Results of Operations

Fluctuations in Operating Results

Our results of operations have fluctuated significantly from period to period in the past and are likely to continue to do so in the future. We anticipate that our quarterly and annual results of operations will be impacted for the foreseeable future by several factors, including the progress and timing of expenditures related to our commercial activities associated with NUPLAZID and the extent to which we generate revenue from product sales, our development of pimavanserin in additional indications other than PDP, our development of trofinetide, ACP-044, ACP-319, and the M1 PAM program, and the progress and timing of expenditures related to studies of NUPLAZID in PDP pursuant to our post-marketing commitments. Further, we expect our sales allowances to vary from quarter to quarter due to fluctuations in our Medicare Part D Coverage Gap liability and the volume of purchases eligible for government mandated discounts and rebates, as well as changes in discount percentages that may be impacted by potential future price increases and other factors. We cannot predict with certainty what the full impact of the COVID-19 pandemic may have on our business, results of operations, financial condition and prospects. Due to these fluctuations, we believe that the period-to-period comparisons of our operating results are not a good indication of our future performance.

Comparison of the Three Months Ended March 31, 2021 and 2020

Product Sales, Net

Net product sales, comprised of NUPLAZID, were $106.6 million and $90.1 million for the three months ended March 31, 2021 and 2020, respectively. The increase in net product sales of $16.5 million was primarily due to growth in NUPLAZID unit sales of approximately 4% in the three months ended March 31, 2021 as compared to the same period in 2020. Also contributing to the increase was a higher average gross selling price of NUPLAZID in 2021 compared to 2020.

The following table provides a summary of activity with respect to our sales allowances and accruals for the three months ended March 31, 2021 (in thousands):

	Distribution Fees, Discounts & Chargebacks	Co-Pay Assistance	Rebates, Data Fees & Returns	Total
Balance as of December 31, 2020	$ 4,221	$ (152)	$ 14,116	$ 18,185
Provision related to current period sales	15,767	578	21,187	37,532
Credits/payments for current period sales	(10,824)	(192)	—	(11,016)
Credits/payments for prior period sales	(4,221)	152	(11,417)	(15,486)
Balance as of March 31, 2021	$ 4,943	$ 386	$ 23,886	$ 29,215

Cost of Product Sales

Cost of product sales was $2.2 million and $2.8 million for the three months ended March 31, 2021 and 2020, respectively, or approximately 2% and 3% of net product sales, respectively. The cost of product sales as a percentage of net sales decreased during the three months ended March 31, 2021 as compared to the same period in 2020 due primarily to a higher average selling price for NUPLAZID in the current period.

License Fees and Royalties

License fees and royalties were $2.5 million and $2.2 million for the three months ended March 31, 2021 and 2020, respectively, and included royalties due to the Ipsen Group of two percent of net sales of NUPLAZID and amortization related to the milestone paid to the Ipsen Group upon FDA approval of NUPLAZID in 2016. The increase in license fees and royalties during the three months ended March 31, 2021 as compared to the same period in 2020 was primarily due to the increase in net sales during the current period.

Research and Development Expenses

Research and development expenses decreased to $57.0 million for the three months ended March 31, 2021, including $4.8 million in stock-based compensation expense, from $72.6 million for the three months ended March 31, 2020, including $8.5 million in stock-based compensation expense. The decrease in research and development expenses was mainly due to the $10.0 million upfront payment to Vanderbilt University for the M1 PAM program incurred during the three months ended March 31, 2020 and decreased costs associated with the cessation of development of pimavanserin for major depressive disorder.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased to $111.7 million for the three months ended March 31, 2021, including $8.2 million in stock-based compensation expense, from $102.0 million for the three months ended March 31, 2020, including $13.0 million in stock-based compensation expense. The increase in selling, general and administrative expenses was primarily due to increased costs associated with preparations for the potential DRP launch, partially offset by a decrease in stock-based compensation expense.

Liquidity and Capital Resources

We have funded our operations primarily through sales of our equity securities, payments received under our collaboration agreements, debt financings, interest income, and, since 2016, with revenues from sales of NUPLAZID. In August 2020, we issued common stock with a value of approximately $44.3 million to CerSci's former equity holders. In September 2019, we raised net proceeds of approximately $271.5 million in a follow-on public offering of our common stock. In November 2018, we raised net proceeds of approximately $298.5 million in a follow-on public offering of our common stock. In January and August 2016, we raised total net proceeds of approximately $497.5 million in follow-on public offerings of our common stock, and in 2014 we raised net proceeds of $196.8 million in a public offering of our common stock. We anticipate that the level of cash used in our operations will increase in future periods in order to fund our ongoing and planned commercial activities for NUPLAZID, our ongoing and planned development activities for pimavanserin in additional indications other than PDP, studies to be conducted pursuant to our post-marketing commitments and our ongoing and planned development activities for trofinetide for the treatment of Rett syndrome, ACP-044 for pain management, and for various M1 PAM compounds, including ACP-319, under the agreement with Vanderbilt University. We expect that our cash, cash equivalents, and investment securities will be sufficient to fund our planned operations through at least the next 12 months.

We may require significant additional financing in the future to fund our operations. Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the progress in, and the costs of, our ongoing and planned development activities for pimavanserin, post-marketing studies for NUPLAZID to be conducted over the next several years, and ongoing and planned commercial activities for NUPLAZID;
- the costs of our development activities for trofinetide;
- the costs of our development activities for ACP-044;
- the costs of our development activities for ACP-319;
- the costs of our development activities for the M1 PAM program;
- the costs of commercializing NUPLAZID, including the maintenance and development of our sales and marketing capabilities;
- the costs of establishing, or contracting for, sales and marketing capabilities for other product candidates;
- the amount of U.S. product sales from NUPLAZID;
- the costs of preparing applications for regulatory approvals for NUPLAZID in jurisdictions other than the U.S., and in additional indications other than PDP and for other product candidates, as well as the costs required to support review of such applications;
- the costs of manufacturing and distributing NUPLAZID for commercial use in the U.S.;
- our ability to obtain regulatory approval for, and subsequently generate product sales from, NUPLAZID in jurisdictions other than the U.S. or in additional indications other than PDP, or from trofinetide, ACP-044, ACP-319 and other product candidates;
- the costs of acquiring additional product candidates or research and development programs;
- the scope, prioritization and number of our research and development programs;
- the ability of our collaborators and us to reach the milestones and other events or developments triggering payments under our collaboration or license agreements, or our collaborators' ability to make payments under these agreements;
- our ability to enter into new collaboration and license agreements;
- the extent to which we are obligated to reimburse collaborators or collaborators are obligated to reimburse us for costs under collaboration agreements;
- the costs involved in filing, prosecuting, enforcing, and defending patent claims and other intellectual property rights;
- the costs of maintaining or securing manufacturing arrangements for clinical or commercial production of pimavanserin, trofinetide or other product candidates; and
- the costs associated with litigation, including the costs incurred in defending against any product liability claims that may be brought against us related to NUPLAZID.

Unless and until we can generate significant cash from our operations, we expect to satisfy our future cash needs through our existing cash, cash equivalents and investment securities, public or private sales of our securities, debt financings, strategic collaborations, or by licensing all or a portion of our product candidates or technology. In the past, periods of turmoil and volatility in the financial markets have adversely affected the market capitalizations of many biotechnology companies, and generally made equity and debt financing more difficult to obtain. For example, due to the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. These events, coupled with other factors, may limit our access to additional financing in the future. We cannot be certain that additional funding will be available to us on acceptable terms, or at all. If adequate funds are not available when needed, we will be required to delay, reduce the scope of, or eliminate one or more of our research or development programs or our commercialization efforts. We also may be required to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. Additional funding, if obtained, may significantly dilute existing stockholders and could negatively impact the price of our stock.

We have invested a substantial portion of our available cash in money market funds, U.S. treasury notes, and high quality, marketable debt instruments of corporations and government sponsored enterprises in accordance with our investment policy. Our investment policy defines allowable investments and establishes guidelines relating to credit quality, diversification, and maturities of our investments to preserve principal and maintain liquidity. All investment securities have a credit rating of at least Aa3/AA- or better, or P-1/A-1 or better, as determined by Moody's Investors Service or Standard & Poor's. Our investment portfolio has not been adversely impacted by the disruptions in the credit markets that have occurred in the past. However, if there are future disruptions in the credit markets, there can be no assurance that our investment portfolio will not be adversely affected.

At March 31, 2021, we had $577.8 million in cash, cash equivalents, and investment securities, compared to $632.0 million at December 31, 2020. This $54.2 million decrease was primarily due to cash used in operating activities. Net cash used in operating activities increased to $60.1 million for the three months ended March 31, 2021 compared to $49.0 million for the three months ended March 31, 2020. This increase in cash used in operations was primarily due to an increased payment of accrued liabilities and increase in selling, general and administrative expense, partially offset by increased net revenues.

Net cash provided by investing activities totaled $30.9 million for the three months ended March 31, 2021 compared to net cash provided by investing activities of $29.6 million for the three months ended March 31, 2020. The increase in net cash provided by investing activities for the three months ended March 31, 2021 compared to the three months ended March 31, 2020 was primarily due to increased net maturities of investment securities.

Net cash provided by financing activities increased to $7.7 million for the three months ended March 31, 2021 compared to $3.8 million for the three months ended March 31, 2020. This increase in net cash provided by financing activities for the three months ended March 31, 2021 was attributable primarily to an increase in proceeds resulting from the exercise of employee stock options.

Off-Balance Sheet Arrangements

To date, we have not had any relationships with unconsolidated entities or financial partnerships, such as entities referred to as structured finance or special purpose entities, which are established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. As such, we are not materially exposed to any financing, liquidity, market, or credit risk that could arise if we had engaged in these relationships.

Recent Accounting Pronouncements

See Item 1 of Part I, "Notes to Condensed Consolidated Financial Statements — Note 10 — Recent Accounting Pronouncements".

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

We invest our excess cash in investment-grade, interest-bearing securities. The primary objective of our investment activities is to preserve principal and liquidity. To achieve this objective, we invest in money market funds, U.S. Treasury notes, and high quality marketable debt instruments of corporations and government sponsored enterprises with contractual maturity dates of generally less than one years. All investment securities have a credit rating of at least Aa3/AA- or better, or P-1/A-1 or better, as determined by Moody's Investors Service or Standard & Poor's. We do not have any direct investments in auction-rate securities or securities that are collateralized by assets that include mortgages or subprime debt. If a 10 percent change in interest rates were to have occurred on March 31, 2021, this change would not have had a material effect on the fair value of our investment portfolio as of that date.

ITEM 4. CONTROLS AND PROCEDURES

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As of March 31, 2021, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of March 31, 2021.

An evaluation was also performed under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of any change in our internal control over financial reporting that occurred during our last fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. That evaluation did not identify any changes in our internal control over financial reporting that occurred during our latest fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

Between July 19 and August 3, 2018, following negative publicity about NUPLAZID, three purported company stockholders filed putative securities class action complaints (captioned Staublein v. Acadia Pharmaceuticals, Inc., Case No. 18-cv-01647, Stone v. Acadia Pharmaceuticals Inc., Case No. 18-cv-01672, and Barglow v. Acadia Pharmaceuticals Inc., Case No. 18-cv-01812) in the U.S. District Court for the Southern District of California against us and certain of our current and former executive officers. Thereafter, several putative lead plaintiffs filed motions to consolidate the cases and to appoint a lead plaintiff. On January 3, 2019, the Court consolidated the cases under the caption In re Acadia Pharmaceuticals Inc. Securities Litigation, Case No. 18-cv-01647, and took the lead plaintiff motions under submission. On February 26, 2019, the Court appointed a lead plaintiff and lead counsel. Lead plaintiff filed a consolidated complaint on April 15, 2019. The consolidated complaint generally alleges that defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 by making materially false and misleading statements regarding our business, operations, and prospects by failing to disclose that adverse events and safety concerns regarding NUPLAZID threatened initial and continuing FDA approval, and by failing to disclose that we engaged in business practices likely to attract regulatory scrutiny. The consolidated complaint seeks unspecified monetary damages and other relief. Defendants filed a motion to dismiss the consolidated complaint on June 7, 2019. On June 1, 2020, the Court granted the motion in part and gave lead plaintiff leave to file an amended complaint. On July 16, 2020, lead plaintiff filed the amended complaint. Defendants filed a motion to dismiss the amended complaint on August 28, 2020. Lead plaintiff opposed the motion on September 15, 2020. Defendants' reply in support of the motion to dismiss was filed on November 11, 2020. On March 29, 2021, the Court granted the defendants' motion to dismiss with leave to amend. On April 16, 2021, lead plaintiff filed a third amended complaint. On April 20, 2021, the Court entered a schedule for filing and briefing a motion to dismiss the third amended complaint. The defendants' motion to dismiss the third amended complaint is due on May 31, 2021. The plaintiff's opposition to the motion is due on July 12, 2021. The defendants' reply in support of the motion is due on August 11, 2021. The motion is set to be heard on October 1, 2021.

On February 7, 2020, a purported company stockholder filed a derivative complaint (captioned Barney v. Davis et al., Case No. 20-cv-0238) in the U.S. District Court for the Southern District of California against our directors and certain of our current and former executive officers. The complaint asserts claims for breach of fiduciary duty, waste of corporate assets, and unjust enrichment arising from allegations similar to those in the federal securities class action described above. On September 9, 2020, the Court substituted plaintiffs and re-captioned the case Shumacher v. Davis et al., Case No. 20-cv-0238. On June 23, 2020, a second derivative complaint (captioned Lazarus v. Davis et al., Case No. 20-cv-0843) was filed in the U.S. District Court for the District of Delaware. On September 9, 2020, the Court transferred the Lazarus case to the U.S. District Court for the Southern District of California and re-captioned the case Lazarus v. Davis et al., Case No. 20-cv-1774. On January 15, 2021, the Court consolidated the cases under the name In re ACADIA Pharmaceuticals Inc. Stockholder Derivative Litigation, Case No. 20-cv-0238, appointed lead counsel for the plaintiffs, and designated the complaint in the Shumacher case as the operative complaint. The consolidated case is stayed until the defendants in the federal securities class action answer, or the federal securities class action is dismissed with prejudice and all appeals are exhausted, or any party to the stipulation to stay gives 15 days' written notice that it no longer consents to the voluntary stay.

On July 24, 2020, we filed complaints against (i) Aurobindo Pharma Limited and its affiliate Aurobindo Pharma USA, Inc. and (ii) Teva Pharmaceuticals USA, Inc. and its affiliate Teva Pharmaceutical Industries Ltd., and on July 30, 2020, we filed complaints against (i) Hetero Labs Limited and its affiliates Hetero Labs Limited Unit-V and Hetero USA Inc., (ii) MSN Laboratories Private Ltd. and its affiliate MSN Pharmaceuticals, Inc., and (iii) Zydus Pharmaceuticals (USA) Inc. and its affiliate Cadila Healthcare Limited. These complaints, which were filed in the U.S. District Court for the District of Delaware, allege infringement of certain of our Orange Book-listed patents covering NUPLAZID. The cases have been assigned to the Honorable Richard G. Andrews. On September 1, 2020, Aurobindo filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On September 22, 2020, we filed our answer to Aurobindo's counterclaims. On August 31, 2020, Teva filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On September 21, 2020, we filed our answer to Teva's counterclaims. On October 5, 2020, Hetero filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On October 26, 2020, we filed our answer to Hetero's counterclaims. On September 30, 2020, MSN filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity regarding certain of our Orange Book-listed patents covering NUPLAZID. On November 5, 2020, we filed our first amended complaint against MSN in the U.S. District Court for the District of Delaware, alleging infringement of certain of our Orange Book-listed patents covering NUPLAZID. On November 19, 2020, MSN filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity regarding certain of our Orange Book-listed patents covering NUPLAZID. On December 10, 2020, we filed our answer to MSN's counterclaims. On November 2, 2020, Zydus filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On November 23, 2020, we filed our answer to Zydus's counterclaims. On December 8, 2020, the parties' joint proposed scheduling order was entered by Judge Andrews. On April 7, 2021, we filed our first amended complaints against Hetero and Teva and our second amended complaint against Hetero, to include an additional Orange Book-listed patent covering NUPLAZID. On April 8, 2021, we filed our first amended complaint against Zydus and on April 9, 2021, we filed our first amended complaint against Aurobindo. On April 20, 2021, MSN filed its answer, affirmative defenses, and counterclaims to our second amended complaint, seeking declaratory judgments of noninfringement and invalidity regarding certain of our Orange Book-listed patents covering NUPLAZID. On April 21, 2021, Teva filed its answer, affirmative defenses, and counterclaims to our first amended complaint, seeking declaratory judgments of noninfringement and invalidity. On April 22, 2021, Zydus filed its answer, affirmative defenses, and counterclaims to our first amended complaint, seeking declaratory judgments of noninfringement and invalidity. A joint trial in the matters is scheduled for May 15, 2023.

We entered into an agreement effective April 22, 2021 with Hetero settling all claims and counterclaims in the litigation. The agreement allows Hetero to launch its generic pimavanserin product on July 27, 2038, subject to certain triggers for earlier launch. The Hetero case was dismissed by joint agreement on May 3, 2021.

On April 19, 2021, a purported Company stockholder filed a putative securities class action complaint (captioned Marechal v. Acadia Pharmaceuticals, Inc., Case No. 21-cv-0762) in the U.S. District Court for the Southern District of California against us and certain of our current executive officers. The complaint generally alleges that defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 by making materially false and misleading statements regarding the Company's business, operations, and prospects by failing to disclose that the materials submitted in support of its sNDA seeking approval of pimavanserin for the treatment of hallucinations and delusions associated with dementia-related psychosis contained statistical and design deficiencies and that the FDA unlikely to approve the sNDA in its current form. The complaints seek unspecified monetary damages and other relief.

We currently believe that none of the foregoing claims or actions pending against us as of March 31, 2021 is likely to have, individually or in the aggregate, a material adverse effect on our business, liquidity, financial position, or results of operations. Given the unpredictability inherent in litigation, however, we cannot predict the outcome of these matters. We are unable to estimate possible losses or ranges of losses that may result from these matters, and therefore we have not accrued any amounts in connection with these matters other than attorneys' fees incurred to date.

ITEM 1A. RISK FACTORS

You should consider carefully the following information about the risks described below, together with the other information contained in this Quarterly Report and in our other public filings in evaluating our business. The risk factors set forth below that are marked with an asterisk (*) did not appear as separate risk factors in, or contain changes to the similarly titled risk factor included in, Item 1A of our Annual Report. If any of the following risks actually occurs, our business, financial condition, results of operations, and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline.

Summary Risk Factors

We face risks and uncertainties related to our business, many of which are beyond our control. In particular, risks associated with our business include:

- Our prospects are highly dependent on the successful commercialization of NUPLAZID. To the extent NUPLAZID is not commercially successful, our business, financial condition and results of operations may be materially adversely affected and the price of our common stock may decline.
- If we do not obtain regulatory approval of pimavanserin for other indications in addition to treatment of PDP in the U.S., or for any indication in foreign jurisdictions, or regulatory approval of trofinetide for Rett syndrome, we will not be able to market pimavanserin for other indications in the U.S. or in other jurisdictions or market trofinetide at all, which will limit our commercial revenues.
- Even though the FDA has granted approval of NUPLAZID for the treatment of hallucinations and delusions associated with PDP, the terms of the approval may limit its commercial potential. Additionally, NUPLAZID is still subject to substantial, ongoing regulatory requirements.
- NUPLAZID has only been studied in a limited number of patients and in limited populations. As we continue to commercialize NUPLAZID, it is becoming available to a much larger number of patients and in broader populations, and we do not know whether the results of NUPLAZID use in such larger number of patients and broader populations will be consistent with the results from our clinical studies.
- We currently market and sell NUPLAZID, our only commercial product, and rely on a limited network of third-party distributors and pharmacies. If we are unable to continue to effectively commercialize NUPLAZID, we may not be able to generate adequate product revenues.
- If we are unable to effectively train and equip our sales force, our ability to successfully commercialize NUPLAZID will be harmed.
- NUPLAZID may not gain maximal acceptance among physicians, patients, and the medical community, thereby limiting our potential to generate revenues.
- Our ability to generate product revenues will be diminished if NUPLAZID does not receive coverage from payors or sells for inadequate prices, or if patients have unacceptably high co-pay amounts.
- Delays, suspensions and terminations in our clinical trials could result in increased costs to us and delay our ability to generate product revenues.
- Healthcare reform measures may negatively impact our ability to sell NUPLAZID or our product candidates, if approved, profitably.
- If we are unable to attract, retain, and motivate key management, research and development, and sales and marketing personnel, our drug development programs, our research and discovery efforts, and our commercialization plans may be delayed and we may be unable to successfully commercialize our products, including NUPLAZID, or develop our product candidates, including pimavanserin for indications beyond PDP.
- We expect our net losses to continue for the next few years and are unable to predict the extent of future losses or when we will become profitable, if ever.
- If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully continue the development and commercialization of NUPLAZID or successfully develop and commercialize our other product candidate opportunities.
- We expect that our results of operations will fluctuate, which may make it difficult to predict our future performance from period to period.

- Public health threats, including the current global COVID-19 pandemic have impacted our clinical trials and could have an adverse effect on our operations and financial results, or may cause us to modify or suspend our financial guidance.
- We previously have depended, and in the future may depend, on collaborations with third parties to develop and commercialize selected product candidates other than pimavanserin, and we have limited control over how those third parties conduct development and commercialization activities for such product candidates.
- We currently depend, and in the future will continue to depend, on third parties to manufacture NUPLAZID, trofinetide and our other product candidates. If these manufacturers fail to provide us or our collaborators with adequate supplies of clinical trial materials and commercial product or fail to comply with the requirements of regulatory authorities, we may be unable to develop or commercialize NUPLAZID, trofinetide or any other product candidates.
- If we fail to comply with the obligations in agreements under which we license intellectual property rights from third parties, we could lose the right to develop certain of our product candidates.
- Our ability to compete may decline if we do not adequately protect our proprietary rights.
- If our competitors develop and market products that are more effective than NUPLAZID or our product candidates, they may reduce or eliminate our commercial opportunity.
- Our stock price historically has been, and is likely to remain, highly volatile.

Risks Related to Our Business

Our prospects are highly dependent on the successful commercialization of NUPLAZID. To the extent NUPLAZID is not commercially successful, our business, financial condition and results of operations may be materially adversely affected and the price of our common stock may decline.*

NUPLAZID is our only drug that has been approved for sale and it has only been approved for the treatment of hallucinations and delusions associated with PDP, in the U.S. since April 2016. We are currently focusing most of our activities and resources on NUPLAZID, because we believe that our prospects are highly dependent on, and the vast majority of the value of our company relates to, our ability to successfully commercialize NUPLAZID in the U.S.

Successful commercialization of NUPLAZID is subject to many risks, and there is no guarantee that we will be able to successfully commercialize NUPLAZID for additional approved indications beyond PDP. There are numerous examples of failures to meet high expectations of market potential, including by pharmaceutical companies with more experience and resources than us. While we have established our commercial team and have hired our U.S. sales force, we will need to further expand and develop the team in order to successfully commercialize NUPLAZID for additional indications. Even if we are successful in developing our commercial team, there are many factors that could cause the commercialization of NUPLAZID to be unsuccessful, including a number of factors that are outside our control. Because no drug has previously been approved by the FDA for the treatment of hallucinations and delusions associated with PDP, it is especially difficult to estimate NUPLAZID's market potential for its approved indication and potential additional indications. The commercial success of NUPLAZID currently depends on the extent to which patients and physicians recognize and diagnose PDP and accept and adopt NUPLAZID as a treatment for hallucinations and delusions associated with PDP, and we do not know whether our or others' estimates in this regard will be accurate. For example, if the patient population suffering from hallucinations and delusions associated with PDP is smaller than we estimate or if physicians are unwilling to prescribe or patients are unwilling to take NUPLAZID, perceived safety issues, or for other reasons, the commercial potential of NUPLAZID will be limited. We have limited information about how physicians, patients and payors have responded and will respond to the pricing of NUPLAZID. We have changed, and may continue to change, the price of NUPLAZID from time to time. Physicians may not prescribe NUPLAZID and patients may be unwilling to use NUPLAZID if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, any negative publicity related to NUPLAZID, or negative development for NUPLAZID in our post-marketing commitments, in clinical development in additional indications, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of NUPLAZID. Thus, significant uncertainty remains regarding the commercial potential of NUPLAZID.

In addition, our business could be adversely affected by the effects of public health threats, including the COVID-19 pandemic. During the first quarter of 2021, sales of NUPLAZID were negatively impacted by ongoing conditions related to the pandemic, including a reduction in patient office visits and a further decline in census at long-term care facilities. The impacts and pace of recovery resulting from the pandemic are difficult to predict at this time, and no assurances can be given that the pandemic will not have significant additional impacts on our business, results of operations, financial condition and prospects.

If the commercialization of NUPLAZID is less successful than expected or perceived as disappointing, our stock price could decline significantly and the long-term success of the product and our company could be harmed.

If we do not obtain regulatory approval of pimavanserin for other indications in addition to treatment of PDP in the U.S., or for any indication in foreign jurisdictions, or regulatory approval of trofinetide for Rett syndrome, we will not be able to market pimavanserin for other indications in the U.S. or in other jurisdictions or market trofinetide at all, which will limit our commercial revenues.*

While pimavanserin has been approved in the U.S. by the FDA for the treatment of hallucinations and delusions associated with PDP, it has not been approved by the FDA for any other indications, and it has not been approved in any other jurisdiction for this indication or for any other indication. In order to market pimavanserin for other indications or in other jurisdictions, we must obtain regulatory approval for each of those indications and in each of the applicable jurisdictions, and we may never be able to obtain such approval. Approval of NUPLAZID by the FDA for the treatment of hallucinations and delusions associated with PDP does not ensure that foreign jurisdictions will also approve NUPLAZID for that indication, nor does it ensure that NUPLAZID will be approved by the FDA for any other indication. For example, following the successful completion of our Phase 3 HARMONY study, we submitted an sNDA to the FDA for the treatment of DRP on June 3, 2020. In July 2020 the FDA notified us of its filing of our sNDA with a filing date of August 2, 2020 and a PDUFA target action date of April 3, 2021. As part of its filing communication, the FDA advised us that it had not identified any potential review issues at that point in its evaluation and at that time was not planning to hold an Advisory Committee meeting. On March 3, 2021, we received a notification from the FDA stating that it had identified deficiencies that preclude discussion of labeling and post-marketing requirements/commitments. The notification did not specify the deficiencies identified by the FDA. On April 2, 2021, we received a CRL from the FDA, indicating that the FDA had completed its review of the application and determined that it could not be approved in its present form. In the CRL, the FDA cited a lack of statistical significance in some of the subgroups of dementia, and insufficient numbers of patients with certain less common dementia subtypes as lack of substantial evidence of effectiveness to support approval. We plan to meet with the FDA to address the CRL and determine potential next steps toward approval of pimavanserin in DRP. In light of these developments, it is currently unclear when, or whether, approval of pimavanserin in DRP can be obtained. Depending on the outcome of our future discussions with the FDA, we could be required to conduct additional costly and time-consuming clinical trials or other studies to support a subsequent request for approval in DRP, or to forego further development of pimavanserin in DRP, which could substantially delay or prevent approval of pimavanserin in DRP or limit our market opportunity in that indication.

We initiated a Phase 3 program for pimavanserin as an adjunctive treatment for MDD in April 2019. In July 2020, we announced that our Phase 3 CLARITY study, which combined two identical, double-blind, placebo-controlled studies, did not achieve statistical significance on the primary endpoint. As a result, at this time we do not plan on initiating any additional Phase 3 studies to evaluate pimavanserin for adjunctive use with SSRI/SNRI drugs for the treatment of MDD.

We initiated the Phase 3 LAVENDER study of trofinetide for Rett syndrome in October 2019. We initiated the Phase 3 ADVANCE-2 study of pimavanserin for the treatment of the negative symptoms of schizophrenia in August 2020. There is no guarantee that our ongoing studies will be successful, or that the FDA or any regulatory authority in foreign jurisdictions will approve pimavanserin or trofinetide for any of those indications.

The research, testing, manufacturing, labeling, approval, sale, import, export, marketing, and distribution of pharmaceutical product candidates are subject to extensive regulation by the FDA and other regulatory authorities in the U.S. and other countries, whose regulations differ from country to country. We will be required to comply with different regulations and policies of the jurisdictions where we seek approval for our product candidates, and we have not yet identified all of the requirements that we will need to satisfy to submit NUPLAZID for approval for other indications or in other jurisdictions or to submit trofinetide for approval for Rett syndrome. This will require additional time, expertise and expense, including the potential need to conduct additional studies or development work for other jurisdictions beyond the work that we have conducted to support our NDA submission in PDP. In addition, strategic considerations need to be taken into account when determining whether and when to submit NUPLAZID for approval in other jurisdictions. For example, in the fourth quarter of 2016, the European Medicines Agency (EMA), approved our proposed pediatric investigation plan related to our planned submission of a marketing authorization application (MAA), for NUPLAZID for the treatment of PDP in Europe. However, in light of our continuing clinical development of pimavanserin in indications other than in PDP, and the time-limited data exclusivity currently granted by the EMA that commences on first approval of a product in Europe, we deferred submission of the MAA and we do not yet have a revised estimate of when we will make that filing. If we do not receive marketing approval for NUPLAZID for any other indication or from any regulatory agency outside of the U.S. or any marketing approval for trofinetide, we will never be able to commercialize NUPLAZID for any other indication in the U.S. or for any indication in any other jurisdiction or be able to commercialize trofinetide at all. Even if we do receive additional regulatory approvals, we may not be successful in commercializing those opportunities.

If the results or timing of regulatory filings, the regulatory process, regulatory developments, clinical trials or preclinical studies, or other activities, actions or decisions related to NUPLAZID do not meet our or others' expectations, the market price of our common stock could decline significantly.

Even though the FDA has granted approval of NUPLAZID for the treatment of hallucinations and delusions associated with PDP, the terms of the approval may limit its commercial potential. Additionally, NUPLAZID is still subject to substantial, ongoing regulatory requirements.

Even though the FDA has granted approval of NUPLAZID, the scope and terms of the approval may limit our ability to commercialize NUPLAZID and, therefore, our ability to generate substantial sales revenues. The FDA has approved NUPLAZID only for the treatment of hallucinations and delusions associated with PDP. The label for NUPLAZID also contains a "boxed" warning that elderly patients with DRP treated with antipsychotic drugs are at an increased risk of death, and that NUPLAZID is not approved for the treatment of patients with DRP unrelated to the hallucinations and delusions associated with PDP. This "boxed" warning may discourage physicians from prescribing NUPLAZID to patients diagnosed with PDP, including those with dementia.

In connection with the FDA approval, we committed to conduct the following post-marketing studies: (i) a randomized, placebo-controlled withdrawal study in patients treated with NUPLAZID, (ii) studies to collect additional data to add to the NUPLAZID safety database from an aggregate of at least 500 predominantly frail and elderly subjects on NUPLAZID in one or more randomized, placebo-controlled studies of eight or more weeks duration, (iii) a drug-drug interaction study with NUPLAZID and a strong CYP3A4 inducer, and (iv) re-analysis of tissue samples from certain previously conducted pre-clinical studies. We have completed the (iii) drug-drug interaction study with NUPLAZID and a strong CYP3A4 inducer and (iv) the re-analysis of tissue samples. We have received FDA approval of an sNDA for labeling revisions related to the completed CYP3A4 study. If we fail to comply with our remaining post-marketing commitments, or if the results of the post-marketing studies, or any other ongoing or planned clinical studies of NUPLAZID, are negative, the FDA could decide to withdraw approval, add warnings or narrow the approved indication in the product label.

The manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for NUPLAZID will also continue to be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing processes, good clinical practices, international council for harmonization guidelines and good laboratory practices, which are regulations and guidelines enforced by the FDA for all of our nonclinical and clinical development and for any clinical trials that we conduct post-approval.

Discovery of any issues post-approval, including any safety concerns, such as unexpected side effects or drug-drug interaction problems, adverse events of unanticipated severity or frequency, or concerns over misuse or abuse of the product, problems with the facilities where the product is manufactured, packaged or distributed, or failure to comply with regulatory requirements, may result in, among other things, restrictions on NUPLAZID or on us, including:

- withdrawal of approval, addition of warnings or narrowing of the approved indication in the product label;
- requirement of a Risk Evaluation and Mitigation Strategy to mitigate the risk of off-label use in populations where the FDA may believe that the potential risks of use may outweigh its benefits;
- voluntary or mandatory recalls;
- warning letters;
- suspension of any ongoing clinical studies;
- refusal by the FDA or other regulatory authorities to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product approvals;
- restrictions on operations, including restrictions on the marketing or manufacturing of the product or the imposition of costly new manufacturing requirements; or
- seizure or detention, or refusal to permit the import or export of products.

If any of these actions were to occur, we may have to discontinue the commercialization of NUPLAZID, limit our sales and marketing efforts, conduct further post-approval studies, and/or discontinue or change any other ongoing or planned clinical studies, which in turn could result in significant expense and delay or limit our ability to generate sales revenues.

NUPLAZID has only been studied in a limited number of patients and in limited populations. As we continue to commercialize NUPLAZID, it is becoming available to a much larger number of patients and in broader populations, and we do not know whether the results of NUPLAZID use in such larger number of patients and broader populations will be consistent with the results from our clinical studies.

Prior to commencing our commercial launch of NUPLAZID in May 2016, NUPLAZID was administered only to a limited number of patients and in limited populations in clinical studies, including our successful pivotal -020 Phase 3 trial with NUPLAZID for the treatment of PDP. We do not know whether the results, when broader populations are exposed to NUPLAZID, including results related to safety and efficacy, will be consistent with the results from the clinical studies of NUPLAZID that served as the basis for its approval. New data relating to NUPLAZID, including from adverse event reports and post-marketing studies in the U.S., and from other ongoing clinical studies, may result in changes to the product label and may adversely affect sales, or result in withdrawal of NUPLAZID from the market. The FDA and regulatory authorities in other jurisdictions may also consider the new data in reviewing NUPLAZID marketing applications for indications other than in PDP and/or in other jurisdictions, or impose additional post-approval requirements. If any of these actions were to occur, it could result in significant expense and delay or limit our ability to generate sales revenues.

We currently market and sell NUPLAZID, our only commercial product, and rely on a limited network of third-party distributors and pharmacies. If we are unable to continue to effectively commercialize NUPLAZID, we may not be able to generate adequate product revenues.*

NUPLAZID is our only drug that has been approved for sale by any regulatory body, and it became available for prescription in the U.S. in May 2016. In order to successfully market NUPLAZID, we must continue to develop our sales, marketing, managerial, compliance, and related capabilities or make arrangements with third parties to perform these services. If we are unable to maintain and develop adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not be able to appropriately commercialize NUPLAZID and may not become profitable.

We employ our own internal specialty sales force to commercialize NUPLAZID for the treatment of PDP as part of our commercialization strategy in the U.S. We will need to refine and further develop our sales force as we continue our commercialization efforts, and we will be competing with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. These efforts will continue to be expensive and time-consuming, and we cannot be certain that we will be able to successfully refine and further develop our sales force. If we receive marketing approval for pimavanserin in DRP, we will need to increase our U.S. sales force significantly, and expand our commercial, medical affairs and general and administrative support functions to support commercialization for that indication.

Additionally, our strategy in the U.S. includes distributing NUPLAZID solely through a limited network of third-party specialty distributors and specialty pharmacies. While we have entered into agreements with each of these distributors and pharmacies to distribute NUPLAZID in the U.S., they may not perform as agreed or they may terminate their agreements with us. Also, we may need to enter into agreements with additional distributors or pharmacies, and there is no guarantee that we will be able to do so on commercially reasonable terms or at all. If we are unable to maintain and, if needed, expand, our network of specialty distributors and specialty pharmacies, we would be exposed to substantial distribution risk.

In the event we are unable to maintain, or expand, if needed, our commercial team, including our U.S. sales force, or maintain and, if needed, expand, our network of specialty distributors and specialty pharmacies, our ability to effectively commercialize NUPLAZID and generate product revenues would be limited.

If we are unable to effectively train and equip our sales force, our ability to successfully commercialize NUPLAZID will be harmed.

NUPLAZID is the first drug approved by the FDA for the treatment of hallucinations and delusions associated with PDP. As a result, we are and will continue to be required to expend significant time and resources to train our sales force to be credible, persuasive, and compliant with applicable laws in marketing NUPLAZID for the treatment of hallucinations and delusions associated with PDP to neurologists, psychiatrists, and pharmacists and physicians in long-term care facilities. In addition, we must ensure that consistent and appropriate messages about NUPLAZID are being delivered to our potential customers by our sales force. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate potential customers about the benefits of NUPLAZID and its proper administration, our efforts to successfully commercialize NUPLAZID could be put in jeopardy, which would negatively impact our ability to generate product revenues.

NUPLAZID may not gain maximal acceptance among physicians, patients, and the medical community, thereby limiting our potential to generate revenues.*

The degree of market acceptance by physicians, healthcare professionals and third-party payors of NUPLAZID, and any other product for which we obtain regulatory approval, and our profitability and growth, will depend on a number of factors, including:

- the ability to provide acceptable evidence of safety and efficacy;
- the scope of the approved indication(s) for the product;
- the inclusion of any warnings or contraindications in the product label;
- the relative convenience and ease of administration;
- the prevalence and severity of any adverse side effects;
- the availability of alternative treatments;
- pricing and cost effectiveness, which may be subject to regulatory control;
- effectiveness of our or our collaborators' sales and marketing strategy; and
- our ability to obtain sufficient third-party insurance coverage or adequate reimbursement levels.

If a product does not provide a treatment regimen that is at least as beneficial as the current standard of care or otherwise does not provide patient benefit, that product will not achieve market acceptance and will not generate sufficient revenues to achieve or maintain profitability.

With respect to NUPLAZID specifically, successful commercialization will depend on whether and to what extent physicians, long-term care facilities and pharmacies, over whom we have no control, determine to utilize NUPLAZID. NUPLAZID is available to treat hallucinations and delusions associated with PDP, an indication for which no other FDA-approved pharmaceutical treatment currently exists. Because of this, it is particularly difficult to estimate NUPLAZID's market potential and how physicians, payors and patients will respond to changes in the price of NUPLAZID. Additionally, although we did not see a material impact on NUPLAZID net sales for the year ended December 31, 2020 due to the COVID-19 pandemic, we have seen a negative impact in the first quarter of 2021, and the ultimate effects of COVID-19, and the duration thereof, are difficult to assess or predict at this time. Industry sources and analysts have a divergence of estimates for the near- and long-term market potential of NUPLAZID, and a variety of assumptions directly impact the estimates for NUPLAZID's market potential, including assumptions regarding the prevalence of PDP, the rate of diagnosis of PDP, the prevalence and rate of hallucinations and delusions in patients diagnosed with PDP, the rate of physician adoption of NUPLAZID, the potential impact of payor restrictions regarding NUPLAZID, and patient adherence and compliance rates. Small differences in these assumptions can lead to widely divergent estimates of the market potential of NUPLAZID. For example, certain research suggests that patients with Parkinson's disease may be hesitant to report symptoms of PDP to their treating physicians for a variety of reasons, including apprehension about societal stigmas relating to mental illness. Research also suggests that physicians who typically treat patients with Parkinson's disease may not ask about or identify symptoms of PDP. For these reasons, even if PDP occurs in high rates among patients with Parkinson's disease, it may be underdiagnosed. Even if PDP is diagnosed, physicians may not prescribe treatment for hallucinations and delusions associated with PDP, and if they do prescribe treatment, they may prescribe other drugs, even though they are not approved in PDP, instead of NUPLAZID. In addition, even if NUPLAZID is prescribed for the treatment of hallucinations and delusions associated with PDP, issues may arise with respect to patient adherence and compliance rates. If patients do not adhere to the recommended dosing of NUPLAZID, patients and physicians may believe that NUPLAZID is less effective, and as a result they may stop taking it and prescribing it.

The label for NUPLAZID also contains a "boxed" warning that elderly patients with DRP treated with antipsychotic drugs are at an increased risk of death, and that NUPLAZID is not approved for the treatment of patients with DRP unrelated to the hallucinations and delusions associated with PDP. There has also been recent attention to publicly reported deaths of patients that were prescribed NUPLAZID, and the FDA conducted an evaluation of available information about NUPLAZID. On September 20, 2018 the U.S. FDA issued a statement concluding: "The U.S. FDA has completed a review of all post marketing reports of deaths and serious adverse events (SAEs) reported with the use of NUPLAZID. Based on an analysis of all available data, FDA did not identify any new or unexpected safety findings with NUPLAZID, or findings that are inconsistent with the established safety profile currently described in the drug label. After a thorough review, FDA's conclusion remains unchanged that the drug's benefits outweigh its risks for patients with hallucinations and delusions of Parkinson's disease psychosis." Although the FDA did not identify any new or unexpected safety risks, the FDA indicated that some potentially concerning prescribing patterns were observed, such as the concomitant use of other antipsychotic drugs or drugs that can cause QT prolongation, a potential cause of heart rhythm disorder. The FDA reminded health care providers to be aware of the risks described in the NUPLAZID prescribing information and that none of the other antipsychotic medications are approved for the treatment of PD psychosis. Regardless, perceptions that NUPLAZID is unsafe, even if unfounded, may discourage physicians from prescribing or patients from taking NUPLAZID.

The commercial success of NUPLAZID depends on acceptance by patients and physicians, and there are a number of factors that could skew our or others' estimates about prescribing behaviors and market adoption.

Our ability to generate product revenues will be diminished if NUPLAZID does not receive coverage from payors or sells for inadequate prices, or if patients have unacceptably high co-pay amounts.

Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors, including governmental healthcare programs, such as Medicare and Medicaid, managed care organizations and commercial payors, among others, to reimburse all or part of the costs associated with their prescription drugs. Coverage and adequate reimbursement from third-party commercial payors is critical to product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor drug products when lower cost therapeutic alternatives are already available or subsequently become available. Even with coverage for NUPLAZID, or other products we may market, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients may not use NUPLAZID if coverage is not provided or reimbursement is inadequate to cover a significant portion of its cost.

In addition, the market for NUPLAZID depends significantly on access to third-party payors' drug formularies, or 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. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly alternative is available, even if not approved for the indication for which NUPLAZID is approved.

In many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. 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. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with NUPLAZID, and any other products we may market, which could negatively impact our profitability.

Third-party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. The current environment is putting pressure on companies to price products below what they may feel is appropriate. Selling NUPLAZID at less than an optimized price could impact our revenues and overall success as a company. We have changed, and may continue to change, the price of NUPLAZID from time to time, however, we do not know if the price we have selected, or may select in the future, for NUPLAZID is or will be the optimized price. Additionally, we do not know whether and to what extent third-party payors will react to any possible future changes in the price of NUPLAZID. In the U.S., no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Further, one payor's determination to provide coverage and reimbursement for a product does not assure that other payors also will provide coverage and reimbursement for the product. Therefore, coverage and reimbursement for NUPLAZID may differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of NUPLAZID to each payor separately, with no assurance that coverage will be obtained. Coverage policies and third-party payor reimbursement rates may change at any time. Therefore, even if favorable coverage and reimbursement status is attained, less favorable coverage policies and reimbursement rates may be implemented in the future. If we are unable to obtain coverage of, and adequate payment levels for, NUPLAZID or any other products we may market to 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 could affect our ability to successfully commercialize NUPLAZID, or any other products we may market, and thereby adversely impact our profitability, results of operations, financial condition, and future success.

There is no guarantee that future studies with pimavanserin will be successful.*

The historical rate of failures for product candidates in clinical development is extremely high. In November 2012, we announced successful results from the Phase 3 -020 Study of pimavanserin for PDP. Additionally, in December 2016, we announced positive top-line results from our Phase 2 exploratory study of pimavanserin in patients with AD Psychosis, those results may not be predictive of the results of any additional studies that we are currently undertaking or may undertake in the future with pimavanserin, including the post-marketing studies we committed to conduct in connection with FDA approval of NUPLAZID and the ongoing studies of pimavanserin in various indications. We believe that pimavanserin also may have utility in indications other than in PDP, such as in DRP and schizophrenia. However, prior to the Phase 3 HARMONY study that we initiated in the fourth quarter of 2017, which was stopped early for efficacy in September 2019, we had never tested pimavanserin in clinical studies where the primary outcome was for the broad indication of DRP, and prior to the studies in schizophrenia that we initiated in the fourth quarter of 2016, we had only conducted a Phase 2 trial for pimavanserin as a co-therapy treatment in schizophrenia. There is no guarantee that we will have the same level of success with pimavanserin in other studies that we had with the -020 Study, the HARMONY study and the ADVANCE study. For example, in July 2020 we announced top-line results from the Phase 3 CLARITY study evaluating pimavanserin as an adjunctive treatment with SSRI/SNRI drugs in MDD. In this study pimavanserin did not achieve statistical significance on the primary endpoint. Further, there is no guarantee that we will be successful at all in ongoing or future studies for additional indications or in our post-marketing studies, or that future results of studies of NUPLAZID for treatment in PDP or for other indications will be positive.

If we do not successfully complete additional development of NUPLAZID, we will be unable to market and sell NUPLAZID or products derived from it for indications other than the treatment of hallucinations and delusions associated with PDP, or to generate related product revenues.

We are solely responsible for the development and commercialization of pimavanserin.*

We have full responsibility for the pimavanserin program throughout the world. We expect our research and development costs for continued development of pimavanserin to be substantial. We are currently undertaking ongoing development work for pimavanserin, including clinical trials of pimavanserin for indications other than in PDP. In the event of approval for additional indications, we would need to add significant resources, and possibly raise additional capital, in order to further commercialize pimavanserin, and to conduct the necessary sales and marketing activities, and to conduct further development activities. Our current strategy is to continue to commercialize NUPLAZID for the treatment of hallucinations and delusions associated with PDP in the U.S. using our specialty sales force focused primarily on neurologists, a small group of psychiatrists, and pharmacists and physicians in long-term care facilities who treat PDP patients. If we receive marketing approval for pimavanserin in DRP, we will need to increase our U.S. sales force significantly, and expand our commercial, medical affairs and general and administrative support functions in connection with commercializing pimavanserin in DRP. In addition, if we are approved to commercialize NUPLAZID in markets outside of the U.S., we may need to establish one or more strategic alliances in the future for that purpose. Without future additional resources or collaboration partners in the U.S. and abroad, we might not be able to realize the full value of NUPLAZID.

Furthermore, even though NUPLAZID is approved for the treatment of hallucinations and delusions associated with PDP, a failure in a subsequent pimavanserin study for another indication, including our ongoing studies in schizophrenia and our previous studies in depression, or any additional studies that may be required in DRP, or a failure in our post-marketing studies could harm our

ability to successfully market NUPLAZID for the treatment of hallucinations and delusions associated with PDP or could lead to it being withdrawn from the market. If we are unable to develop pimavanserin for other indications, we may not be able to maximize the potential of the compound and that could have a material adverse effect on our future revenues and our success as a company.

Pimavanserin is currently in late-stage development for additional indications other than in PDP, and we have initiated Phase 3 development of trofinetide for Rett syndrome. Drug development is a long, expensive and unpredictable process with a high risk of failure.*

Preclinical testing and clinical trials are long, expensive and unpredictable processes that can be subject to delays. It may take several years to complete the preclinical testing and clinical development necessary to commercialize a drug, and delays or failure can occur at any stage. Interim results of clinical trials do not necessarily predict final results, and success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials even after promising results in earlier trials.

Our drug development programs are at various stages of development and the historical rate of failures for product candidates is extremely high. In fact, we had an unsuccessful Phase 3 trial with NUPLAZID in 2009. An unfavorable outcome in any of our ongoing or future development efforts or in the post-marketing studies for NUPLAZID could be a major set-back for the program and for us, generally. In particular, an unfavorable outcome in our NUPLAZID program or in the post-marketing studies may require us to delay, devote additional substantial resources to, reduce the scope of, or eliminate this program and could have a material adverse effect on us and the value of our common stock.

In addition, based on positive top-line results from CLARITY, a Phase 2 study evaluating pimavanserin as an adjunctive treatment for MDD, we initiated our Phase 3 CLARITY program, consisting of two Phase 3 studies, CLARITY-2 and CLARITY-3, evaluating pimavanserin as an adjunctive treatment with SSRI/SNRI drugs for MDD. Despite the positive results observed in the Phase 2 CLARITY study, our Phase 3 CLARITY study, did not achieve statistical significance on the primary endpoint. In July 2019, we announced top-line results from the Phase 3 ENHANCE study evaluating pimavanserin as a treatment in inadequate response schizophrenia. In this study pimavanserin did not achieve statistical significance on either the primary endpoint or the key secondary endpoint.

Following the successful completion of our Phase 3 HARMONY study, we submitted an sNDA to the FDA for the treatment of DRP on June 3, 2020. In July 2020 the FDA advised us that it had not identified any potential review issues at that point in its evaluation. On April 2, 2021, we received a CRL indicating that the FDA had completed its review of the application and determined that it could not be approved in its present form. In the CRL, the FDA cited a lack of statistical significance in some of the subgroups of dementia, and insufficient numbers of patients with certain less common dementia subtypes as lack of substantial evidence of effectiveness to support approval. While we plan to meet with the FDA to address the CRL and determine potential next steps towards approval of pimavanserin in DRP, it is currently unclear when, or whether, approval of pimavanserin in DRP can be obtained. Depending on the outcome of our future discussions with the FDA, we could be required to conduct additional costly and time-consuming clinical trials or other studies to support a subsequent request for approval in DRP, or to forego further development of pimavanserin in DRP, any of which could substantially delay or prevent approval of pimavanserin in DRP or limit our market opportunity in that indication.

We may plan and conduct additional studies in the future, and have initiated the Phase 3 LAVENDER study of trofinetide in Rett syndrome in October 2019 and the Phase 3 ADVANCE-2 study of pimavanserin in negative symptoms of schizophrenia.

In connection with clinical trials, we face risks that:

- a product candidate may not prove to be efficacious or safe;
- patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested;
- the results may not be consistent with positive results of earlier trials; and
- the results may not meet the level of statistical significance required by the FDA or other regulatory agencies.

If we do not successfully complete preclinical and clinical development, we will be unable to market and sell products derived from our product candidates and to generate product revenues. Even if we do successfully complete clinical trials, those results are not necessarily predictive of results of additional trials that may be needed before an NDA may be submitted to the FDA. Of the large number of drugs in development, only a small percentage result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

Delays, suspensions and terminations in our clinical trials could result in increased costs to us and delay our ability to generate product revenues.

The commencement of clinical trials can be delayed for a variety of reasons, including delays in:

- demonstrating sufficient safety and efficacy to obtain regulatory approval to commence a clinical trial;
- reaching agreement on acceptable terms with prospective contract research organizations and clinical trial sites;
- manufacturing sufficient quantities of a product candidate;
- obtaining clearance from the FDA to commence clinical trials pursuant to an Investigational New Drug application;
- obtaining institutional review board approval to conduct a clinical trial at a prospective clinical trial site; and
- patient recruitment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical trial sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial.

Once a clinical trial has begun, it may be delayed, suspended or terminated due to a number of factors, including:

- competition for internal and external resources, including clinical sites and study patients, that we may choose to allocate to other programs;
- ongoing discussions with regulatory authorities regarding the scope or design of our clinical trials or requests by them for supplemental information with respect to our clinical trial results;
- imposition of clinical holds by regulatory authorities or institutional review boards;
- failure to conduct clinical trials in accordance with regulatory requirements;
- patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical trial sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial;
- lower than anticipated screening or retention rates of patients in clinical trials;
- serious adverse events or side effects experienced by participants; and
- insufficient supply or deficient quality of product candidates or other materials necessary for the conduct of our clinical trials.

In addition, enrollment and retention of patients in clinical trials could be disrupted by man-made or natural disasters or public health emergencies. For example, as a result of the COVID-19 pandemic, we temporarily paused enrollment of new patients in our ongoing clinical trials, as well as commencement of new trials. However, we have re-initiated enrollment in clinical trials on a study-by-study and site-by-site basis. It is possible that future enrollment in these studies, or enrollment in future studies, could be impacted due to COVID-19. If patients withdraw from our trials, miss scheduled doses or follow-up visits or otherwise fail to follow trial protocols, or if our trial results are otherwise disputed due to COVID-19 or actions taken to slow its spread, the integrity of data from our trials may be compromised or not accepted by the FDA or other regulatory authorities, which would represent a significant setback for the applicable program.

Many of these factors may also ultimately lead to denial of regulatory approval of a current or potential product candidate. If we experience delays, suspensions or terminations in a clinical trial, the commercial prospects for the related product candidate will be harmed, and our ability to generate product revenues will be delayed.

If we are unable to attract, retain, and motivate key management, research and development, and sales and marketing personnel, our drug development programs, our research and discovery efforts, and our commercialization plans may be delayed and we may be unable to successfully commercialize our products, including NUPLAZID, or develop our product candidates, including pimavanserin for indications beyond PDP.

Our success depends on our ability to attract, retain, and motivate highly qualified management, scientific, and commercial personnel. In particular, our development programs depend on our ability to attract and retain highly skilled development personnel, especially in the fields of central nervous system disorders, including neuropsychiatric and related disorders. We are currently hiring, and in the future we expect to need to continue to hire, additional personnel as we expand our research and development efforts for pimavanserin and commercial activities for NUPLAZID. We face competition for experienced scientists, clinical operations personnel, commercial and other personnel from numerous companies and academic and other research institutions. Competition for qualified personnel is particularly intense in the San Diego, California area. Many of the other biotechnology and pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than that which we have to offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize products and product candidates will be limited. If we are unable to attract and retain the necessary personnel, it will significantly impede our commercialization efforts for NUPLAZID and the achievement of our research and development objectives.

All of our employees are “at will” employees, which means that any employee may quit at any time and we may terminate any employee at any time. We do not carry “key person” insurance covering members of senior management.

We have recently increased the size of our organization, and if we receive approval of NUPLAZID in additional indications, including DRP, we would need to continue to increase the size of our organization. We may encounter difficulties with managing our growth, which could adversely affect our results of operations.*

As of March 31, 2021, we employed approximately 640 employees. Although we have already added several capabilities, we will need to add additional qualified personnel and resources. Our current infrastructure may be inadequate to support our development and commercialization efforts and expected growth. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, and integrate additional employees, and may take time away from running other aspects of our business, including development and commercialization of our product candidates.

Our future financial performance and our ability to commercialize NUPLAZID and any other product candidates that receive regulatory approval and to compete effectively will depend, in part, on our ability to manage any future growth effectively. In particular, as we commercialize NUPLAZID, we will need to support the training and ongoing activities of our sales force and expect to need to expand the size of our employee base for managerial, operational, financial, and other resources. In addition, if we receive regulatory approval for pimavanserin for the treatment of DRP, we would need to increase our U.S. sales force and additional functions significantly to support a commercial launch in DRP. In light of the FDA’s recent actions regarding our sNDA, however, and the resulting uncertainty as to the timing of such commercial launch, we may need to re-evaluate both current staffing levels and future hiring plans. To that end, we must be able to:

- manage our development efforts effectively;
- integrate additional management, administrative and manufacturing personnel;
- develop our marketing and sales organization; and
- maintain sufficient administrative, accounting and management information systems and controls.

We may not be able to accomplish these tasks or successfully manage our operations and, accordingly, may not achieve our research, development, and commercialization goals. Our failure to accomplish any of these goals could harm our financial results and prospects.

If we fail to develop, acquire or in-license other product candidates or products, our business and prospects would be limited. Even if we obtain rights to other product candidates or products, we will incur a variety of costs and may never realize the anticipated benefits.

A key element of our strategy is to develop, acquire or in-license businesses, technologies, product candidates or products that we believe are a strategic fit with our business. The success of this strategy depends in large part on the combination of our regulatory, development and commercial capabilities and expertise and our ability to identify, select and acquire or in-license clinically-enabled product candidates for the treatment of neurological disorders, or for therapeutic indications that complement or augment our current product candidates, or that otherwise fit into our development or strategic plans on terms that are acceptable to us. Identifying, selecting and acquiring or in-licensing promising product candidates requires substantial technical, financial and human resources expertise, and we have limited experience in identifying acquisition targets, successfully completing proposed acquisitions and integrating any acquired businesses, technologies, services or products into our current infrastructure. Efforts to do so may not result in the actual acquisition or in-license of a particular product candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit. If we are unable to identify, select and acquire or license suitable product candidates from third parties on terms acceptable to us, our business and prospects will be limited. In particular, if we are unable to add additional commercial products to our portfolio, we may not be able to successfully leverage our commercial organization that we have assembled for the marketing and sale of NUPLAZID.

The process of integrating any acquired business, technology, service, or product may result in unforeseen operating difficulties and expenditures and may divert significant management attention from our ongoing business operations. As a result, we will incur a variety of costs in connection with an acquisition and may never realize its anticipated benefits. Moreover, any product candidate we identify, select and acquire or license may require additional, time-consuming development or regulatory efforts prior to commercial sale, including preclinical studies, if applicable, and extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to the risk of failure that is inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective or desired than other commercially available alternatives.

In addition, if we fail to successfully commercialize and further develop NUPLAZID or our product candidates, there is a greater likelihood that we will fail to successfully develop a pipeline of other product candidates, and our business and prospects would therefore be harmed.

We expect our net losses to continue for the next few years and are unable to predict the extent of future losses or when we will become profitable, if ever.*

We have experienced significant net losses since our inception. As of March 31, 2021, we had an accumulated deficit of approximately $2.1 billion. We expect to incur net losses over the next few years as we invest in the commercialization of NUPLAZID and advance our development programs.

Even though we began commercializing NUPLAZID in the U.S. in May 2016, we still expect to incur significant expenses and net losses for at least the next few years as we continue our commercialization efforts for NUPLAZID and pursue the further development of NUPLAZID and our product candidates. Substantially all of our revenues since May 2016 were from net product sales of NUPLAZID.

We expect that our revenues over the next few years will be entirely dependent on our ability to generate net product sales of NUPLAZID. To the extent that we cannot generate significant revenues from the sale of NUPLAZID to cover our expenses, including the significant expenses associated with commercializing NUPLAZID and continuing to develop pimavanserin in additional indications, we may never achieve profitability and/or may have to reduce our commercialization and/or research and development activities to become profitable, which would harm our future growth prospects. Additionally, to obtain revenues from product candidates other than NUPLAZID, we must succeed, either alone or with others, in developing, obtaining regulatory approval for, manufacturing and marketing compounds with significant market potential. We may never succeed in these activities and may never generate revenues from our commercialization of NUPLAZID, or from other product candidates that may be approved, that are significant enough to achieve profitability.

If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully continue the development and commercialization of NUPLAZID or successfully develop and commercialize our other product candidate opportunities.*

We have consumed substantial amounts of capital since our inception. Our cash, cash equivalents, and investment securities totaled $577.8 million at March 31, 2021. While we believe that our existing cash resources will be sufficient to fund our cash requirements through at least the next twelve months, we may require significant additional financing in the future to continue to fund our operations. Our future capital requirements will depend on, and could increase significantly as a result of, many factors including:

- the progress in, and the costs of, our ongoing and planned development activities for pimavanserin, post-marketing studies for NUPLAZID to be conducted over the next several years, ongoing and planned commercial activities for NUPLAZID, and other research and development programs;
- the costs of our development activities for trofinetide, ACP-044, ACP-319 and the M1 PAM program and any other product candidates;
- the costs of commercializing NUPLAZID, including the maintenance and development of our sales and marketing capabilities;
- the costs of establishing, or contracting for, sales and marketing capabilities for other product candidates;
- the amount of U.S. product sales from NUPLAZID;
- the costs of preparing applications for regulatory approvals for NUPLAZID in jurisdictions other than the U.S., and in additional indications other than in PDP, and for other product candidates, as well as the costs required to support review of such applications;
- the costs of manufacturing and distributing NUPLAZID for commercial use in the U.S.;
- our ability to obtain regulatory approval for, and subsequently generate product sales from, NUPLAZID in jurisdictions other than the U.S. or in additional indications other than in PDP, or from trofinetide, ACP-044, ACP-319 and the M1 PAM program and any other product candidates;
- the costs of acquiring additional product candidates or research and development programs;
- the scope, prioritization and number of our research and development programs;
- the ability of our collaborators and us to reach the milestones and other events or developments triggering payments under our collaboration or license agreements, or our collaborators' ability to make payments under these agreements;
- our ability to enter into new collaboration and license agreements;
- the extent to which we are obligated to reimburse collaborators or collaborators are obligated to reimburse us for costs under collaboration agreements;
- the costs involved in filing, prosecuting, enforcing, and defending patent claims and other intellectual property rights;
- the costs of maintaining or securing manufacturing arrangements and supply for clinical or commercial production of pimavanserin, trofinetide or other product candidates; and
- the costs associated with litigation, including the costs incurred in defending against any product liability claims that may be brought against us related to NUPLAZID.

Unless and until we can generate significant cash from our operations, we expect to satisfy our future cash needs through our existing cash, cash equivalents and investment securities, strategic collaborations, public or private sales of our securities, debt financings, grant funding, or by licensing all or a portion of our product candidates or technology. In the past, periods of turmoil and volatility in the financial markets have adversely affected the market capitalizations of many biotechnology companies, and generally made equity and debt financing more difficult to obtain. For example, as a result of the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. These events, coupled with other factors, may limit our access to additional financing in the future. This could have a material adverse effect on our ability to access sufficient funding. We cannot be certain that additional funding will be available to us on acceptable terms, or at all. If funds are not available, we will be required to delay, reduce the scope of, or eliminate one or more of our research or development programs or our commercialization efforts. We also may be required to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. Additional funding, if obtained, may significantly dilute existing stockholders and could negatively impact the price of our stock.

We expect that our results of operations will fluctuate, which may make it difficult to predict our future performance from period to period.

Our operating results have fluctuated in the past and are likely to do so in future periods. Some of the factors that could cause our operating results to fluctuate from period to period include:

- the success of our commercialization of NUPLAZID in the U.S. for the treatment of hallucinations and delusions associated with PDP;
- the impact of the COVID-19 pandemic on our business, including the ability of our field sales force to meet with healthcare providers, visit physician's offices, hospitals and other healthcare facilities (including long-term care and skilled nursing facilities);
- the status and cost of our post-marketing commitments for NUPLAZID;
- the variation in our gross-to-net adjustments from quarter to quarter, primarily because of the fluctuation in our share of the donut hole for Medicare Part D patients;
- the status and cost of development and commercialization of pimavanserin for indications other than in PDP and in jurisdictions other than the U.S.;
- the status and cost of development and commercialization of our product candidates, including compounds being developed under our collaborations;
- whether we acquire or in-license additional product candidates or products, and the status of development and commercialization of such product candidates or products;
- whether we generate revenues or reimbursements by achieving specified research, development or commercialization milestones under any agreements or otherwise receive potential payments under these agreements;
- whether we are required to make payments due to achieving specified milestones under any licensing or similar agreements or otherwise make payments under these agreements;
- the incurrence of preclinical or clinical expenses that could fluctuate significantly from period to period, including reimbursement obligations pursuant to our collaboration agreements;
- the initiation, termination, or reduction in the scope of our collaborations or any disputes regarding these collaborations;
- the timing of our satisfaction of applicable regulatory requirements;
- the rate of expansion of our clinical development, other internal research and development efforts, and pre-commercial and commercial efforts;
- the effect of competing technologies and products and market developments;
- the costs associated with litigation, including the costs incurred in defending against any product liability claims that may be brought against us related to NUPLAZID; and
- general and industry-specific economic conditions.

We believe that comparisons from period to period of our financial results are not necessarily meaningful and should not be relied upon as indications of our future performance.

From time to time, we provide guidance relating to our expectations for NUPLAZID net sales and certain expense line items based on estimates and the judgment of management. If, for any reason, our actual net sales or expenses differ materially from our guidance, we may have to revise our previously announced financial guidance. If we change, update or fail to meet any element of such guidance, our stock price could decline.

Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Tax Cut and Jobs Act of 2017 (2017 Tax Act) enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the 2017 Tax Act may affect us, and certain aspects of the 2017 Tax Act could be repealed or modified in future legislation. For example, the CARES Act, modified certain provisions of the 2017 Tax Act. In addition, it is uncertain if and to what extent various states will conform to the 2017 Tax Act or any newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the 2017 Tax Act or future reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

Our ability to use net operating losses and certain other tax attributes to offset future taxable income or taxes may be limited.

Portion of our net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the 2017 Tax Act, as modified by the CARES Act, federal net operating losses incurred in tax years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal net operating losses in tax years beginning after December 31, 2020, is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to the 2017 Tax Act or the CARES Act. In addition, 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,” which is generally defined as a greater than 50 percent change, by value, in its equity ownership over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We have experienced ownership changes in the past and we may experience additional ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations. In addition, at the state level, there may be periods during which the use of net operating loss carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, California imposed limits on the usability of California state net operating losses to offset taxable income in tax years beginning after 2019 and before 2023. As a result, if we earn net taxable income, we may be unable to use all or a material portion of our net operating loss carryforwards and other tax attributes, which could potentially result in increased future tax liability to us and adversely affect our future cash flows.

Changes to U.S. and non-U.S. tax laws or challenges by tax authorities to our intercompany arrangements could materially adversely affect us.

In 2015, we licensed worldwide intellectual property rights related to pimavanserin in certain indications to Acadia Pharmaceuticals GmbH, our wholly owned Swiss subsidiary (Acadia GmbH), and in July 2020 we licensed additional related rights to Acadia GmbH. Our goals for the establishment of Acadia GmbH, and the licensing of worldwide intellectual property rights for pimavanserin, include building a platform for long-term operational and financial efficiencies, including tax-related efficiencies. Future changes in U.S. and non-U.S. tax laws, including implementation of international tax reform relating to the tax treatment of multinational corporations, if enacted, may reduce or eliminate any potential financial efficiencies that we hoped to achieve by establishing this operational structure. Additionally, taxing authorities, such as the U.S. Internal Revenue Service, may audit and otherwise challenge these types of arrangements, and have done so with other companies in the pharmaceutical industry. If any such changes in tax law are enacted, or our licensing of worldwide intellectual property rights for pimavanserin to our Swiss subsidiary is otherwise challenged, this could materially adversely affect our business.

Public health threats, including the current global COVID-19 pandemic have impacted our clinical trials and could have an adverse effect on our operations and financial results, or may cause us to modify or suspend our financial guidance.*

On March 11, 2020, the World Health Organization declared a pandemic resulting from the disease known as COVID-19 caused by a novel strain of coronavirus, SARS-CoV-2. The rapid global spread of COVID-19 has had a major impact on the financial markets, the global economy and the economies of particular countries or regions, and led to travel restrictions, quarantines, "work-at-home" and "shelter-in-place" orders imposed by authorities and the extended shutdown of certain non-essential businesses in the U.S. throughout the world, including in countries where we have planned or active clinical trials. In an effort to protect the health and safety of our employees, we adopted recommended policies applicable to office-based employees as well as our field-based commercial and medical affairs personnel, such as working from home, limiting employees to essential on-site work only, and suspending business travel. The effects and duration of such measures could have a material adverse impact on our business, results of operations, financial condition and prospects.

Our sales force has had physical access to hospitals, clinics, long-term care and skilled nursing facilities, healthcare providers and pharmacies curtailed, which may have a material adverse effect on our future sales. Currently, health care providers are conducting patient visits in-person and through telemedicine and our sales force has been able to call upon medical clinics, hospitals, long-term care facilities and skilled nursing facilities either in person in accordance with applicable regulatory guidance and local policies or virtually. While digital tools are available to our field employees to facilitate remote meetings with healthcare providers that are unable to meet in-person, we cannot ensure that these methods will be effective. Additionally, patients who are currently using NUPLAZID or who are eligible to use NUPLAZID, may be unable to meet with their healthcare providers in person, which may reduce the number of prescription refills or new patient starts, affecting our revenues both in our currently approved indication and potentially impacting our anticipated launches in other indications, if approved.

Our clinical trials have been impacted by the COVID-19 pandemic. We temporarily paused enrollment of new patients in our ongoing clinical trials as well as commencement of new trials, and our data collection and site monitoring activities relating to currently active clinical trials could be delayed or otherwise impeded by travel and access restrictions and diversion of healthcare resources toward treating COVID-19 patients, among other things. However, we have re-initiated enrollment in clinical trials on a study-by-study and site-by-site basis. It is possible that future enrollment in these studies, or enrollment in future studies, could be impacted due to COVID-19.

In addition, our business could be adversely affected by the effects of public health threats, including the COVID-19 pandemic. During the first quarter of 2021, sales of NUPLAZID were negatively impacted by ongoing conditions related to the pandemic, including a reduction in patient office visits and a further decline in census at long-term care facilities. The impacts and pace of recovery resulting from the pandemic are difficult to predict at this time, and no assurances can be given that the pandemic will not have significant additional impacts on our business, results of operations, financial condition and prospects.

Earthquake or fire damage to our facilities could delay our research and development efforts and adversely affect our business.

Our headquarters and research and development facilities in San Diego are located in a seismic zone, and there is the possibility of an earthquake, which could be disruptive to our operations and result in delays in our research and development efforts. In addition, while our facilities have not been adversely impacted by local wildfires, there is the possibility of future fires in the area. In the event of an earthquake or fire, if our facilities or the equipment in our facilities is significantly damaged or destroyed for any reason, we may not be able to rebuild or relocate our facilities or replace any damaged equipment in a timely manner and our business, financial condition, and results of operations could be materially and adversely affected. We do not have insurance for damages resulting from earthquakes. While we do have fire insurance for our property and equipment located in San Diego, any damage sustained in a fire could cause a delay in our research and development efforts and our results of operations could be materially and adversely affected.

Our business involves the use of hazardous materials, and we and our third-party manufacturers and suppliers must comply with environmental, health and safety laws and regulations, which can be expensive and restrict how we do, or interrupt our, business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the generation, storage, use and disposal of hazardous materials, including the components of our products and product candidates and other hazardous compounds and wastes. We and our manufacturers and suppliers are subject to environmental, health and safety laws and regulations governing, among other matters, the use, manufacture, generation, storage, handling, transportation, discharge and disposal of these hazardous materials and wastes and worker health and safety. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination or injury, which could result in an interruption of our commercialization efforts, research and development efforts and business operations, damages and significant cleanup costs and liabilities under applicable environmental, health and safety laws and regulations. We also cannot guarantee that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials and wastes generally comply with the standards prescribed by these laws and regulations. We may be held liable for any resulting damages costs or liabilities, which could exceed our resources, and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental, health and safety laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. Failure to comply with these environmental, health and safety laws and regulations may result in substantial fines, penalties or other sanctions. We do not currently carry hazardous waste insurance coverage.

Risks Related to Our Relationships with Third Parties

We previously have depended, and in the future may depend, on collaborations with third parties to develop and commercialize selected product candidates other than pimavanserin, and we have limited control over how those third parties conduct development and commercialization activities for such product candidates.

In the past, we have selectively entered into collaboration agreements with third parties. We relied on our collaborators for financial resources and for development, regulatory, and commercialization expertise for selected product candidates and we had limited control over the amount and timing of resources that our collaborators devoted to our product candidates. We may choose to rely on collaborations in the future for certain portions of our pimavanserin program or other product candidates, or for the commercialization of NUPLAZID in certain territories outside of the U.S.

Our collaborators may fail to develop or effectively commercialize products using our product candidates or technologies because they:

- do not have sufficient resources or decide not to devote the necessary resources due to internal constraints such as limited cash or human resources or a change in strategic focus;
- decide to pursue a competitive product developed outside of the collaboration; or
- cannot obtain the necessary regulatory approvals.

We also face competition in our search for new collaborators, if we seek a new partner for our pimavanserin program or other programs. Given the current economic and industry environment, it is possible that competition for new collaborators may increase. If we are unable to find new collaborations, we may not be able to continue advancing our programs alone.

If conflicts arise with our collaborators, they may act in their self-interests, which may be adverse to our interests.

Conflicts may arise in our collaborations due to one or more of the following:

- disputes or breaches with respect to payments that we believe are due under the applicable agreements, particularly in the current environment when companies, including large established ones, may be seeking to reduce external payments;
- disputes on strategy as to what development or commercialization activities should be pursued under the applicable agreements;
- disputes as to the responsibility for conducting development and commercialization activities pursuant to the applicable collaboration, including the payment of costs related thereto;
- disagreements with respect to ownership of intellectual property rights;

- unwillingness on the part of a collaborator to keep us informed regarding the progress of its development and commercialization activities, or to permit public disclosure of these activities;
- delay or reduction of a collaborator's development or commercialization efforts with respect to our product candidates; or
- termination or non-renewal of the collaboration.

Conflicts arising with our collaborators could impair the progress of our product candidates, harm our reputation, result in a loss of revenues, reduce our cash position, and cause a decline in our stock price.

In addition, in our past collaborations, we generally have agreed not to conduct independently, or with any third party, any research that is directly competitive with the research conducted under the applicable program. Any collaborations we establish in the future may have the effect of limiting the areas of research that we may pursue, either alone or with others. Conversely, the terms of any collaboration we may establish in the future might not restrict our collaborators from developing, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by our collaborators or to which our collaborators have rights, may result in the allocation of resources by our collaborators to competing products and their withdrawal of support for our product candidates or may otherwise result in lower demand for our potential products.

We rely on third parties to conduct our clinical trials and perform data collection and analysis, which may result in costs and delays that prevent us from successfully commercializing product candidates.

Although we design and manage our current preclinical studies and clinical trials, we currently do not have the ability to conduct clinical trials for our product candidates on our own. We rely on contract research organizations, medical institutions, clinical investigators, and contract laboratories to perform data collection and analysis and other aspects of our clinical trials. In addition, we also rely on third parties to assist with our preclinical studies, including studies regarding biological activity, safety, absorption, metabolism, and excretion of product candidates. Some of these third parties may experience shutdowns or other disruptions as a result of the COVID-19 pandemic and therefore may be unable to provide the level of service that we have received in the past.

Our preclinical activities or clinical trials may be delayed, suspended, or terminated if:

- these third parties do not successfully carry out their contractual duties or fail to meet regulatory obligations or expected deadlines;
- these third parties need to be replaced; or
- the quality or accuracy of the data obtained by these third parties is compromised due to their failure to adhere to our clinical protocols or regulatory requirements or for other reasons.

Failure to perform by these third parties may increase our development costs, delay our ability to obtain regulatory approval, and delay or prevent the commercialization of our product candidates. We currently use several contract research organizations to perform services for our preclinical studies and clinical trials. While we believe that there are numerous alternative sources to provide these services, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without delays or additional expenditures.

Even if we or our collaborators successfully complete the clinical trials of product candidates, the product candidates may fail for other reasons.

Of the large number of product candidates in development, only a small percentage result in the submission of an NDA to the FDA or comparable regulatory filing to regulatory authorities in other jurisdictions, and even fewer are approved for marketing. We cannot assure you that, even if clinical trials are completed, either we or our collaborators will submit applications for required authorizations to manufacture and/or market potential products or that any such application will be reviewed and approved by the appropriate regulatory authorities in a timely manner, if at all. Even if we or our collaborators successfully complete the clinical trials of product candidates and apply for such required authorizations, the product candidates, such as pimavanserin, may fail for other reasons, including the possibility that the product candidates will:

- fail to receive the regulatory clearances required to market them as drugs;
- be subject to proprietary rights held by others requiring the negotiation of a license agreement prior to marketing;
- be difficult or expensive to manufacture on a commercial scale;

- have adverse side effects that make their use less desirable; or
- fail to compete with product candidates or other treatments commercialized by competitors.

We currently depend, and in the future will continue to depend, on third parties to manufacture NUPLAZID, trofinetide and any other product candidates. If these manufacturers fail to provide us or our collaborators with adequate supplies of clinical trial materials and commercial product or fail to comply with the requirements of regulatory authorities, we may be unable to develop or commercialize NUPLAZID, trofinetide or any other product candidates.

We have no manufacturing facilities and only limited experience as an organization in the manufacturing of drugs or in designing drug-manufacturing processes. We have contracted with third-party manufacturers to produce, in collaboration with us, NUPLAZID and our product candidates.

We have contracted with Patheon Pharmaceuticals Inc. to manufacture NUPLAZID 10 mg tablet and 34 mg capsule drug product for commercial use in the U.S. We have also contracted with a second contract manufacturing organization to manufacture NUPLAZID 34 mg drug product for commercial use in the U.S. Additionally, we have contracted with Siegfried AG to manufacture active pharmaceutical ingredient (API), to be used in the manufacture of NUPLAZID drug product for commercial use. However, we have not entered into any agreements with any alternate suppliers for 10 mg NUPLAZID drug product or NUPLAZID API, and we may face delays or increased costs in our supply chain that could jeopardize the commercialization of NUPLAZID. While we currently have sufficient pimavanserin API and NUPLAZID finished product on hand to continue our commercial and clinical operations as planned, depending on the length of the COVID-19 pandemic and whether further disruptions occur, we may face such delays or costs in future years. If any third party in our supply or distribution chain for materials or finished product is adversely impacted by restrictions resulting from the COVID-19 outbreak, including staffing shortages, production slowdowns and disruptions in delivery systems, our supply chain may be disrupted, limiting our ability to manufacture and distribute NUPLAZID for commercial sales and our product candidates for our clinical trials and research and development operations. Additionally, if NUPLAZID is approved for commercial sale in jurisdictions outside the U.S., we will need to contract with a third party to manufacture such products for commercial sale in the U.S. and/or in such other jurisdictions.

We have contracted with manufacturers to produce clinical supplies of trofinetide to support the development program. If trofinetide or any other product candidate is approved by the FDA or other regulatory agencies for commercial sale, we will need to contract with a third party to manufacture such products for commercial sale in the U.S. and/or in such other jurisdictions.

Even though we have agreements with Patheon for the manufacture of NUPLAZID 10 mg tablet and agreements with Patheon and another manufacturer for the manufacture of 34 mg capsule drug product, and with Siegfried for the manufacture of NUPLAZID API for commercial use, and even if we successfully enter into long-term agreements with other manufacturers, the FDA may not approve the facilities of such manufacturers, the manufacturers may not perform as agreed, or the manufacturers may terminate their agreements with us. Presently, we have only one supplier of API, two suppliers for the 34 mg capsule and one supplier for the 10mg tablet of NUPLAZID. If any of the foregoing circumstances occur, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, maintain or obtain, as applicable, regulatory approval for or market NUPLAZID or trofinetide or any other product candidates. While we believe that there will be alternative sources available to manufacture NUPLAZID and trofinetide and any other product candidates, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without delays or additional expenditures. We cannot estimate these delays or costs with certainty but, if they were to occur, they could cause a delay in our development and commercialization efforts.

The manufacturers of NUPLAZID and trofinetide and any other product candidates, including Patheon and Siegfried, are obliged to operate in accordance with FDA-mandated current good manufacturing practices (cGMPs), and we have limited control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel to ensure compliance with cGMPs. In addition, the facilities used by our third-party manufacturers to manufacture NUPLAZID and trofinetide and any other product candidates must be approved by the FDA pursuant to inspections that will be conducted prior to any grant of regulatory approval by the FDA. If any of our third-party manufacturers are unable to successfully manufacture material that conforms to our specifications and the FDA's strict regulatory requirements, or pass regulatory inspection, they will not be able to secure or maintain approval for the manufacturing facilities. Additionally, a failure by any of our third-party manufacturers to establish and follow cGMPs or to document their adherence to such practices may lead to significant delays in clinical trials or in obtaining regulatory approval of product candidates, or result in issues maintaining regulatory approval of NUPLAZID and trofinetide and any other product candidate that receives regulatory approval, negatively impact our commercialization of NUPLAZID, or lead to significant delays in the launch and commercialization of trofinetide or any other products we may have in the future. Failure by our third-party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of the government to grant pre-market approval of drugs, delays, suspension or withdrawal of approvals, seizures or recalls of products, operating restrictions, and criminal prosecutions.

The manufacture of pharmaceutical products requires significant capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. We cannot assure you that any issues relating to the manufacture of NUPLAZID or trofinetide or any other product candidates will not occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to commercialize NUPLAZID in the U.S., or provide trofinetide or any other product candidates to patients in clinical trials, would be jeopardized. Any delay or interruption in our ability to meet commercial demand for NUPLAZID and any other approved products will result in the loss of potential revenues and could adversely affect our ability to gain market acceptance for these products. In addition, any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Failures or difficulties faced at any level of our supply chain could materially adversely affect our business and delay or impede the development and commercialization of NUPLAZID or trofinetide or any other product candidates and could have a material adverse effect on our business, results of operations, financial condition and prospects.

If we fail to comply with the obligations in agreements under which we license intellectual property rights from third parties, we could lose license rights to certain of our product candidates.

In August 2018, we entered into a license agreement with Neuren, and obtained exclusive North American rights to develop and commercialize trofinetide for Rett syndrome and other indications. In March 2020, we entered into a license agreement with Vanderbilt University, and obtained exclusive worldwide license to develop and commercialize our M1 PAM program, and we may enter into additional license agreements in the future.

Our agreements with Neuren and Vanderbilt University impose, and we expect that future agreements where we in-license intellectual property will impose, various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to bankruptcy-related proceedings, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license.

Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patents and other rights to third parties;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- our right to transfer or assign the license; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may not be able to successfully develop and commercialize the related product candidates, which would have a material adverse effect on our business.

We may not be able to continue or fully exploit our collaborations with outside scientific and clinical advisors, which could impair the progress of our clinical trials and our research and development efforts.

We work with scientific and clinical advisors at academic and other institutions who are experts in the field of central nervous system disorders. They assist us in our research and development efforts and advise us with respect to our clinical trials. These advisors are not our employees and may have other commitments that would limit their future availability to us. Although our scientific and clinical advisors generally agree not to engage in competing work, if a conflict of interest arises between their work for us and their work for another entity, we may lose their services, which may impair our reputation in the industry and delay the development or commercialization of our product candidates.

Risks Related to Our Intellectual Property

Our ability to compete may decline if we do not adequately protect our proprietary rights.*

Our commercial success depends on obtaining and maintaining intellectual property rights to our products and product candidates, including NUPLAZID, and technologies, as well as successfully defending these rights against third-party challenges. Successful challenges to, or misappropriation of, our intellectual property could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. To protect our intellectual property, we rely on a combination of patents, trade secret protection and contracts requiring confidentiality and nondisclosure. If our patents are successfully challenged, we may face generic competition prior to the expiration dates of our U.S. Orange Book listed patents. In June 2020, Aurobindo Pharma Limited (Aurobindo), Hetero Labs Limited (Hetero), MSN Laboratories Private Ltd. (MSN Labs), Teva Pharmaceuticals USA, Inc. (Teva) and Zydus Pharmaceuticals (USA) Inc. (Zydus) notified us that they had filed an Abbreviated New Drug Application (ANDA) with the FDA for generic versions of NUPLAZID, seeking approval prior to the expiration of our patents. On July 24, 2020, we filed complaints against Aurobindo and its affiliate Aurobindo Pharma USA, Inc. and Teva and its affiliate Teva Pharmaceutical Industries Ltd., and on July 30, 2020, we filed complaints against Hetero and its affiliates Hetero Labs Limited Unit-V and Hetero USA Inc., MSN Labs and its affiliate MSN Pharmaceuticals, Inc., and Zydus and its affiliate Cadila Healthcare Limited. These complaints, which were filed in the U.S. District Court for the District of Delaware, allege infringement of certain of our Orange Book-listed patents covering NUPLAZID. The cases have been assigned to the Honorable Richard G. Andrews. On September 1, 2020, Aurobindo filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On September 22, 2020, we filed our answer to Aurobindo's counterclaims. On August 31, 2020, Teva filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On October 26, 2020, we filed our answer to Hetero's counterclaims. On September 21, 2020, we filed our answer to Teva's counterclaims. On October 5, 2020, Hetero filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On September 30, 2020, MSN filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity regarding certain of our Orange Book-listed patents covering NUPLAZID. On November 5, 2020, we filed our first amended complaint against MSN in the U.S. District Court for the District of Delaware, alleging infringement of certain of our Orange Book-listed patents covering NUPLAZID. On November 19, 2020, MSN filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity regarding certain of our Orange Book-listed patents covering NUPLAZID. On December 10, 2020, we filed our answer to MSN's counterclaims. On November 2, 2020, Zydus filed its answer and counterclaims seeking declaratory judgments of noninfringement and invalidity. On November 23, 2020, we filed our answer to Zydus's counterclaims. On December 8, 2020, the parties' joint proposed scheduling order was entered by Judge Andrews. A joint trial in the matters is scheduled for May 15, 2023. On April 7, 2021, we filed our first amended complaints against Hetero and Teva and our second amended complaint against Hetero, to include an additional Orange Book-listed patent covering NUPLAZID. On April 8, 2021, we filed our first amended complaint against Zydus and on April 9, 2021, we filed our first amended complaint against Aurobindo. On April 20, 2021, MSN filed its answer, affirmative defenses, and counterclaims to our second amended complaint, seeking declaratory judgments of noninfringement and invalidity regarding certain of our Orange Book-listed patents covering NUPLAZID. On April 21, 2021, Teva filed its answer, affirmative defenses, and counterclaims to our first amended complaint, seeking declaratory judgments of noninfringement and invalidity. On April 22, 2021, Zydus filed its answer, affirmative defenses, and counterclaims to our first amended complaint, seeking declaratory judgments of noninfringement and invalidity. We entered into an agreement effective April 22, 2021 with Hetero settling all claims and counterclaims in the litigation. The agreement allows Hetero to launch its generic pimavanserin product on July 27, 2038, subject to certain triggers for earlier launch. The Hetero case was dismissed by joint agreement on May 3, 2021. While we intend to defend the validity of such patents vigorously, and will seek to use all appropriate methods to prevent their infringement, such efforts are expensive and time consuming. Any substantial decrease in the revenue and income derived from NUPLAZID would have an adverse effect on our results of operations.

With regard to patents, although we have filed numerous patent applications worldwide with respect to pimavanserin, not all of our patent applications resulted in an issued patent, or they resulted in an issued patent that is susceptible to challenge by a third party. Our ability to obtain, maintain, and/or defend our patents covering our product candidates and technologies is uncertain due to a number of factors, including:

- we may not have been the first to make the inventions covered by our pending patent applications or issued patents;
- we may not have been the first to file patent applications for our product candidates or the technologies we rely upon;
- others may develop similar or alternative technologies or design around our patent claims to produce competitive products that fall outside of the scope of our patents;
- our disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;
- we may not seek or obtain patent protection in all countries that will eventually provide a significant business opportunity;
- any patents issued to us or our collaborators may not provide a basis for commercially viable products, may not provide us with any competitive advantages, or are easily susceptible to challenges by third parties;
- our proprietary technologies may not be patentable;
- changes to patent laws that limit the exclusivity rights of patent holders or make it easier to render a patent invalid;
- recent decisions by the U.S. Supreme Court limiting patent-eligible subject matter;
- litigation regarding our patents may include challenges to the validity, enforceability, scope and term of one or more patents;
- the passage of The Leahy-Smith America Invents Act (the America Invents Act), introduced new procedures for challenging pending patent applications and issued patents; and
- technology that we may in-license may become important to some aspects of our business, however, we generally would not control the patent prosecution, maintenance or enforcement of any such in-licensed technology.

Even if we have or obtain patents covering our product candidates or technologies, we may still be barred from making, using and selling our product candidates or technologies because of the patent rights of others. Others have or may have filed, and in the future are likely to file, patent applications covering compounds, assays, genes, gene products or therapeutic products that are similar or identical to ours. There are many issued U.S. and foreign patents relating to genes, nucleic acids, polypeptides, chemical compounds or therapeutic products, and some of these may encompass reagents utilized in the identification of candidate drug compounds or compounds that we desire to commercialize. Numerous U.S. and foreign issued patents and pending patent applications owned by others exist in the area of central nervous system disorders and the other fields in which we are developing products. These could materially affect our freedom to operate. Moreover, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, that may later result in issued patents that our product candidates or technologies may infringe. These patent applications may have priority over patent applications filed by us.

We regularly conduct searches to identify patents or patent applications that may prevent us from obtaining patent protection for our proprietary compounds or that could limit the rights we have claimed in our patents and patent applications. Disputes may arise regarding the ownership or inventorship of our inventions. For applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the U.S. Patent and Trademark Office (U.S. PTO), to determine who was the first to invent the invention at issue. It is difficult to determine how such disputes would be resolved. Applications containing a claim not entitled to priority before March 16, 2013, are not subject to interference proceedings due the change brought by the America Invents Act to a “first-to-file” system. However, a derivation proceeding can be brought by a third-party alleging that the inventor derived the invention from another.

Periodic maintenance fees on any issued patent are due to be paid to the U.S. PTO and foreign patent agencies in several stages over the lifetime of the patent. The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Some of our academic institutional licensors, research collaborators and scientific advisors have rights to publish data and information to which we have rights. We generally seek to prevent our collaborators from disclosing scientific discoveries until we have the opportunity to file patent applications on such discoveries, but in some cases, we are limited to relatively short periods to review a proposed publication and file a patent application. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, then our ability to receive patent protection or protect our proprietary information may be impaired.

Confidentiality agreements with employees and others may not adequately prevent disclosure of our trade secrets and other proprietary information and may not adequately protect our intellectual property, which could limit our ability to compete.

Because we operate in the highly technical field of drug discovery and development of small molecule drugs, we rely in part on trade secret protection in order to protect our proprietary technology and processes. However, trade secrets are difficult to protect. We enter into confidentiality, nondisclosure, and intellectual property assignment agreements with our corporate partners, employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party's relationship with us. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming and the outcome is unpredictable. In addition, courts outside the U.S. may be less willing to protect trade secrets. We also have not entered into any noncompete agreements with any of our employees. Although each of our employees is required to sign a confidentiality agreement with us at the time of hire, we cannot guarantee that the confidential nature of our proprietary information will be maintained in the course of future employment with any of our competitors. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

A dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time-consuming and costly, and an unfavorable outcome could harm our business.

There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including post-issuance review proceedings before the U.S. PTO or oppositions and other comparable proceedings in foreign jurisdictions.

Central provisions of the America Invents Act went into effect on September 16, 2012 and on March 16, 2013. The America Invents Act includes a number of significant changes to U.S. patent law. These changes include provisions that affect the way patent applications are being filed, prosecuted and litigated. For example, the America Invents Act enacted proceedings involving post-issuance patent review procedures, such as inter partes review (IPR), and post-grant review, that allow third parties to challenge the validity of an issued patent in front of the U.S. PTO Patent Trial and Appeal Board. Each proceeding has different eligibility criteria and different patentability challenges that can be raised. IPRs permit any person (except a party who has been litigating the patent for more than a year) to challenge the validity of the patent on the grounds that it was anticipated or made obvious by prior art. Patents covering pharmaceutical products have been subject to attack in IPRs from generic drug companies and from hedge funds. If it is within nine months of the issuance of the challenged patent, a third party can petition the U.S. PTO for post-grant review, which can be based on any invalidity grounds and is not limited to prior art patents or printed publications.

In post-issuance proceedings, U.S. PTO rules and regulations generally tend to favor patent challengers over patent owners. For example, unlike in district court litigation, claims challenged in post-issuance proceedings are given their broadest reasonable meaning, which increases the chance a claim might be invalidated by prior art or lack support in the patent specification. As another example, unlike in district court litigation, there is no presumption of validity for an issued patent, and thus, a challenger's burden to prove invalidity is by a preponderance of the evidence, as opposed to the heightened clear and convincing evidence standard. As a result of these rules and others, statistics released by the U.S. PTO show a high percentage of claims being invalidated in post-issuance proceedings. Moreover, with few exceptions, there is no standing requirement to petition the U.S. PTO for inter partes review or post-grant review. In other words, companies that have not been charged with infringement or that lack commercial interest in the patented subject matter can still petition the U.S. PTO for review of an issued patent. Thus, even where we have issued patents, our rights under those patents may be challenged and ultimately not provide us with sufficient protection against competitive products or processes.

We may be exposed to future litigation by third parties based on claims that our product candidates, technologies or activities infringe the intellectual property rights of others. In particular, there are many patents relating to specific genes, nucleic acids, polypeptides or the uses thereof to identify product candidates. Some of these may encompass genes or polypeptides that we utilize in our drug development activities. If our drug development activities are found to infringe any such patents, and such patents are held to be valid and enforceable, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from using the patented genes or polypeptides for the identification or development of drug compounds. There are also many patents relating to chemical compounds and the uses thereof. If our compounds are found to infringe any such patents, and such patents are held to be valid and enforceable, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from making, using or selling the patented compounds.

In addition to the patent infringement lawsuits that we have recently initiated against the filers of ANDAs pertaining to NUPLAZID, we may need to resort to litigation to enforce other patents issued to us, protect our trade secrets or determine the scope and validity of third-party proprietary rights. From time to time, we may hire scientific personnel formerly employed by other companies involved in one or more areas similar to the activities conducted by us. Either we or these individuals may be subject to allegations of trade secret misappropriation or other similar claims as a result of their prior affiliations. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. We may not be able to afford the costs of litigation. Any legal action against us or our collaborators could lead to:

- payment of damages, which could potentially be trebled if we are found to have willfully infringed a party's patent rights;
- injunctive or other equitable relief that may effectively block our ability to further develop, commercialize, and sell products; or
- we or our collaborators having to enter into license arrangements that may not be available on commercially acceptable terms, or at all.

As a result, we could be prevented from commercializing current or future products.

Furthermore, because of the substantial amount of pre-trial document and witness discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the trading price of our common stock.

The patent applications of pharmaceutical and biotechnology companies involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our patent position.

The strength of patents in the pharmaceutical and biotechnology field can be highly uncertain and involve complex legal and factual questions. For example, some of our patent applications may cover the uses of gene sequences. The patentability of gene sequences and the use of gene sequences has been seriously undermined by recent decisions of the U.S. Supreme Court. The U.S. PTO's interpretation of the Supreme Court's decisions and the standards for patentability it sets forth are uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. U.S. patents and patent applications may also be subject to interference proceedings as mentioned above, and U.S. patents may be subject to reexamination and post-issuance proceedings in the U.S. PTO (and foreign patents may be subject to opposition or comparable proceedings in the corresponding foreign patent office), which proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. Similarly, opposition or invalidity proceedings could result in loss of rights or reduction in the scope of one or more claims of a patent in foreign jurisdictions. In addition, such interference, reexamination, post-issuance and opposition proceedings may be costly. Accordingly, rights under any issued patents may not provide us with sufficient protection against competitive products or processes.

In addition, changes in or different interpretations of patent laws in the U.S. and foreign countries may permit others to use our discoveries or to develop and commercialize our technology and products without providing any compensation to us or may limit the number of patents or claims we can obtain. In particular, there have been proposals to shorten the exclusivity periods available under U.S. patent law that, if adopted, could substantially harm our business. The product candidates that we are developing are protected by intellectual property rights, including patents and patent applications. If any of our product candidates becomes a marketable product, we will rely on our exclusivity under patents to sell the compound and recoup our investments in the research and development of the compound. If the exclusivity period for patents is shortened, then our ability to generate revenues without competition will be reduced and our business could be materially adversely impacted. The laws of some countries do not protect intellectual property rights to the same extent as U.S. laws and those countries may lack adequate rules and procedures for defending our intellectual property rights. For example, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans and, in these countries, patent protection may not be available at all to protect our product candidates. In addition, U.S. patent laws may change which could prevent or limit us from filing patent applications or patent claims to protect our products and/or technologies or limit the exclusivity periods that are available to patent holders. For example, the America Invents Act (2012) included a number of significant changes to U.S. patent law. These included changes to transition from a “first-to-invent” system to a “first-to-file” system and to the way issued patents are challenged. These changes may favor larger and more established companies that have more resources to devote to patent application filing and prosecution. It is still not clear what, if any, impact the America Invents Act will ultimately have on the cost of prosecuting our patent applications, our ability to obtain patents based on our discoveries and our ability to enforce or defend our issued patents.

If we fail to obtain and maintain patent protection and trade secret protection of our product candidates, proprietary technologies and their uses, we could lose our competitive advantage and competition we face would increase, reducing our potential revenues and adversely affecting our ability to attain or maintain profitability.

Risks Related to Government Regulation and Our Industry

Healthcare reform measures may negatively impact our ability to sell NUPLAZID or our product candidates, if approved, profitably.*

In both the U.S. and certain foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell NUPLAZID, and any other potential products, as described in greater detail in the Government Regulation section of our Annual Report.

For example, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively the ACA), as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we may receive for any approved product, including NUPLAZID. With respect to pharmaceutical products, the ACA, among other things, expanded and increased industry rebates for drugs covered by Medicaid and made changes to the coverage requirements under Medicare Part D, Medicare's prescription drug benefits program. There have been legal and political challenges to certain aspects of the ACA. For example, former President Trump signed several executive orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the ACA have been enacted. The 2017 Tax Act included a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and the medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. The Bipartisan Budget Act of 2018 (BBA), among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole", and also increased the percentage that a drug manufacturer must discount the cost of prescription drugs from 50% to 70%. Given that the current patient population for NUPLAZID is primarily Medicare beneficiaries, accelerating the closure of the coverage gap and the increase in the discount that must be paid, could have a significant impact on the Company's business in 2021 and beyond. On December 14, 2018, a federal judge in Texas ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the 2017 Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the Fifth Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing this case, but it is unknown when a decision will be reached. On February 10, 2021, the Biden administration withdrew the federal government's support for overturning the ACA. Although the U.S. Supreme Court has yet ruled on the constitutionality of the ACA, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and will remain open through August 15, 2021. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the ACA and our business.

Other legislative changes have been proposed and adopted in the U.S. since the ACA. Through the process created by the Budget Control Act of 2011, there are automatic reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, following passage of the BBA, will remain in effect through 2030 unless additional Congressional action is taken. However, COVID-19 pandemic relief legislation suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2021. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to certain providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

An expansion in the government's role in the U.S. healthcare industry may increase existing congressional or governmental agency scrutiny on price increases, such as the ones we have implemented for NUPLAZID, cause general downward pressure on the prices of prescription drug products, lower reimbursements for providers using NUPLAZID or any other product for which we obtain regulatory approval, reduce product utilization and adversely affect our business and results of operations. There have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. For example, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals. The FDA also recently released a final rule, effective November 30, 2020, implementing a portion of former President Trump's importation executive order announced in July 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the Department of Health and Human Services (HHS) finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of this rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2031. In addition, on November 20, 2020, the Centers for Medicare and Medicaid Services (CMS) issued an interim final rule implementing former President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the U.S. District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. However, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. Individual states in the U.S. have also increasingly passed legislation and implemented regulations designed to control pharmaceutical 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.

The implementation of cost-containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize NUPLAZID or any other products for which we may receive regulatory approval. It is also possible that additional governmental action may be taken in response to the COVID-19 pandemic.

We are subject, directly and indirectly, to federal, state and foreign healthcare and data protection laws and regulations, including healthcare fraud and abuse laws, false claims laws, physician payment transparency laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.*

Our operations are directly, and indirectly through our customers and third-party payors, subject to various U.S. federal and state healthcare laws and regulations, including, without limitation, the U.S. federal Anti-Kickback Statute, the U.S. federal False Claims Act, and physician payment sunshine laws and regulations. These laws may impact, among other things, our clinical research, sales, marketing, grants, charitable donations, and education programs and constrain the business or financial arrangements with healthcare providers, physicians, charitable foundations that support Parkinson's disease patients generally, and other parties that have the ability to directly or indirectly influence the prescribing, ordering, marketing, or distribution of our products for which we obtain marketing approval. In addition, we and any potential future collaborators, partners or service providers are subject to data privacy and security regulation by both the U.S. federal government and the states in which we conduct our business. Finally, we may be subject to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. The laws that may affect our ability to operate include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs 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;
- the U.S. federal civil and criminal false claims laws, including the civil False Claims Act, which can be enforced through civil whistleblower or *qui tam* actions, and civil monetary penalties laws, which impose criminal and civil penalties on individuals or entities for, among other things, knowingly presenting, or causing to be presented to the U.S. federal government, claims for payment or approval that are false or fraudulent or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute 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), which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device 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 U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, and its implementing regulations, and as amended again by the Final HIPAA Omnibus Rule, Modifications to the HIPAA Privacy, Security, Enforcement and Breach Notification Rules Under the Health Information Technology for Economic and Clinical Health Act (HITECH) and the Genetic Information Nondiscrimination Act; Other Modifications to the HIPAA Rules, published in January 2013, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information on covered entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers as well as their business associates, individuals or entities that perform certain services involving the use or disclosure of individually identifiable health information on behalf of a covered entity and their subcontractors that use, disclose or otherwise process individually identifiable health information;
- the U.S. Federal Food, Drug and Cosmetic Act (FDCA), which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. federal physician payment transparency requirements, sometimes referred to as the “Physician Payments Sunshine Act”, which was enacted as part of the ACA and its implementing regulations and requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children’s Health Insurance Program to report annually to CMS information related to certain payments and other transfers of value made to physicians (as defined to include doctors of medicine, dentists, optometrists, podiatrists and chiropractorsunder such law), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members, which will be expanded beginning in 2022, to require applicable manufacturers to report such information regarding its payments and other transfers of value made during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives;
- analogous state and local laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and local laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities and/or the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers, and the European General Data Protection Regulation (EU) 2016/679 (GDPR), which became effective in May 2018 and contains new provisions specifically directed at the processing of health information, higher sanctions and extra-territoriality measures intended to bring non-EU companies under the regulation, including companies like us that conduct clinical trials in the EU; we anticipate that over time we may expand our business operations to include additional operations in the EU and with such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including the GDPR.

The GDPR has increased our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Failure to comply with the GDPR carries significant risk; potential fines for noncompliant companies of are up to the greater of €20 million or 4% of annual global revenue. Compliance with the GDPR and applicable EU Member States and the United Kingdom privacy laws is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, and reputational harm in connection with our European activities. In addition, our failure to comply with GDPR and privacy laws of EU Member States or the United Kingdom may result in regulators prohibiting our processing of the personal information of EU data subjects, which could impact our operations and ability to develop our products and provide our services, including interrupting or ending EU clinical trials.

In addition, the GDPR includes restrictions on cross-border data transfers. A recent decision by the Court of Justice of the European Union (the "Schrems II" ruling), however, has invalidated the EU-U.S. Privacy Shield Framework, which was one of the primary mechanisms used by U.S. Companies to import personal information from Europe, and raised questions about whether the European Commission's Standard Contractual Clauses (SCCs), one of the primary alternatives to the Privacy Shield, can lawfully be used for personal information transfers from Europe to the U.S. or most other countries. Similarly, the Swiss Federal Data Protection and Information Commissioner recently opined that the Swiss-U.S. Privacy Shield is inadequate for transfers of data from Switzerland to the U.S. The United Kingdom, whose data protection laws are similar to those of the European Union, may similarly determine that the EU-U.S. Privacy Shield is not a valid mechanism for lawfully transferring personal information from the UK to the U.S. The European Commission recently proposed updates to the SCCs, and additional regulatory guidance has been released that seeks to impose additional obligations on companies seeking to rely on the SCCs. Given that, at present, there are few, if any, viable alternatives to the EU-U.S. Privacy Shield and the SCCs, any transfers by us or our vendors of personal data from Europe may not comply with European data protection law, which may increase our exposure to the GDPR's heightened sanctions for violations of its cross-border data transfer restrictions and may prohibit our transfer of EU personal data outside of the EU (including clinical trial data), and may adversely impact our operations, product development and ability to provide our products.

Further, the United Kingdom's vote in favor of exiting the EU, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. Beginning in 2021, the UK will be a "third country" under the GDPR and transfers of European personal information to the U.K. will require an adequacy mechanism to render such transfers lawful under the GDPR. Compliance with the GDPR and applicable EU Member States and the United Kingdom privacy laws will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. In addition, our failure to comply with GDPR and privacy laws of EU Member States or the United Kingdom may result in regulators prohibiting our processing of the personal information of EU data subjects, which could impact our operations and ability to develop our products and provide our services, including interrupting or ending EU clinical trials.

Moreover, states are constantly adopting new data protection laws or amending existing laws, requiring attention to frequently changing regulatory requirements. For example, California recently enacted legislation, which became effective on January 1, 2020, that has been dubbed the first "GDPR-like" law in the U.S. Known as the California Consumer Privacy Act (CCPA), gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used by requiring covered companies to provide new disclosures to California consumers (as that term is broadly defined and can include any of our current or future employees who may be California residents) and provide such residents new ways to opt-out of certain sales of personal information. As we expand our operations and trials, the CCPA may increase our compliance costs and potential liability.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Data protection laws and data protection worldwide is, and is likely to remain, uncertain for the foreseeable future. While we strive to comply with applicable data protection laws, external and internal privacy and security policies, and contractual data protection obligations to the extent possible, we may at times fail to do so, or may be perceived to have failed to do so. Moreover, despite our efforts, we may not be successful in achieving compliance if our personnel, collaborators, partners or vendors do not comply with applicable data protection laws, external and internal privacy and security policies, and contractual data protection obligations. Actual or perceived failure to comply with U.S. and international data protection laws could result in government enforcement actions (which could include civil or criminal penalties), private litigation or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individual's privacy rights, even if we are found not liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business.

We are also subject to the terms of our external and internal privacy and security policies, representations, certifications, publications and frameworks, and contractual obligations to third parties related to privacy, information security and processing. Failure or a perceived failure to comply with these policies, or if these policies are, in whole or part, found or perceived to be inaccurate, incomplete, deceptive, unfair, or misrepresentative of our actual practices, could result in reputational harm; result in litigation; cause a material adverse impact to business operations or financial results, and; otherwise result in other material harm to our business.

Additionally, California recently enacted legislation, which became effective on January 1, 2020, that has been dubbed the first "GDPR-like" law in the U.S. Known as the California Consumer Privacy Act (CCPA), it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. As currently written, the CCPA will likely impact (possibly significantly) our business activities and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. For example, contributions to third-party charitable foundations are a current area of significant governmental and congressional scrutiny, and we could face action if a federal or state governmental authority were to conclude that our charitable contributions to foundations that support Parkinson's disease patients generally are not compliant. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government-funded healthcare programs, such as Medicare and Medicaid, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits, additional reporting requirements and/or oversight, and the curtailment or restructuring of our operations. Moreover, while we do not bill third-party payors directly and our customers make the ultimate decision on how to submit claims, from time-to-time, for NUPLAZID, and any other product candidates that may be approved, we may provide reimbursement guidance to patients and healthcare providers. If a government authority were to conclude that we provided improper advice and/or encouraged the submission of a false claim for reimbursement, we could face action against us by government authorities. If any of the physicians or other providers or entities with whom we expect 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 government-funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of NUPLAZID, or any other product candidates that may be approved, outside the U.S. will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the U.S., we could be subject to additional reimbursement requirements, fines, sanctions and exposure under other laws which could have a material adverse effect on our business, results of operations and financial condition.*

We participate in the Medicaid Drug Rebate Program, as administered by CMS, and other federal and state government pricing programs in the U.S., and we may participate in additional government pricing programs in the future. These programs generally require us to pay rebates or otherwise provide discounts to government payors in connection with drugs that are dispensed to beneficiaries/recipients of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing that we report on a monthly and quarterly basis to the government agencies that administer the programs. Pricing requirements and rebate/discount calculations are complex, vary among products and programs, and are often subject to interpretation by governmental or regulatory agencies and the courts. The requirements of these programs, including, by way of example, their respective terms and scope, change frequently. For example, on March 11, 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, for single source and innovator multiple source drugs, beginning January 1, 2024. Responding to current and future changes may increase our costs, and the complexity of compliance will be time consuming. Invoicing for rebates is provided in arrears, and there is frequently a time lag of up to several months between the sales to which rebate notices relate and our receipt of those notices, which further complicates our ability to accurately estimate and accrue for rebates related to the Medicaid program as implemented by individual states. Thus, there can be no assurance that we will be able to identify all factors that may cause our discount and rebate payment obligations to vary from period to period, and our actual results may differ significantly from our estimated allowances for discounts and rebates. Changes in estimates and assumptions may have a material adverse effect on our business, results of operations and financial condition.

In addition, the HHS Office of Inspector General and other Congressional, enforcement and administrative bodies have recently increased their focus on pricing requirements for products, including, but not limited to the methodologies used by manufacturers to calculate average manufacturer price (AMP), and best price (BP), for compliance with reporting requirements under the Medicaid Drug Rebate Program. We are liable for errors associated with our submission of pricing data and for any overcharging of government payors. For example, failure to submit monthly/quarterly AMP and BP data on a timely basis could result in significant civil monetary penalties for each day the submission is late beyond the due date. Failure to make necessary disclosures and/or to identify overpayments could result in allegations against us under the civil False Claims Act and other laws and regulations. Any required refunds to the U.S. government or responding to a government investigation or enforcement action would be expensive and time consuming and could have a material adverse effect on our business, results of operations and financial condition. In addition, in the event that the CMS were to terminate our rebate agreement, no federal payments would be available under Medicaid or Medicare for our covered outpatient drugs.

The FDA granted marketing approval of NUPLAZID for the treatment of hallucinations and delusions associated with PDP, and we could face liability if a regulatory authority determines that we are promoting NUPLAZID for any "off-label" uses.

A company may not promote "off-label" uses for its drug products. An off-label use is the use of a product for an indication or patient population that is not described in the product's FDA-approved label in the U.S. or for uses in other jurisdictions that differ from those approved by the applicable regulatory agencies. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from pharmaceutical companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. A company that is found to have promoted off-label use of its product may be subject to significant liability, including civil and criminal sanctions. We intend to comply with the requirements and restrictions of the FDA and other regulatory agencies with respect to our promotion of NUPLAZID, and any other products we may market, but we cannot be sure that the FDA or other regulatory agencies will agree that we have not violated their restrictions. As a result, we may be subject to criminal and civil liability. In addition, our management's attention could be diverted to handle any such alleged violations. A significant number of pharmaceutical companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice (DOJ), and various U.S. Attorneys' Offices, the HHS Office of Inspector General, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the FDCA, the civil False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. If the FDA, DOJ, or any other governmental agency initiates an enforcement action against us, or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects, and reputation.

Changes at the FDA and other government agencies could delay or prevent new products from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our 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 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 other government agencies on which our 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 new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including beginning on December 22, 2018 and ending on January 25, 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical government employees and stop critical activities. If repeated or prolonged government shutdowns occur, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, and negatively impact other government operations on which we rely, which could have a material adverse effect on our business. In addition, the COVID-19 pandemic may affect processing times as the FDA reallocates resources to immediate needs such as the review and approval of viral and antibody tests, therapeutic treatments for use by COVID-19 patients and SARS-CoV-2 vaccines.

We are subject to stringent regulation in connection with the marketing of NUPLAZID and any other products derived from our product candidates, which could delay the development and commercialization of our products.

The pharmaceutical industry is subject to stringent regulation by the FDA and other regulatory agencies in the U.S. and by comparable authorities in other countries. Neither we nor our collaborators can market a pharmaceutical product, including NUPLAZID, in the U.S. until it has completed rigorous preclinical testing and clinical trials and an extensive regulatory clearance process implemented by the FDA. Satisfaction of regulatory requirements typically takes many years, depends upon the type, complexity and novelty of the product, and requires substantial resources. Even if regulatory approval is obtained, the FDA and other regulatory agencies may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, and/or marketing of such products, and requirements for post-approval studies, including additional research and development and clinical trials. These limitations may limit the size of the market for the product or result in the incurrence of additional costs. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular product candidate.

Outside the U.S., the ability to market a product is contingent upon receiving approval from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing, and reimbursement vary widely from country to country. Only after the appropriate regulatory authority is satisfied that adequate evidence of safety, quality, and efficacy has been presented will it grant a marketing authorization. Approval by the FDA does not automatically lead to the approval by regulatory authorities outside the U.S. and, similarly, approval by regulatory authorities outside the U.S. will not automatically lead to FDA approval.

In addition, U.S. and foreign government regulations control access to and use of some human or other tissue samples in our research and development efforts. U.S. and foreign government agencies may also impose restrictions on the use of data derived from human or other tissue samples. Accordingly, if we fail to comply with these regulations and restrictions, the commercialization of our product candidates may be delayed or suspended, which may delay or impede our ability to generate product revenues.

If our competitors develop and market products that are more effective than NUPLAZID or our product candidates, they may reduce or eliminate our commercial opportunity.*

Competition in the pharmaceutical and biotechnology industries is intense and expected to increase. We face competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, both in the U.S. and abroad. Some of these competitors have products or are pursuing the development of drugs that target the same diseases and conditions that are the focus of our drug development programs.

For example, the use of NUPLAZID for the treatment of PDP competes with off-label use of various antipsychotic drugs, including the generic drugs quetiapine, clozapine, risperidone, aripiprazole, and olanzapine. If approved, pimavanserin for the treatment of DRP would also compete with off-label use of various antipsychotic drugs, including the generic drugs quetiapine, clozapine, risperidone, aripiprazole, and olanzapine, as well as generic mood stabilizers such as valproate. Other generic agents for the treatment of underlying dementia such as donepezil and memantine may also be secondarily used for the treatment of DRP, although NUPLAZID would not be promoted to replace these agents. Pimavanserin for the treatment of negative symptoms of schizophrenia, if approved for that indication, would compete with off-label use of Vraylar, marketed by Allergan, Rexulti, marketed by Otsuka Pharmaceutical Co., Ltd., Latuda, marketed by Sunovion Pharmaceuticals Inc., Caplyta, marketed by IntraCellular Therapeutics and various generic drugs, including quetiapine, clozapine, risperidone, aripiprazole, and olanzapine. In addition, trofinetide, if approved would compete indirectly with off-label usage of branded and generic prescription medications targeted at individual symptoms of Rett syndrome, including antiepileptics, antipsychotics, antidepressants and benzodiazepines. Several academic institutions and pharmaceutical companies are currently conducting clinical trials for the treatment of various symptoms of Rett syndrome.

Many of our competitors and their collaborators have significantly greater experience than we do in the following:

- identifying and validating targets;
- screening compounds against targets;
- preclinical studies and clinical trials of potential pharmaceutical products;
- obtaining FDA and other regulatory approvals; and
- commercializing pharmaceutical products.

In addition, many of our competitors and their collaborators have substantially greater capital and research and development resources, manufacturing, sales and marketing capabilities, and production facilities. Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaboration arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved or are in advanced development and may develop superior technologies or methods to identify and validate drug targets and to discover novel small molecule drugs. Our competitors, either alone or with their collaborators, may succeed in developing drugs that are more effective, safer, more affordable, or more easily administered than ours and may achieve patent protection or commercialize drugs sooner than us. Our competitors may also develop alternative therapies that could further limit the market for any drugs that we may develop. Our failure to compete effectively could have a material adverse effect on our business.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of NUPLAZID or any other product for which we obtain regulatory approval, or development or commercialization of our product candidates.

We face an inherent risk of product liability as a result of the commercial sales of NUPLAZID in the U.S. and the clinical testing of our product candidates, and will face an even greater risk following commercial launch of NUPLAZID in additional jurisdictions, if approved, or if we engage in the clinical testing of new product candidates or commercialize any additional products. For example, we may be sued if NUPLAZID or any other product we develop allegedly causes injury or is found to be otherwise unsuitable for administration in humans. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products or product candidates that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management’s time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize our products or product candidates; and
- a decline in our stock price.

Although we currently have product liability insurance that covers our clinical trials and the commercialization of NUPLAZID, we may need to increase and expand this coverage, including if we commence larger scale trials and if other product candidates are approved for commercial sale. This insurance may be prohibitively expensive or may not fully cover our 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 products that we or our collaborators develop. If we determine that it is prudent to increase our product liability coverage, we may be unable to obtain such increased coverage on acceptable terms or at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. Our liability could exceed our total assets if we do not prevail in a lawsuit from any injury caused by our drug products. Product liability claims could have a material adverse effect on our business and results of operations.

We are dependent on information technology systems, infrastructure and data, which exposes us to data security risks. If our security measures are compromised now, or in the future, or the security, confidentiality, integrity or availability of, our information technology, software, services, communications or data is compromised, limited or fails, this could result in a materially adverse impact, including without limitation, a material operation or service interruption, harm to our reputation, significant fines, penalties and liability, breach or triggering of data protection laws, privacy policies and data protection and data protection obligations, loss of customers or sales, or users curtailing or ceasing their use of our products.

We are dependent upon our own or third-party information technology systems, infrastructure and data, including mobile technologies, to operate our business. The multitude and complexity of our computer systems may make them vulnerable to service interruption or destruction, disruption of data integrity, malicious intrusion, or random attacks. Likewise, data privacy or security incidents or breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients, customers or other business partners may be exposed to unauthorized persons or to the public. Cyber-attacks are increasing in their frequency, sophistication and intensity. In addition to traditional computer "hackers," threat actors, software bugs, malicious code (such as viruses and worms), employee theft or misuse, denial-of-service attacks (such as credential stuffing), phishing and ransomware attacks, sophisticated nation-state and nation-state supported actors now engage in attacks (including advanced persistent threat intrusions). Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. Cyber-attacks could include the deployment of harmful malware, denial-of-service, social engineering and other means to affect service reliability and threaten data confidentiality, integrity and availability. Our business partners, collaborators, and service providers face similar risks and any security breach of their systems could adversely affect our security posture.

While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, there can be no assurance that our efforts will prevent service interruptions, or identify, prevent or mitigate breaches of or disruptions to our systems in our systems. We may be required to expend significant resources, fundamentally change our business activities and practices or modify our operations or information technology in an effort to protect against security breaches and to mitigate, detect, and remediate actual and potential vulnerabilities. , that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. A security breach or privacy violation that leads to disclosure or modification of or prevents access to patient sensitive information, including personally identifiable information or protected health information, or a perceived security breach or violation, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, subject us to investigations by federal or state authorities, require us to verify the correctness of database contents, harm our reputation and otherwise subject us to litigation or other liability under laws and regulations that protect personal data, any of which could disrupt our business and/or result in increased costs or loss of revenue. Additionally, violations of our external contractual commitments and internal privacy and security policies may require us to notify relevant stakeholders if there has been a security breach, including affected individuals, business partners and regulators. Such disclosures are costly, and the disclosures or the failure to comply with such requirements could lead to a materially adverse impact on the business, including negative publicity, a loss of confidence in our services or security measures by our business partners or breach of contract claims. There can be no assurances that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages if we fail to comply with applicable data protection laws, privacy policies or other data protection obligations related to information security or security breaches. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, there can be no assurance that our efforts will prevent service interruptions, or identify breaches in our systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks and other related breaches. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large deductible or co-insurance requirements), could have an adverse effect on our business.

Risks Related to Our Common Stock

Our stock price historically has been, and is likely to remain, highly volatile.*

The market prices for securities of biotechnology companies in general, and drug discovery and development companies in particular, have been highly volatile and may continue to be highly volatile in the future. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

- the success of our commercialization of NUPLAZID in the U.S. for the treatment of hallucinations and delusions associated with PDP;

- the status and cost of our post-marketing commitments for NUPLAZID;
- the status and cost of development and commercialization of pimavanserin for indications other than in PDP, including DRP, and in jurisdictions other than the U.S.;
- the status and cost of development and commercialization of our product candidates, including compounds being developed under our collaborations;
- whether we acquire or in-license additional product candidates or products, and the status of development and commercialization of such product candidates or products;
- any other communications or guidance from the FDA or other regulatory authorities that pertain to NUPLAZID or our product candidates;
- the initiation, termination, or reduction in the scope of our collaborations or any disputes or developments regarding our collaborations;
- market conditions or trends related to biotechnology and pharmaceutical industries, or the market in general;
- announcements of technological innovations, new products, or other material events by our competitors or us, including any new products that we may acquire or in-license;
- disputes or other developments concerning our proprietary and intellectual property rights;
- changes in, or failure to meet, securities analysts' or investors' expectations of our financial performance;
- our failure to meet applicable Nasdaq listing standards and the possible delisting of our common stock from the Nasdaq Stock Market;
- additions or departures of key personnel;
- discussions of our business, products, financial performance, prospects, or stock price by the financial and scientific press and online investor communities such as blogs and chat rooms;
- public concern as to, and legislative action with respect to, genetic testing or other research areas of biopharmaceutical companies, the pricing and availability of prescription drugs, or the safety of drugs and drug delivery techniques;
- regulatory developments in the U.S. and in foreign countries;
- changes in the structure of healthcare payment systems;
- the announcement of, or developments in, any litigation matters;
- disruptions caused by man-made or natural disasters or public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic; and
- economic and political factors, including but not limited to economic and financial crises, wars, terrorism, and political unrest.

In the past, following periods of volatility in the market price of a particular company's securities, securities class action litigation has often been brought against that company. For example, we, and certain of our current and former officers and directors, are subject to numerous lawsuits related to prior statements about NUPLAZID and our sNDA seeking approval of pimavanserin for the treatment of hallucinations and delusions associated with DRP, as described above in "Legal Proceedings". If we are not successful in defense of these claims, we may have to make significant payments to, or other settlements with, our stockholders and their attorneys. Even if such claims are not successful, the litigation could result in substantial costs and divert our management's attention and resources, which could have a material adverse effect on our business, operating results or financial condition.

If we or our stockholders sell substantial amounts of our common stock, the market price of our common stock may decline.

A significant number of shares of our common stock are held by a small number of stockholders. Sales of a significant number of shares of our common stock, or the expectation that such sales may occur, could significantly reduce the market price of our common stock. In connection with our March 2014 public offering of common stock, we agreed to provide resale registration rights for the shares of our common stock held by entities affiliated with one of our principal stockholders and two of our directors, Julian C. Baker and Dr. Stephen R. Biggar, which we refer to as the Baker Entities. In connection with our January 2016 public offering of common stock, we entered into a formal registration rights agreement with the Baker Entities to provide for these rights. Under the registration rights agreement we have agreed that, if at any time and from time to time, the Baker Entities demand that we register their shares of our common stock for resale under the Securities Act, we would be obligated to effect such registration. On May 3, 2019, we filed a registration statement covering the sale of up to 40,203,111 shares of our common stock, which includes 489,269 shares of our common stock issuable upon the exercise of warrants that were owned by the Baker Entities as of April 29, 2019, and which represented approximately 28 percent of our outstanding shares at the time. Our registration obligations under this registration rights agreement cover all shares now held or later acquired by the Baker Entities will be in effect for up to 10 years, and include our obligation to facilitate certain underwritten public offerings of our common stock by the Baker Entities in the future. If the Baker Entities sell a large number of our shares, or the market perceives that the Baker Entities intend to sell a large number of our shares, this could adversely affect the market price of our common stock. We also may elect to sell an indeterminate number of shares on our own behalf pursuant to a registration statement or in a private placement, from time to time. Our stock price may decline as a result of the sale of the shares of our common stock included in any of these registration statements or future financings.

If our officers, directors, and largest stockholders choose to act together, they may be able to significantly influence our management and operations, acting in their best interests and not necessarily those of our other stockholders.

Our directors, executive officers and holders of 5% or more of our outstanding common stock and their affiliates beneficially own a substantial portion of our outstanding common stock. As a result, these stockholders, acting together, have the ability to significantly influence all matters requiring approval by our stockholders, including the election of all of our board members, amendments to our certificate of incorporation, going-private transactions, and the approval of mergers or other business combination transactions. The interests of this group of stockholders may not always coincide with our interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of our other stockholders.

Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us more complicated and may make the removal and replacement of our directors and management more difficult.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may delay or prevent a change in control, discourage bids at a premium over the market price of our common stock and adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. These provisions may also make it difficult for stockholders to remove and replace our board of directors and management. These provisions:

- establish that members of the board of directors may be removed only for cause upon the affirmative vote of stockholders owning at least a majority of our capital stock;
- authorize the issuance of “blank check” preferred stock that could be issued by our board of directors to increase the number of outstanding shares and prevent or delay a takeover attempt;
- limit who may call a special meeting of stockholders;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings;
- prohibit our stockholders from making certain changes to our amended and restated certificate of incorporation or amended and restated bylaws except with $66^{2/3}$% stockholder approval; and
- provide for a board of directors with staggered terms.

We are also subject to provisions of the Delaware corporation law that, in general, prohibit any business combination with a beneficial owner of 15% or more of our common stock for three years unless the holder’s acquisition of our stock was approved in advance by our board of directors. Although we believe these provisions collectively provide for an opportunity to receive higher bids by requiring potential acquirors to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders.

We do not intend to pay dividends on our common stock in the foreseeable future; as such, you must rely on stock appreciation for any return on your investment.

To date, we have not paid any cash dividends on our common stock, and we do not intend to pay any dividends in the foreseeable future. Instead, we intend to retain any future earnings to fund the development and growth of our business. For this reason, the success of an investment in our common stock, if any, will depend on the appreciation of our common stock, which may not occur. There is no guarantee that our common stock will appreciate, and therefore, a holder of our common stock may not realize a return on his or her investment.

General Risk Factors

Our management has broad discretion over the use of our cash and we may not use our cash effectively, which could adversely affect our results of operations.

Our management has significant flexibility in applying our cash resources and could use these resources for corporate purposes that do not increase our market value, or in ways with which our stockholders may not agree. We may use our cash resources for corporate purposes that do not yield a significant return or any return at all for our stockholders, which may cause our stock price to decline.

We have incurred, and expect to continue to incur, significant costs as a result of laws and regulations relating to corporate governance and other matters.

Laws and regulations affecting public companies, including provisions of the Dodd-Frank Wall Street Reform and Consumer Protection Act that was enacted in July 2010, the provisions of the Sarbanes-Oxley Act of 2002 (SOX), and rules adopted or proposed by the SEC and by The Nasdaq Stock Market, have resulted in, and will continue to result in, significant costs to us as we evaluate the implications of these rules and respond to their requirements. In the future, if we are not able to issue an evaluation of our internal control over financial reporting, as required, or we or our independent registered public accounting firm determine that our internal control over financial reporting is not effective, this shortcoming could have an adverse effect on our business and financial results and the price of our common stock could be negatively affected. New rules could make it more difficult or more costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the coverage that is the same or similar to our current coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors and board committees, and as our executive officers. We cannot predict or estimate the total amount of the costs we may incur or the timing of such costs to comply with these rules and regulations.

Changes or modifications in financial accounting standards, including those related to revenue recognition, may harm our results of operations.

From time to time, the Financial Accounting Standards Board (FASB), either alone or jointly with other organizations, promulgates new accounting principles that could have an adverse impact on our financial position, results of operations or reported cash flows. In February 2016, the FASB issued Accounting Standards Update (ASU) No. 2016-02, *Leases (Topic 842)*, which requires a lessee to recognize a lease liability and a right-of-use asset for all leases with lease terms of more than 12 months. We adopted this new standard for the year beginning January 1, 2019. Consequently, all of our operating lease commitments were recognized as lease liabilities, with corresponding right-of-use assets, based on the present value of the remaining minimum rental payments under current leasing standards for existing operating leases. Upon adoption of the standard, we recorded a right-of-use asset and lease liability of approximately $12.0 million in our condensed consolidated balance sheets. We have elected the standard's package of practical expedients on adoption requiring no reassessment of whether any expired or existing agreements contain a lease, the classification of any expired or existing lease agreements, or initial direct costs for any existing leases. The majority of our leases are facility and equipment leases and are classified as operating leases under current lease guidance. Any difficulties in implementing this standard, or in adopting or implementing any other new accounting standard, and to update or modify our internal controls as needed on a timely basis, could result in our failure to meet our financial reporting obligations, which could result in regulatory discipline and harm investors' confidence in us. Finally, if we were to change our critical accounting estimates, including those related to the recognition of product revenue, our operating results could be significantly affected.

Adverse securities and credit market conditions may significantly affect our ability to raise capital.

Historically, turmoil and volatility in the financial markets (including recent volatility as a result of the COVID-19 pandemic) have adversely affected the market capitalizations of many biotechnology companies, and generally made equity and debt financing more difficult to obtain. These events, coupled with other factors, may limit our access to financing in the future. This could have a material adverse effect on our ability to access funding on acceptable terms, or at all, and our stock price may suffer further as a result.

ITEM 6. EXHIBITS

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation, as amended (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q, filed August 6, 2015).
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.2 to the Registrant's Annual Report on Form 10-K, filed February 24, 2021).
3.3	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed September 12, 2013).
4.1	Form of common stock certificate of the Registrant (incorporated by reference to Exhibit 4.1 to Registration Statement No. 333-52492).
4.2	Form of Amended and Restated Warrant to Purchase Common Stock issued to purchasers in a private placement on December 17, 2012 (incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K, filed on February 27, 2019).
10.1*	Master Manufacturing Services Agreement and Product Agreement, dated August 3, 2015, by and between the Registrant and Patheon Pharmaceuticals Inc.
10.2*	First Amendment to Product Agreement, dated April 25, 2016, by and between the Registrant and Patheon Pharmaceuticals Inc.
10.3*	Second Amendment to Product Agreement, dated October 6, 2016, by and between the Registrant and Patheon Pharmaceuticals Inc.
10.4*	Third Amendment to Product Agreement, dated December 11, 2017, by and between the Registrant and Patheon Pharmaceuticals Inc.
31.1	Certification of Stephen R. Davis, Chief Executive Officer, pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Elena Ridloff, Executive Vice President and Chief Financial Officer, pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Stephen R. Davis, Chief Executive Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of Elena Ridloff, Executive Vice President and Chief Financial Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following financial statements from the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2021, filed on May 5, 2021, formatted in iXBRL (Inline Extensible Business Reporting Language), are filed herewith: (i) Condensed Consolidated Balance Sheets, (ii) Condensed Consolidated Statements of Operations, (iii) Condensed Consolidated Statements of Comprehensive Loss, (iv) Condensed Consolidated Statements of Cash Flows, and (v) Notes to Condensed Consolidated Financial Statements.
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)

* Certain portions of this exhibit (indicated by asterisks) have been excluded pursuant to Item 601(b)(10) of Regulation S-K because they are both not material and are the type that the Registrant treats as private or confidential.

SIGNATURES

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

Acadia Pharmaceuticals Inc.

Date: May 5, 2021

By: /s/ Elena Ridloff
Elena Ridloff
Executive Vice President and Chief Financial Officer
(on behalf of the registrant and as the registrant's Principal Financial Officer)

Exhibit 10.1

Master Manufacturing Services Agreement

August 3, 2015

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MASTER MANUFACTURING SERVICES AGREEMENT

THIS MASTER MANUFACTURING SERVICES AGREEMENT (the "Agreement") is made as of August 3**,** 2015 (the "**Effective Date**")

B E T W E E N:

PATHEON PHARMACEUTICALS INC.,
a corporation existing under the laws of the State of Delaware

("**Patheon**"),

- and -

ACADIA PHARMACEUTICALS INC.,
a corporation existing under the laws of the State of Delaware

("**Client**").

THIS AGREEMENT WITNESSES THAT in consideration of the rights conferred and the obligations assumed herein, and for other good and valuable consideration (the receipt and sufficiency of which are acknowledged by each Party), and intending to be legally bound the Parties agree as follows:

STRUCTURE OF AGREEMENT AND INTERPRETATION

1.1 Master Agreement.

This Agreement establishes the general terms and conditions under which Patheon or any Affiliate of Patheon may perform Manufacturing Services for Client or any Affiliate of Client, at the manufacturing site where the Affiliate of Patheon resides. This "master" form of agreement is intended to allow the Parties, or any of their Affiliates, to contract for the manufacture of multiple Products through Patheon's global network of manufacturing sites through the issuance of site specific Product Agreements without having to re-negotiate the basic terms and conditions contained herein.

1.2 Product Agreements.

This Agreement is structured so that a Product Agreement may be entered into by the Parties for the manufacture of a particular Product or multiple Products at a Patheon manufacturing site. Each Product Agreement will be governed by the terms and conditions of this Agreement unless the Parties to the Product Agreement expressly modify the terms and conditions of this Agreement in the Product Agreement. Unless otherwise agreed by the Parties, each Product Agreement will be in the general form and contain the information set forth in Appendix 1 hereto.

1.3 Definitions.

The following terms will have the respective meanings set out below and grammatical variations of these terms will have corresponding meanings:

"**Active Materials**", **"Active Pharmaceutical Ingredients" or "API"** means the materials listed in a Product Agreement on Schedule D;

"**Active Materials Credit Value**" means the value of the Active Materials for certain purposes of this Agreement, as set forth in a Product Agreement on Schedule D;

"**Actual Annual Yield**" or "**AAY**" has the meaning specified in Section 2.2(a);

"**Affiliate**" means:

(a) a business entity which owns, directly or indirectly, a controlling interest in a Party to this Agreement, by stock ownership or otherwise; or

(b) a business entity which is controlled by a Party to this Agreement, either directly or indirectly, by stock ownership or otherwise; or

(c) a business entity, the controlling interest of which is directly or indirectly common to the controlling interest of a Party to this Agreement;

For this definition, "control" means the ownership of shares carrying at least a majority of the votes for the election of the directors of a corporation or other business entity (with corresponding meanings for "controlling interest" and "controlled by");

"Annual Minimum" will have the meaning specified in Section 2.1;

"Annual Product Review Report" means the annual product review report prepared by Patheon as described in Title 21 of the United States Code of Federal Regulations, Section 211.180(e);

"**Annual Report"** means the annual report to the FDA prepared by Client regarding the Product as described in Title 21 of the United States Code of Federal Regulations, Section 314.81(b)(2);

"**Annual Volume**" means the minimum volume of Product to be manufactured in any Year of this Agreement as set forth in a Product Agreement on Schedule B;

"**Applicable Laws**" means the applicable provisions of any and all national, supranational, regional, state, provincial, county and local laws, statutes, treaties, ordinances, regulations, rules, administrative codes, guidance, ordinances, by-laws, judgments, decrees, directives, injunctions, permits (including marketing approvals) or orders of or from any Authority having jurisdiction over or related to the subject item;

"**Authority**" means any governmental or regulatory authority, department, body or agency or any court, tribunal, bureau, commission or other similar body, whether national, supranational, regional, state, provincial, county or local;

“Batch” means a specific quantity of Product or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of Manufacturing Services;

“Bill Back Items” means the reasonable documented actual expenses in accordance with Section 2.1(g) for all third party supplier fees for the purchase or use of columns, standards, tooling, non-standard pallets, PAPR or PPE suits (where applicable), RFID tags and supporting equipment, and other Product-specific items, in each case, as necessary for Patheon to perform the Manufacturing Services, and which are not included as Components;

“**Breach Notice**” will have the meaning specified in Section 8.2(a);

"**Business Day**" means a day other than a Saturday, Sunday or a day that is a statutory holiday in the jurisdiction where the Manufacturing Site is located or in the State of California;

“**Capital Equipment Agreement**” means a separate agreement that the Parties may enter into that will address responsibility for the purchase of capital equipment and facility modifications that may be required to perform the Manufacturing Services under a particular Product Agreement;

"**cGMPs**" means, as applicable, current good manufacturing practices as described in:

(a) Division 2 of Part C of the *Food and Drug Regulations* (Canada);

(b) Parts 210 and 211 of Title 21 of the United States' Code of Federal Regulations;

(c) EC Directive 2003/94/EC; and

(d) ICH guidelines;

together with the latest Health Canada, FDA, and EMA and any other jurisdiction agreed to by the Parties guidance documents pertaining to manufacturing and quality control practice, all as updated, amended and revised from time to time, and any foreign equivalents to any such regulations which may apply to the Manufacturing Site or be applicable to Products sold outside of the United States, Canada or the European Union;

“Certificate of Analysis” means, with respect to a Batch, that document setting for the measured and observable characteristics of Product from the Batch, as required by the Specifications, as dated, executed and provided to Client by Patheon prior to delivery of the Product;

“Certificate of Compliance” means a statement signed by Patheon that certifies that all Manufacturing Services of a Batch of Product was performed or otherwise implemented, packaged, stored and tested in accordance with cGMP and all other regulatory requirements;

“**Claims**” has the meaning specified in Section 10.3;

“**Client Indemnitees**” has the meaning specified in Section 10.3;

“Client Intellectual Property” means Intellectual Property generated or derived by Client or any of its Affiliates before entering into this Agreement or independent of this Agreement, or by Patheon or any of its Affiliates while performing any Manufacturing Services or otherwise

generated or derived by Patheon or any of its Affiliates in its business, which Intellectual Property is directly related to, specific to, or dependent upon, Client's Active Materials or Product;

"**Client Property**" will have the meaning specified in Section 8.4(e);

"**Client-Supplied Components**" means those Components to be supplied by Client or that have been supplied by Client;

"**CMC**" has the meaning specified in Section 7.8(c);

"**Components**" means, collectively, all packaging components, raw materials, ingredients, and other materials (including labels, product inserts and other labelling for the Products) required to manufacture the Products in accordance with the Specifications, other than the Active Materials;

"**Confidential Information**" has the meaning specified in Section 11.1;

"DDP" has the meaning as set forth in the 2010 edition of the International Commercial terms published by the International Chamber of Commerce, as may be amended or modified from time to time (**Incoterms 2010**);

"**Deficiencies**" has the meaning specified in Section 7.8(d);

"**Deficiency Notice**" has the meaning specified in Section 6.1(a);

"Delivery Date" means the date scheduled for shipment of Product under a Firm Order as set forth in Section 5.1(d);

"Delivery Documentation" has the meaning specified in Section 2.1(b);

"Disclosing Party" has the meaning specified in Section 11.1;

"Deviation" means a departure from an established quality standard, including, but not limited to, that set forth in any Product Agreement, any Quality Agreement, cGMP standard operating procedure, manufacturing work order, packaging order, raw material or product specification, analytical control procedure, water monitoring procedure, equipment maintenance schedule, or any unusual occurrence that could affect the Product. Deviations may be either anticipated or unanticipated departures from established quality standards and may have the potential to affect the safety, identity, strength, quality or purity of a Product;

"**EMA**" means the European Medicines Agency or any successor agency thereto which may regulate pharmaceutical products;

"EXW" has the meaning as set forth in Incoterms 2010;

"**FDA**" means the United States Food and Drug Administration or any successor agency thereto which may regulate pharmaceutical products;

"**Firm Order**" has the meaning specified in Section 5.1(c);

"**First Firm Order**" has the meaning specified in Section 5.1(b);

"For Cause Audit" means an audit of manufacturing records of Patheon or its subcontractors and supplies by Client following: (a) an unfavorable observation during regulatory inspections that is material to the quality of Product; or (b) a major or repeated quality excursion that may result in a failed manufacture Batch or Non-Conforming Product;

"**Force Majeure Event**" has the meaning specified in Section 13.7;

"**Health Canada**" means the section of the Canadian Government known as Health Canada and includes, among other departments, the Therapeutic Products Directorate and the Health Products and Food Branch Inspectorate or any successor agency thereto which may regulate pharmaceutical products;

"**Initial Manufacturing Month**" has the meaning specified in Section 5.1(b);

"**Initial Manufacturing Period**" has the meaning specified in Section 5.1(b);

"**Initial Product Term**" has the meaning specified in Section 8.1;

"**Initial Set Exchange Rate**" means as of the Effective Date of a Product Agreement, the initial exchange rate set forth in the Product Agreement to convert one unit of the Patheon Manufacturing Site local currency into one unit of the billing currency, calculated as the daily average interbank exchange rate for conversion of one unit of the Patheon Manufacturing Site local currency into one unit of the billing currency during the 90 day period immediately preceding the Effective Date as published by OANDA.com "The Currency Site" under the heading "FxHistory: historical currency exchange rates" at www.OANDA.com/convert/fxhistory;

"**Initial Term**" has the meaning specified in Section 8.1;

"**Intellectual Property**" means any and all rights in patents, patent applications, formulae, trademarks, trademark applications, trade-names, Inventions, copyrights, industrial designs, trade secrets, and know how;

"**Invention**" means any and all information, results, data, innovation, improvement, development, discovery, computer program, device, trade secret, method, know-how, process, technique or the like, whether or not written or otherwise fixed in any form or medium, regardless of the media on which it is contained and whether or not patentable or copyrightable;

"**Inventory**" means all inventories of Components and work-in-process produced or held by Patheon for the manufacture of the Products but, for greater certainty, does not include the Active Materials;

"**Late Delivery**" will have the meaning specified in Section 5.5(b);

"Latent Defect" means a defect in any Batch of Product, the API or Materials that was not, and could not reasonably be expected to have been, found by exercise of ordinary care, following the approved specifications or in inspection at Delivery;

"Late Product" means Product ordered under a Firm Order that is not delivered on the Delivery Date;

"**Losses**" has the meaning specified in Section 10.3;

"**Manufacturing Services**" means the manufacturing, quality control, quality assurance, stability testing, packaging, labelling, storage and related services provided by Patheon to manufacture Product or Products using the Active Materials, Components, and Bill Back Items pursuant to this Agreement;

"**Manufacturing Site**" means the facility owned and operated by Patheon where the Manufacturing Services will be performed as identified in a Product Agreement;

"Materials" means all Components and Bill Back Items required to manufacture the Products in accordance with the Specifications, other than the Active Materials;

"**Maximum Credit Value**" means the maximum value of Active Materials that may be credited by Patheon under this Agreement, as set forth in a Product Agreement on Schedule D;

"**Minimum Order Quantity**" means the minimum number of Batches of a Product to be produced as set forth in a Product Agreement on Schedule B;

"**Non-Conforming Products**" will have the meaning specified in Section 6.1(a);

"Out of Specification" or **"OOS"** means a confirmed result that falls outside the Specifications.

"Party" or "Parties" means, as the context requires individually or collectively, Patheon and Client;

"**Patheon Competitor**" means a business that derives greater than 50% of its revenues from performing contract pharmaceutical development or commercial manufacturing services for Third Parties;

"**Patheon Indemnitees**" has the meaning specified in Section 10.4;

"Patheon Intellectual Property" means Intellectual Property generated or derived by Patheon before performing any Manufacturing Services, or developed by Patheon while performing the Manufacturing Services or otherwise generated or derived by Patheon in its business which Intellectual Property is not Client Intellectual Property;

"Price" means the price measured in US Dollars to be charged by Patheon for performing the Manufacturing Services, and includes the cost of Components (other than Client-Supplied Components), certain cost items as set forth in a Product Agreement on Schedule B, and annual stability testing costs as set forth in a Product Agreement on Schedule C;

"**Product(s)**" means the product(s) listed in a Product Agreement on Schedule A;

"**Product Agreement**" means the agreement between Patheon and Client issued under this Agreement in the form set forth in Appendix 1 (including Schedules A to D) under which Patheon will perform Manufacturing Services at a particular Manufacturing Site as updated, amended and revised from time to time by the Parties in accordance with the terms of this Agreement;

"**Product Warranties**" will have the meaning specified in Section 9.3(a);

"**Quality Agreement**" means the agreement between the Parties entering into a Product Agreement that sets out the quality assurance standards and responsibilities for the

Manufacturing Services to be performed by Patheon for Client, as such agreement may be amended from time to time in accordance with its terms; the Parties anticipate that the Quality Agreement will be executed within 30 days after the Effective Date of the Product Agreement;

"Quantity Converted" as the meaning specified in Section 2.2(a);

"Quantity Dispensed" has the meaning specified in Section 2.2(a);

"Quantity Received" has the meaning specified in Section 2.2(a);

"Quarter" means each successive period of three calendar months commencing on January 1, April 1, July 1 and October 1;

"Recall" means any action (i) by Client or its Affiliates or licensees to recover title to or possession, or stop distribution, prescription or consumption, of quantities of the Products sold or shipped to Third Parties (including, without limitation, the voluntary withdrawal of Products from the market); or (ii) by any Regulatory Authorities to detain or destroy any of the Products. Recall will also include any action by Client or its Affiliates or licensees to refrain from selling or shipping quantities of the Products to Third Parties that would have been subject to a Recall if sold or shipped.

"**Recipient**" has the meaning specified in Section 11.1;

"**Regulatory Authority**" means the FDA, EMA, and Health Canada and any other foreign regulatory agencies competent to grant marketing approvals for pharmaceutical products including the Products in the Territory;

"RFID" means Radio Frequency Identification Devices which (at present or in the future) may be affixed to Products or Materials to assist in inventory control, tracking, and identification;

"**Remediation Period**" has the meaning specified in Section 8.2(a);

"Set Exchange Rate" means the exchange rate to convert one unit of the Patheon Manufacturing Site local currency into one unit of the billing currency for each Year, calculated as the average daily interbank exchange rate for conversion of the Patheon Manufacturing Site local currency into one unit of the billing currency during the full year period (October 1st [preceding year] to September 30th) as published by OANDA.com "The Currency Site" under the heading "FxHistory: historical currency exchange rates" at www.OANDA.com/convert/fxhistory;

"**Shortfall**" has the meaning specified in Section 2.2(b);

"Significant Quality Event" means any event occurring during the Manufacturing of the Product resulting in a Deviation that materially impacts the quality, performance, safety or reliability of the Product or intermediates thereof. A confirmed Out of Specification result is a Significant Quality Event;

"**Specifications**" means the requirements, for each Material, Component, Active Material or Product, which is given by Client to Patheon in accordance with the procedures listed in a Product Agreement on Schedule A and which contains documents or requirements relating to each Product, including, without limitation:

(a) specifications for Active Materials and Components;

(b) manufacturing specifications, directions, and processes;

(c) storage requirements;

(d) all environmental, health and safety information for each Product including material safety data sheets;

(e) the in-process specifications; and

(f) the finished Product specifications, packaging specifications and shipping requirements for each Product;

all as updated, amended and revised from time to time by Client in accordance with the terms of this Agreement;

"**Target Yield**" has the meaning specified in Section 2.2(a);

"**Target Yield Determination Batches**" has the meaning specified in Section 2.2(a);

"**Technical Dispute**" has the meaning specified in Section 12.2;

"**Technology Transfer**" means the transfer to Client or any Third Party designated by Client by Patheon of all information relating to the process of manufacturing Product, all documents, manufacturing instructions, specifications, and any other relevant documentation, all relevant manufacturing know-how, licenses and materials (including raw materials specifications) related to Product that Patheon or its Affiliates, as applicable, controls or has the right to license at any time during the Term and that is necessary to enable Client or its designee to manufacture Product in accordance with the Specifications, and to comply with applicable regulatory requirements (including obtaining any necessary regulatory approvals, conducting any required studies and developing any other regulatory documentation) and all Applicable Laws in connection with the transfer;

"**Territory**" means any geographic area described in a Product Agreement where Products manufactured by Patheon will be distributed by Client;

"Third Party" means any party other than Client, Patheon or their respective Affiliates;

"**Third Party Rights**" means any Intellectual Property of any party other than Client or Patheon or their respective Affiliates;

"**United States**" means the United States of America including its territories and possessions; and

"**Year**" means in the first year of this Agreement, the period from the Effective Date up to and including December 31 of the same calendar year, and thereafter will mean a calendar year.

1.4

Currency.

Unless otherwise agreed in a Product Agreement, all monetary amounts expressed in this Agreement are in United States Dollars (USD).

1.5 Sections and Headings.

The division of this Agreement into Articles, Sections, Subsections, an Appendix, Schedules and Exhibits and the insertion of headings are for convenience of reference only and will not affect the interpretation of this Agreement. Unless otherwise indicated, any reference in this Agreement to a Section, Appendix, Schedule or Exhibit refers to the specified Section, Appendix, Schedule or Exhibit to this Agreement. In this Agreement, the terms "**this Agreement**", "**hereof**", "**herein**", "**hereunder**" and similar expressions refer to this Agreement as a whole and not to any particular part, Section, Appendix, Schedule or Exhibit of this Agreement.

1.6 Singular Terms.

Except as otherwise expressly stated or unless the context otherwise requires, all references to the singular will include the plural and vice versa, and all references to “includes” or “including” will mean “includes without limitation” or “including without limitation.”

1.7 Appendix 1, Schedules and Exhibits.

Appendix 1 (including Schedules thereto) and the following Exhibits are attached to, incorporated in, and form part of this Agreement:

Appendix 1	-Form of Product Agreement (Including Schedules A to D)
Exhibit A	-Technical Dispute Resolution
Exhibit B	-Monthly Active Materials Inventory Report
Exhibit C	-Report of Annual Active Materials Inventory Reconciliation and Calculation of Actual Annual Yield
Exhibit D	-Example of Price Adjustment Due to Currency Fluctuation

PATHEON'S MANUFACTURING SERVICES

2.1 Manufacturing Services.

Patheon will perform the Manufacturing Services for the Territory for the fees specified in a Product Agreement in Schedules B and C. Schedule B to a Product Agreement sets forth a list of cost items that are included or not included in the unit Price for Products; all cost items that are not included in the Price are subject to additional fees to be paid by the Client as agreed by the Parties. Patheon may amend the fees set out in Schedules B and C to a Product Agreement as set forth and in accordance with Article 4. Patheon will perform the Manufacturing Services in strict compliance with the established Specifications, cGMP and Applicable Laws. Patheon may not change the Specifications or the Manufacturing Site (including facility modifications) or any other aspect of the manufacturing process used to perform the Manufacturing Services with respect to the Products except with the prior written consent of Client, this consent not to be unreasonably withheld. Unless otherwise agreed in a Product

Agreement or in this Agreement, and for so long as Patheon remains in material compliance with its obligations under this Agreement and the applicable Product Agreement, Patheon will manufacture at least […***…] % (**"Annual Minimum"**) of Products manufactured by or on Client's behalf for sale by Client in the Territory in a particular Year. If Patheon does not remain in material compliance, the Annual Minimum will no longer apply in addition to any other remedies the Client may have under this Agreement. In performing the Manufacturing Services, Patheon and Client agree that:

(a) Use of Active Materials and Components. Patheon will use the Active Materials and Components to manufacture Products in accordance with this Agreement. Patheon will not use the Active Materials, any Client-Supplied Components or any other Components paid for by Client for any other use or purpose. Patheon will use all Active Materials and Components on a first-to-expire, first-to-use basis in manufacturing Products under this Agreement.

(b) Quality Control and Quality Assurance. Patheon will perform the quality control and quality assurance testing specified in the Quality Agreement. Batch review and release to Client will be the responsibility of Patheon's quality assurance group, consistent with the Quality Agreement. Patheon will perform its Batch review and release responsibilities in accordance with Patheon's standard operating procedures copies of which have been made available to Client and will not change in a material way related to Product without Client consent (not to be unreasonably withheld), and the Quality Agreement. Each time Patheon ships Products to Client or Client's designee, it will give Client a Certificate of Analysis and Certificate of Compliance, and a list of all Deviations (**"Delivery Documentation"**). Client will have sole responsibility for the release of Products to the market. The Batch documents, including, but not limited to, Batch production records, lot packaging/labeling records, equipment set up control, operating parameters, investigation/non-conformances, and data printouts, raw material data, and laboratory notebooks will be the exclusive property of Client. But any intellectual property comprised of the form and style of those Batch documents are the exclusive property of Patheon and Patheon will not be obligated to disclose to Client confidential or proprietary information of Third Parties contained in any lab notebooks that is unrelated to the Manufacturing Services. Subject to the foregoing, Patheon will provide any information reasonably required by Client to perform, if required, a Technology Transfer or if requested by a Regulatory Authority in a redacted form at Client's expense. Except for Patheon Intellectual Property, all information contained in the Batch documents, including, but not limited to specific Product related information, is Client property.

(c) Components. Patheon will purchase (with the exception of Client-Supplied Components) and test all Components at Patheon's expense and as required by the Product Agreement in accordance with the Specifications and the Quality Agreement.

(d) Stability Testing. Patheon will conduct stability testing on the Products as part of the Manufacturing Services provided hereunder. Patheon will perform this testing in accordance with the protocols set out in the Quality Agreement and the Specifications for the separate fees and during the time periods set out in Schedule C to a Product Agreement, if applicable. Patheon will not make any changes to these testing protocols without prior written approval from Client. If a confirmed stability test failure occurs, Patheon will notify Client within one Business Day, after which Patheon and Client will jointly determine the proceedings and methods to be undertaken to investigate the cause of the failure in accordance with the Quality Agreement, including which Party will bear the cost of the investigation. Patheon will not be liable for these costs unless it has failed to perform the Manufacturing Services in accordance with the Quality Agreement, Specifications, cGMPs or Applicable Laws. Patheon will give Client all stability test data and results (including a final report) at Client's request within […***…] Business Days, upon completion of the testing.

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(e) Packaging. Patheon will package the Products as set out in the Specifications and the applicable master packaging records approved by Client. Client will be responsible for the cost of artwork development, as applicable. Patheon will determine and imprint the Batch numbers and expiration dates for each Product shipped. The expiration dates must be determined in accordance with the Specifications. The Batch numbers and expiration dates will be affixed on the Products and on the shipping carton of each Product as outlined in the Specifications and as required by the Quality Agreement, cGMPs and Applicable Laws. Client may, in its sole discretion, make changes to labels, product inserts, and other packaging for the Products. Those changes will be submitted by Client to all applicable Regulatory Authorities. Client will be responsible for the cost of labelling obsolescence when changes occur, as contemplated in Section 4.4. Patheon's name will not appear on the label or anywhere else on the Products unless: (i) required by any Applicable Laws; or (ii) Patheon consents in writing to the use of its name.

(f) Active Materials and Client-Supplied Components. At least […***…] before the scheduled production date, Client will deliver the Active Materials and any Client-Supplied Components to the Manufacturing Site DDP, in sufficient quantity to enable Patheon to manufacture the desired quantities of Product and to ship Product on the Delivery Date. Upon receipt of the Active Materials, Patheon will test all Active Materials in accordance with the provisions of the Product Agreement and in accordance with the applicable Quality Agreement. If the Active Materials and/or Client-Supplied Components are not received […***…] before the scheduled production date, Patheon may delay the shipment of Product by the same number of days as the delay in receipt of the Active Materials and/or Client-Supplied Components. But if Patheon is unable to manufacture Product to meet this new shipment date due to prior Third Party production commitments, Patheon may delay the shipment until a later date as agreed to by the Parties, but Patheon will make commercially reasonable efforts to make the shipment as soon as possible. All shipments of Active Material will be accompanied by Certificate(s) of Analysis provided by Client, confirming the identity and purity of the Active Materials and its compliance with the Active Material Specifications set forth in the Product Agreement.

(g) Bill Back Items. Bill Back Items purchased by Patheon will be charged to Client at Patheon's actual and reasonable cost plus a […***…]% handling fee for Bill Back Items that cost less than $5,000 and a […***…]% handling fee for Bill Back Items that cost $5,000 or more, but Client must give prior written approval for the purchase of all Bill Back items. Patheon will use commercially reasonable efforts to order Bill Back Items in amounts to minimize the handling fee.

(h) Handling and Storage. Patheon will store at no cost to Client inventory to support […***…] months of production per the forecast of the Active Material and Client-Supplied Components in a controlled and monitored environment and at appropriate conditions in accordance with Specifications, the Quality Agreement, and Applicable Laws.

2.2 Active Material Yield.

(a) Reporting. Patheon will give Client a monthly inventory report of the Active Materials held by Patheon within five Business Days of the end of the most recent monthly using the inventory report form set out in Exhibit B, which will contain the following information for the month:

Quantity Received: The total quantity of Active Materials that complies with the Specifications and is received at the Manufacturing Site during the applicable month (**"Quantity Received"**).

Quantity Dispensed: The total quantity of Active Materials dispensed at the Manufacturing Site during the applicable month (**"Quantity Dispensed"**). The Quantity
Dispensed is calculated by adding the Quantity Received to the inventory of Active Materials that complies with the Specifications and is held by Patheon at the beginning of the applicable month, less the inventory of Active Materials that complies with the Specifications and is held by Patheon at the end of the month. The Quantity Dispensed will only include Active Materials received and dispensed in commercial manufacturing of Products and will not include any (i) Active Materials that must be retained by Patheon as samples, (ii) Active Materials contained in Product that must be retained as samples, (iii) Active Materials used in testing (if applicable), and (iv) Active Materials received or dispensed in technical transfer activities or development activities during the applicable period, including without limitation, any regulatory, stability, validation or test Batches manufactured during the applicable period, in each case of clauses (i) through (iv) in accordance with this Agreement.

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Quantity Converted: The total amount of Active Materials contained in the Product manufactured with the Quantity Dispensed (including any additional Product produced in accordance with Section 6.3(a) or 6.3(b)), delivered by Patheon, and not rejected, recalled or returned in accordance with Section 6.1 or 6.2 because of Patheon's failure to perform the Manufacturing Services in accordance with Specifications, cGMPs, and Applicable Laws.

Client acknowledges that, if there is no change in this information from one month to the next month, the report will reflect that.

Within […***…] days after the end of each Year, Patheon will prepare an annual reconciliation of Active Materials on the reconciliation report form set forth in Exhibit C including the calculation of the "**Actual Annual Yield**" or "**AAY**" for the Product at each Manufacturing Site during the Year. AAY is the percentage of the Quantity Dispensed that was converted to Product and is calculated as follows:

$$\frac{\text{Quantity Converted during the Year}}{\text{Quantity Dispensed during the Year}} \times 100\%$$

After Patheon has produced a minimum of […***…] successful commercial production Batches of Product and has produced commercial production Batches for at least […***…] months at the Manufacturing Site (collectively, the "**Target Yield Determination Batches**"), the Parties will agree on the target yield for the Product at the Manufacturing Site (each, a "**Target Yield**"). The Target Yield will be revised annually to reflect the actual manufacturing experience as agreed to by the Parties.

Additionally, promptly following production of the validation Batches, but prior to production of the […***…] Target Yield Determination Batches described above, the Parties will agree to an interim Target Yield that will apply before determination of the Target Yield set out above, based on data from production of the validation Batches. Promptly following production of the first […***…] Target Yield Determination Batches described above, the Parties will agree to an updated interim Target Yield that will apply before determination of the Target Yield set out above, based on data from production of the first […***…] Target Yield Determination Batches.

(b) Shortfall Calculation. If the Actual Annual Yield falls more than […***…]% below the respective Target Yield in a Year, then the shortfall for the Year (the "**Shortfall**") will be calculated as follows:

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Shortfall = [(Target Yield – […***…]%) – AAY] * Active Materials Credit Value * Quantity Dispensed

(c) Credit for Shortfall. If there is a Shortfall for a Product in a Year, then Patheon will credit Client's account for the amount of the Shortfall not later than […***…] days after the end of the Year.

Each credit under this Section 2.2(c) will be summarized on the reconciliation report form set forth in Exhibit C. Upon expiration or termination of a Product Agreement, any remaining credit owing under this Section 2.2 will be paid to Client within […***…] days of the expiration or termination of the Product Agreement. The Annual Shortfall, if any, will be disclosed by Patheon on the reconciliation report form.

(d) Maximum Credit. Patheon's liability for Active Materials calculated in accordance with this Section 2.2 for any Product Agreement in a Year will not exceed, in the aggregate, the Maximum Credit Value set forth in Schedule D to the Product Agreement.

(e) No Material Breach. It will not be a material breach of this Agreement by Patheon under Section 8.2(a) if the Actual Annual Yield is less than the Target Yield unless the Actual Annual Yield is more than […***…]% below the Target Yield.

CLIENT'S OBLIGATIONS

3.1 Payment.

Client will pay Patheon for performing the Manufacturing Services in accordance with this Agreement according to the Prices specified in Schedules B and C in a Product Agreement. These Prices may be subject to adjustment under Sections 4.2 and 4.3 of this Agreement. Client will also pay Patheon for any Bill Back Items as provided in Section 2.1(g).

3.2 Active Materials and Qualification of Additional Sources of Supply.

Client will at its sole cost and expense, deliver the Active Materials to Patheon (in accordance with Section 2.1(f)). If applicable, Patheon and the Client will reasonably cooperate to permit the import of the Active Materials to the Manufacturing Site. Client's obligation will include obtaining the proper release of the Active Materials from the applicable Customs Agency and Regulatory Authority. Client or Client's designated broker will be the "Importer of Record" for Active Materials imported to the Manufacturing Site. The Active Materials will be held by Patheon on behalf of Client as set forth in this Agreement. The Active Materials will at all times remain the property of Client. Patheon will ensure that the Active Materials will not become subject to any encumbrances, liens or other third-party claims while in Patheon's possession. Any Active Materials received by Patheon will only be used by Patheon to perform the Manufacturing Services.

If Client asks Patheon to qualify an additional source for the Active Material or any Component, Patheon will evaluate the Active Material or Component to be supplied by the additional source to determine if it is suitable for use in the Product. The Parties will agree on the scope of work to be performed by Patheon at Client's cost. For an Active Material, this work at a minimum will include:

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(a) laboratory testing to confirm the Active Material meets existing specifications;

(b) manufacture of an experimental Batch of Product that will be placed on three months accelerated stability; and

(c) manufacture of three full-scale validation Batches that will be placed on concurrent stability (one Batch may be the registration Batch if manufactured at full scale).

Section 6.3(c) will apply to all Product manufactured using the newly approved Active Material or Component because of the limited material characterization that is performed on additional sources of supply.

CONVERSION FEES AND COMPONENT COSTS

4.1 First Year Pricing.

The tiered Price and annual stability Price for the Products through December 31, 2015 are listed in Schedules B and C in a Product Agreement and are subject to the adjustments set forth in Sections 4.2 and 4.3.

4.2 Price Adjustments – Subsequent Years' Pricing.

Beginning January 1, 2016, Patheon may adjust the Price effective January 1st of each Year as follows:

(a) Manufacturing and Stability Testing Costs. For Products manufactured in the United States or Puerto Rico, Patheon may adjust the conversion component of Price for inflation, based upon the preliminary number for any increase or decrease in the Producer Price Index pcu325412325412 for Pharmaceutical Preparation Manufacturing published by the United States Department of Labor, Bureau of Labor Statistics ("**PPI**") in August of the preceding Year compared to the final number for the same month of the Year prior to that, unless the Parties otherwise agree in writing. On or before November 30th of each Year, Patheon will give Client a statement setting forth the calculation for the inflation adjustment to be applied in calculating the Price for the next Year. But Client will have the right to dispute the calculation in good faith and the existing Prices will continue to apply until the dispute is resolved. If necessary, the Price will be retroactively adjusted for the applicable period after the dispute is resolved. For Products manufactured outside the United States or Puerto Rico, Patheon may similarly adjust the Price for inflation using an equivalent inflation index to be agreed by the Parties in a Product Agreement.

(b) Component Costs. Patheon may increase or, if the average price of the Component costs decreases, Patheon will decrease the Price for the next Year to pass through the actual additional or reduced Component costs. In November of each Year, Patheon will give Client reasonably detailed information about the increase or decrease in Component costs which will be applied to the calculation of the Price for the next Year to reasonably demonstrate that the Price increase or decrease is justified. But Patheon will not be required to give information to Client that is subject to obligations of confidentiality between Patheon and its suppliers. But, at Client's request, Patheon will allow an independent third party auditor to review the information supporting the increase or decrease in Component costs and confirm that the information reasonably demonstrates that the Price increase or decrease is justified and reasonable.

(c) Pricing Basis. Client acknowledges that the Price in any Year is quoted based upon the Minimum Order Quantity and the Annual Volume specified in Schedule B to a Product Agreement. The Price is subject to change if the specified Minimum Order Quantity changes or if the Annual Volume is not ordered in a Year. For greater clarity, if Patheon and Client agree that the Minimum Order Quantity will be reduced or the Annual Volume in the lowest tier will not be ordered in a Year whether as a result of a decrease in estimated Annual Volume or otherwise and, as a result of the reduction, Patheon demonstrates to Client's reasonable satisfaction that its costs to perform the Manufacturing Services or to acquire the Components for the Product will increase or decrease on a per unit basis (including the amount of the increase), then Patheon may increase or decrease the Price by an amount sufficient to absorb the documented increased or reduced costs. On or before November 1st of each Year, Patheon will give Client a statement setting forth the information to be applied in calculating those cost increases or decreases for the next Year. But Patheon will not be required to give information to Client that is subject to obligations of confidentiality between Patheon and its suppliers. But, at Client's request, Patheon will allow an independent third party auditor to review the information supporting the increase in Component costs and confirm that the information reasonably demonstrates that the Price increase is justified.

(d) Adjustments Due to Currency Fluctuations. If the Parties agree in a Product Agreement to invoice in a currency other than the local currency for the Manufacturing Site, Patheon will adjust the Price to reflect currency fluctuations in accordance with this Section 4.2(d). If the Set Exchange Rate for a given Year has changed, the adjustment will be calculated after all other annual Price adjustments under this Section 4.2 have been made. The adjustment will proportionately reflect the increase or decrease, if any, in the Set Exchange Rate compared to the Set Exchange Rate established for the prior Year or the Initial Set Exchange Rate, as the case may be. An example of the calculation of the price adjustment (for a Canadian Manufacturing Site invoiced in USD) is set forth in Exhibit D.

(e) Tier Pricing (if applicable). The pricing in Schedule B of a Product Agreement is set forth in Annual Volume tiers based upon the Client's volume forecasts under Section 5.1. The Client will be invoiced during the Year for the unit price set forth in the Annual Volume tier based on the […***…] month forecast provided in September of the previous Year. Within 30 days of the end of each Year or of the termination of the Agreement, Patheon will send Client a reconciliation of the actual volume of Product ordered by the Client during the Year with the pricing tiers. If Client has overpaid during the Year, Patheon will issue a credit to the Client for the amount of the overpayment within 45 days of the end of the Year or will issue payment to the Client for the overpayment within 45 days of the termination of the Agreement. If Client has underpaid during the Year, Patheon will issue an invoice to the Client under Section 5.6 for the amount of the underpayment within 45 days of the end of the Year or termination of the Agreement. If Client disagrees with the reconciliation, the Parties will work in good faith to resolve the disagreement amicably. If the Parties are unable to resolve the disagreement within 30 days, the matter will be handled under Section 12.1.

For all Price adjustments under this Section 4.2, Patheon will deliver to Client on or before November 30th of each Year a revised Schedule B to the Product Agreement to be effective for Product delivered on or after the first day of the next Year, which revised Schedule B must be approved in writing by Client before it becomes binding on the Parties. Client's approval must not be unreasonably withheld.

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4.3 Price Adjustments – Current Year Pricing.

During any Year, the Prices set out in Schedule B of a Product Agreement will be adjusted as follows:

Extraordinary Increases or Decreases in Component Costs. If, at any time, market conditions result in Patheon's cost of Components being materially greater or less than the cost on which the current Price is based, then the Parties will adjust the Price for any affected Product that reflects the increased or decreased Component costs. Changes materially greater than normal forecasted increases or decreases will have occurred if: (i) the cost of a Component increases or decreases by […***…]% of the cost for that Component upon which the most recent fee quote was based; or (ii) the aggregate cost for all Components required to manufacture a Product increases or decreases by […***…]% of the total Component costs for the Product upon which the most recent fee quote was based. If Component costs have been previously adjusted to reflect an increase or decrease in the cost of one or more Components, the adjustments set out in (i) and (ii) above will operate based on the last cost adjustment for the Components.

For a Price adjustment under this Section 4.3, Patheon will deliver to Client a revised Schedule B to the Product Agreement and budgetary pricing information, adjusted Component costs or other documents reasonably sufficient to demonstrate that a Price adjustment is justified, to Client's reasonable satisfaction. Client will have the right to dispute any Price adjustment in good faith, and for the duration of the dispute, the existing Prices will continue to apply. If necessary, the Price will be retroactively adjusted for the applicable period after the dispute is resolved. At Client's request, Patheon will allow an independent Third Party auditor to review the information supporting the increase or decrease in Component costs and confirm that the information reasonably demonstrates that the Price increase or decrease is justified and reasonable. Patheon will have no obligation to deliver any supporting documents that are subject to obligations of confidentiality between Patheon and its suppliers. For an undisputed Price adjustment, the revised Price will be effective for any Product delivered on or after the first day of the month following Client's receipt of the revised Schedule B to the Product Agreement. If the Price is revised pursuant to this Section 4.3, it will not be revised subsequently pursuant to Section 4.2(b) with respect to the same increased Component costs.

4.4 Adjustments Due to Technical Changes.

Amendments to the Specifications or the Quality Agreement requested by Client will only be implemented following a technical and cost review that Patheon will perform at Client's cost, and are subject to Client and Patheon reaching agreement on any Price changes required because of the amendment. Amendments to the Specifications, the Quality Agreement, or the Manufacturing Site requested by Patheon will only be implemented following the written approval of Client. Upon receiving notice of a request by Client for any such amendments, Patheon will promptly advise Client in writing of any scheduling adjustments, any cost increases or decreases or other changes that may result from the change, and (a) will use its best efforts to make any change identified in the Client request that is in response to a regulatory or safety issue pertaining to the Product, and (b) will use commercially reasonable efforts to implement any other change identified in a Client request by the date requested by Client, or as soon thereafter as it is commercially reasonable. If Client accepts a proposed Price change, the proposed change in the Specifications will be implemented, and the Price change will become effective, only for those orders of Products that are manufactured under the revised Specifications. In addition, Client agrees to purchase, at Patheon's actual cost (including all reasonable costs incurred by Patheon for the purchase and handling of the Inventory), all Inventory used under the "old" Specifications and purchased or maintained by Patheon in order to fill Firm Orders or under Section 5.2, but only to the
extent the Inventory can no longer be used under the revised Specifications. Open purchase orders for Components no longer required under any revised Specifications that were placed by Patheon with suppliers in order to fill Firm Orders or under Section 5.2 will be cancelled where possible, and if the orders may not be cancelled without penalty, will, at Client's sole discretion, be assigned to and satisfied by Client or cancelled by Patheon and Client will reimburse Patheon for any penalty it incurs due to the cancellation.

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4.5 Multi-Country Packaging Requirements.

If Client decides to have Patheon perform Manufacturing Services for the Product for countries outside the Territory, then Client will inform Patheon of the packaging requirements for each such country and Patheon will prepare a quotation for consideration by Client of any additional costs for Components (other than Client-Supplied Components) and the change over fees for the Product destined for each such country. The agreed additional packaging requirements and related packaging costs and change over fees will be set out in a written amendment to this Agreement.

ORDERS, SHIPMENT, INVOICING, PAYMENT

5.1 Orders and Forecasts.

(a) Rolling […***…] Month Forecast. When each Product Agreement is executed, Client will give Patheon a non-binding […***…] month forecast of the volume of Product that Client expects to order in the first […***…] months of commercial manufacture of the Product. This forecast will then be updated by Client on or before the […***…] day of each month on a rolling forward basis. Client will update the forecast forthwith if it determines that the volumes estimated in the most recent forecast have changed by more than […***…]%. The most recent […***…] month forecast will prevail.

(b) Firm Orders for Initial Manufacturing Month. At least […***…] months before the start of commercial manufacture of the Product, Client will update the rolling forecast for the first […***…] months of manufacture of the Product (the "**Initial Manufacturing Period**"). Subject to the provisions of Section 5.1(c), the first month of this updated forecast ("**Initial Manufacturing Month**") will constitute a firm written order in the form of a purchase order or otherwise ("**First Firm Order**") by Client to purchase and, when accepted by Patheon, for Patheon to manufacture the quantity of the Product. If manufacturing has not started, Client may cancel any Batches from the First Firm Order at a cost of $[…***…] per cancelled Batch per month until manufacturing starts, if notice of cancellation is received by Patheon […***…] days or more before the scheduled Delivery Date under the First Firm Order. If manufacturing has not started, Client may cancel any Batches from the First Firm Order if notice of cancellation is received by Patheon more than […***…] days but fewer than […***…] days before the scheduled Delivery Date under the First Firm Order, but Client will pay Patheon $[…***…] for each cancelled Batch. The Parties agree that this payment will be considered liquidated damages for Patheon's loss of manufacturing capacity due to the Client's cancellation of manufacturing and will not be considered a penalty. If the First Firm Order is changed or adjusted as described above, then the initial rolling […***…] month forecast will also be adjusted as necessary.

(c) Firm Orders Thereafter. Before and during the Initial Manufacturing Period, and on a rolling basis during the term of the Product Agreement, Client will issue an updated […***…] month forecast on
or before the […***…] day of each month. This forecast will start on the first day of the next month. The first […***…] months of this updated forecast will be considered binding firm orders. But the initial order related to the launch of each Product will not be binding until the Client receives approval from the FDA to market the applicable Product. Concurrent with the delivery of the applicable forecast, Client will issue a firm written order for the first […***…] months of the forecast in the form of a purchase order or otherwise ("**Firm Order**") by Client to purchase and, when accepted by Patheon, for Patheon to manufacture and deliver the agreed quantity of the Products as set forth in the Firm Order. The Delivery Date specified in the Firm Order will not be less than …***… days following the date that the Firm Order is submitted. Firm Orders submitted to Patheon will specify Client's purchase order number, quantities by Product type, monthly delivery schedule, and any other elements necessary to ensure the timely manufacture and shipment of the Products. Upon Patheon's acceptance of a Firm Order, the quantities of Products ordered in the Firm Order will be firm and binding on the Parties and may only be reduced by written agreement of the Parties.

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(d) […***…] Year Forecast. On or before the […***…] day of May of each Year, Client will give Patheon a written non-binding […***…]-year forecast, broken down by Quarters […***…], of the volume of each Product Client then anticipates will be required to be manufactured and delivered to Client during the […***…]-year period.

(e) Acceptance of Firm Order. Patheon will accept Firm Orders by sending an acknowledgement to Client within […***…] Business Days of its receipt of the Firm Order. The acknowledgement will include, subject to confirmation from the Client, the Delivery Date for the Product ordered. The Delivery Date may be amended by written agreement of the Parties or as set forth in Section 2.1(f) or 5.1(b). If Patheon fails to send an acknowledgement to Client within the applicable […***…] Business Day period, then the Firm Order will be deemed to have been accepted by Patheon. Patheon will accept Firm Orders submitted in accordance with this Agreement. If Patheon rejects a Firm Order submitted in accordance with this Agreement, without limiting Client's other rights and remedies hereunder, Client may obtain the Product from another supplier, and this Product will not be included for purposes of calculating the Annual Minimum under this Agreement, and the Annual Minimum will automatically be reduced by […***…]%. If Patheon rejects two or more Firm Orders in a […***…]-month period, the Annual Minimum will no longer apply.

5.2 Reliance by Patheon.

(a) Client understands and acknowledges that Patheon will rely on the Firm Orders and rolling forecasts submitted under Sections 5.1(a) and (b) in ordering the Components (other than Client-Supplied Components) required to meet the Firm Orders. In addition, Client understands that to ensure an orderly supply of the Components, Patheon may want to purchase the Components in reasonable volumes to meet the production requirements for Products during part or all of the forecasted periods referred to in Section 5.1(a) or to meet the production requirements of any longer period agreed to in writing by Patheon and Client. Accordingly, Client authorizes Patheon to purchase Components in quantities reasonably needed to satisfy the Manufacturing Services requirements for Products for the first […***…] months contemplated in the most recent forecast given by Client under Section 5.1(a). Patheon may make other purchases of Components to meet Manufacturing Services requirements for longer periods if agreed to in writing by the Parties. The Client will give Patheon written authorization to order Components for any launch quantities of Product requested by Client which will be considered a Firm Order when accepted by Patheon. If Components ordered by Patheon under Firm Orders or this Section 5.2(a) are not included in finished Products manufactured for Client within […***…] months after the forecasted month for which the purchases have been made (or for a longer period as the Parties may agree) or if the Components have expired during the period, then Client will pay to Patheon its costs therefor (including all reasonable costs incurred by Patheon for the purchase and handling of the Components). But if these
Components are used in Products subsequently manufactured for Client or in third party products manufactured by Patheon, Client will receive credit for any costs of those Components previously paid to Patheon by Client or, at Client's election, a refund in an amount equal to these costs. On a Quarterly basis, Patheon will provide a report summarizing the Inventory held by Patheon.

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(b) If Client fails to take possession or arrange for the destruction of Components purchased by Patheon in accordance with Section 5.2(a) within 12 months of purchase or, in the case of finished Product that is not the subject of a Deficiency Notice, within three months of manufacture, Client will pay Patheon $100.00 per pallet, per month thereafter for storing the Components or finished Product. Storage fees for Components or Product which contain controlled substances or require refrigeration will be charged at $200.00 per pallet per month. Storage fees are subject to a one pallet minimum charge per month. Patheon may ship finished Product that is not the subject of a Deficiency Notice held by it longer than three months to the Client at Client's expense on 14 days' prior written notice to the Client in accordance with the Specifications.

5.3 Minimum Orders.

Client may only order Manufacturing Services for amounts of Products in multiples of the Minimum Order Quantities as set out in Schedule B to a Product Agreement.

5.4 Shipments.

Shipments of Products will be made EXW Patheon's shipping point unless otherwise agreed in a Product Agreement. Risk of loss or of damage to Products will remain with Patheon until Patheon loads the Products onto the carrier's vehicle for shipment at the shipping point at which time risk of loss or damage will transfer to Client. Patheon will, in accordance with Client's instructions and as agent for Client, at Client's risk, (i) arrange for shipping to be paid by Client and (ii) at Client's expense, obtain any export license or other official authorization necessary to export the Products. Client will arrange for insurance and will select the freight carrier used by Patheon to ship Products and may monitor Patheon's shipping and freight practices as they pertain to this Agreement. Products will be transported in accordance with the Specifications.

5.5 Late Delivery.

(a) Patheon will deliver Products ordered under a Firm Order on the applicable Delivery Date. The Parties agree that they will work together closely to expedite deliveries of Product, including, without limitation, any samples of Products and Products for initial launch, and manage the scheduling of the initial Product launch.

(b) If, after the Initial Manufacturing Period, Patheon is unable to deliver […***…]% of the quantity of a particular Product ordered under a Firm Order within […***…] days of the Delivery Date due to an act or omission by Patheon (a "**Late Delivery**"), Client will receive a credit from Patheon for the Late Delivery that will be applied against the purchase price under the next Firm Order. The credit will be […***…]% of the Price of the quantities of Product not delivered by Patheon under the Firm Order (i.e., Client Credit = [Quantity Ordered in the Firm Order – Actual Delivery Quantities of Product] * Price *[…***…]%). Patheon will make commercially reasonable efforts to replace the late Product within […***…] days. If, after the Initial Manufacturing Period, Patheon makes two or more Late Deliveries for the same Product in the same calendar Quarter, Client will receive an additional credit of […***…]% from Patheon for the Late Deliveries that will be applied against the purchase price under the next Firm Order. The total credit will be […***…]% of the Price of the quantities of Product not delivered by Patheon under the Firm Order (i.e., Client Credit = [Quantity Ordered in the Firm Order – Actual Delivery Quantities of Product] * Price *[…***…]%. Without

limiting Client's other rights or remedies in this Agreement, if Patheon makes two or more Late Deliveries within a […***…]-month period, the Annual Minimum will be reduced to […***…]%. In such case, for the remainder of the term of this Agreement, the Parties agree that Patheon will manufacture at least […***…]% of the Products manufactured by or on Client's behalf for sale by Client in the Territory in a particular Year until Patheon has no Late Deliveries for a […***…] month period in which case the Annual Minimum will increase by […***…]% and by […***…]% in each sequential […***…] month period that there are no Late Deliveries up to a maximum of […***…]%. Notwithstanding the foregoing, if Patheon makes two or more Late Deliveries within a […***…]-month period, the Parties will meet and agree on and implement a delivery improvement action plan within five Business Days. If, after the delivery improvement plan is in place, two additional Late Deliveries occur within a […***…]-month period, these Late Deliveries may be considered a material breach of this Agreement by Patheon under Section 8.2(a) and Patheon will not be allowed any further opportunity to remedy the material breach.

(c) A Late Delivery will not include any delay in shipment of Product caused by events outside of Patheon's reasonable control, such as a Force Majeure Event, a delay in delivery of API or Materials, a delay in Product release approval from Client, inaccurate Client forecasts, or receipt of non-conforming API or Client-Supplied Components.

5.6 Invoices and Payment.

Invoices will be sent by fax or email to the fax number or email address given by Client to Patheon in writing. Invoices will be sent when the Product is manufactured and released by Patheon to the Client. Patheon will also submit to Client, with each shipment of Products, a duplicate copy of the invoice covering the shipment and the associated Delivery Documentation. Patheon will also give Client an invoice covering any Inventory or Components which are to be purchased by Client under Section 5.2 of this Agreement. All payments made that are associated with Inventory or Components will be credited against the Price of any Batch of Product that incorporates the Components and/or Inventory. Each invoice will also reflect any credit to Client under Section 5.2. Each invoice will, to the extent applicable, identify Client's Manufacturing Services purchase order number, Product numbers, names and quantities, unit price, freight charges, Delivery Documentation and the total amount to be paid by Client. Client will pay all invoices within […***…] days of the date thereof. If any portion of an invoice is disputed, the Client will pay Patheon for the undisputed amount and the Parties will use good faith efforts to reconcile the disputed amount as soon as practicable, but in no case more than […***…] days. Interest on undisputed past due accounts will accrue at […***…]% per month which is equal to an annual rate of […***…]%. The Late Delivery credits set forth in Section 5.5(b) are only available to Client if all outstanding undisputed invoices have been paid in full or are within […***…] days outstanding from the invoice date when the Late Delivery arose. In the case of a Deficiency Notice, payments will be due within […***…] days following receipt of a replacement Batch or Batches that are not subject to a Deficiency Notice. Batches that are determined to have a Latent Defect due to Patheon will be either credited against future Batches or refunded at the sole discretion of Client. No payments will be due for Non-Conforming Product and Patheon will use commercially reasonable efforts to replace the Non-Conforming Product within […***…] days.

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PRODUCT CLAIMS AND RECALLS

6.1 Product Claims.

(a) Product Claims. Client has the right to reject any shipment of Products or any portion thereof that does not conform to the Product Warranties set forth in Section 9.3(a) ("**Non-Conforming Products**"), without invalidating any portion of the shipment of Products that conforms to the Product Warranties. Client will inspect the Products manufactured by Patheon upon receipt at the third-party site agreed to by Patheon and Client and will give Patheon written notice (a "**Deficiency Notice**") of all claims for Non-Conforming Products within […***…] days after Client's receipt of the Product and the Delivery Documentation thereof (or, in the case of Latent Defect, within […***…] days after confirmation by Client, its Affiliate or any licensee, distributor or other Third Party but not after the expiration date of the Product). If Client fails to give Patheon the Deficiency Notice within the applicable […***…]- or […***…]-day period, then the delivery will be deemed to have been accepted by Client on the […***…] or […***…] day after delivery or confirmation, as applicable. Except as set out in Section 6.3, Patheon will have no liability for any Deviations for which it has not received notice within the applicable […***…]-day period except for a Latent Defect.

(b) Determination of Deficiency. Upon receipt of a Deficiency Notice, Patheon will have […***…] days to advise Client by notice in writing that it disagrees with the contents of the Deficiency Notice. Should Patheon fail to provide such notice to Client within the […***…] day period, then Patheon will be deemed to agree with the contents of the Deficiency Notice. If Client and Patheon fail to agree within […***…] days after Patheon's notice to Client as to whether any Products identified in the Deficiency Notice are Non-Conforming Products, then the Parties will mutually select an independent laboratory or expert to evaluate if the Products are Non-Conforming Products. This evaluation will be binding on the Parties. If the independent laboratory or expert determines that any Products are Non-Conforming Products, Client may reject those Products in the manner contemplated in this Section 6.1 and Patheon will be responsible for the cost of the evaluation. If the independent laboratory determines that the Products conform to the Product Warranties, then Client will be deemed to have accepted delivery of the Products on the […***…] day after delivery (or, in the case of any defects not reasonably susceptible to discovery upon receipt of the Product, on the […***…] day after confirmation thereof by Client, but not after the expiration date of the Product) and Client will be responsible for the cost of the evaluation.

(c) Shortages. Claims for shortages in the amount of Products shipped by Patheon will be dealt with by reasonable agreement of the Parties.

6.2 Product Recalls and Returns.

(a) Records and Notice. Patheon and Client will each maintain records necessary to permit a Recall of any Products delivered to Client or customers of Client. Each Party will promptly notify the other by telephone to the contacts designated in the Quality Agreement (to be confirmed in writing) of any information which might affect the marketability, safety or effectiveness of the Products or which might result in the Recall or seizure of the Products within one Business Day. Upon receiving this notice or upon this discovery, each Party will stop making any further shipments of any Products in either Party's possession or control until Client has made a decision as to whether a Recall or some other corrective action is necessary. The decision to initiate a Recall or to take some other corrective action, if any, will be made and implemented by Client.

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(b) Recalls. If (i) any Regulatory Authority issues a directive, order or, following the issuance of a safety warning or alert about a Product, a written request that any Product be Recalled, (ii) a court of competent jurisdiction orders a Recall, or (iii) Client determines that any Product should be Recalled or that a "Dear Doctor" letter is required relating the restrictions on the use of any Product, Patheon will co-operate as reasonably required by Client, having regard to all Applicable Laws.

(c) Product Returns. Client will have the responsibility for handling customer returns of the Products. Patheon will give Client any assistance that Client may reasonably require to handle the returns including, if requested by Client, appropriate investigations.

6.3 Patheon's Responsibility for Non-Conforming and Recalled Products.

(a) Non-Conforming Product. If Client rejects Products under Section 6.1, Client will not be required to pay for the Product under Section 3.1. Patheon will promptly, at Client's election, either: (i) refund the amount paid for the Non-Conforming Products if Client previously paid for the Products, and the cost incurred by Client for the Bill Back Items and Client-Supplied Components used in the Products; (ii) offset the amount paid for the Non-Conforming Products, if Client previously paid for the Products, and the cost incurred by Client for the Bill Back Items and Client-Supplied Components used in the Products, against other amounts due to Patheon hereunder; or (iii) at Patheon's sole expense (excluding expense to incur replacement Active Materials, but including the replacement of Client-Supplied Components and Bill Back Items), replace the Products with conforming Products without Client being liable for payment therefor under Section 3.1, contingent upon the receipt from Client of all Active Materials and Client-Supplied Components required for the manufacture of the replacement Products. For greater certainty, Patheon's responsibility for any loss of Active Materials in Non-Conforming Product will be captured and calculated in the Active Materials Yield under Section 2.2.

(b) Recalled Product. If a Recall or return of Products results from, or arises out of, a failure by Patheon to perform the Manufacturing Services in accordance with the terms of this Agreement, including the warranties set forth in Sections 9.3 and 9.4 or other negligence or willful misconduct of Patheon, Patheon will be responsible for the documented costs and out-of-pocket expenses of the Recall or return and will promptly, at the election of Client, either: (i) refund the amount paid for the Recalled or returned Products and the cost incurred by Client for the Bill Back Items and Client-Supplied Components used in the Products; (ii) offset the amount paid for the Recalled or returned Products and the cost incurred by Client for the Bill Back Items and Client-Supplied Components used in the Products, against other amounts due to Patheon hereunder; or (iii) replace the Recalled or returned Products with conforming Products, at Patheon's sole expense (excluding expense to incur replacement Active Materials, but including the expense to obtain replacement Bill Back Items and Client-Supplied Components), as promptly as practical without Client being liable for payment therefor under Section 3.1, contingent upon the receipt from Client of all Active Materials and Client-Supplied Components required for the manufacture of the replacement Products. For greater certainty, Patheon's responsibility for any loss of Active Materials in Recalled Product will be captured and calculated in the Active Materials Yield under Section 2.2. In all other circumstances, Recalls, returns, or other corrective actions will be made at Client's cost and expense. For clarification, any refund of the amount paid by Client for the Recall or return of Products that is paid by Patheon subject to this Section 6.3(b) will not be considered a liability under, and therefore will not be subject to, Section 10.2(a).

(c) Product Rejection for Finished Product Specification Failure. Internal process specifications will be defined and agreed upon. If a Batch or portion of a Batch of Product does not meet a finished Product Specification despite Patheon's assertion that it manufactured the Product in accordance with the agreed upon process specifications, the Batch production record, and Patheon's standard operating procedures for manufacturing, the Parties agree that they will mutually select an

independent laboratory or expert to evaluate if such laboratory or expert can determine why the Products do not meet a finished Product Specification. The evaluation will be binding on the Parties. If the independent laboratory or expert determines that the Product is Non-Conforming due to an act or omission by Patheon or does not otherwise comply with the Terms of the Agreement, Client may reject those Products in the manner contemplated by Section 6.1 and Patheon will be responsible for the cost of the evaluation. If the independent laboratory determines that the Patheon complied with the agreed upon process specifications, the Batch production record, and Patheon's standard operating procedures and that the Product does not meet a finished Product specification, Client will be responsible for the cost of the evaluation and will pay Patheon the applicable fee per unit for the Non-Conforming Product. In which case, the API in the Non-Conforming Product will be included in the "Quantity Converted" for purposes of calculating the "Actual Annual Yield" under Section 2.2(a).

(d) Except as set forth in Sections 6.3(a) and (b) above, Patheon will not be liable to Client nor have any responsibility to Client for any deficiencies in, or other liabilities associated with, any Product manufactured by it (collectively, "**Product Claims**"). For greater clarity, Patheon will have no obligation for any Product Claims to the extent the Product Claim (i) is caused by deficiencies in the Specifications, the safety, efficacy, or marketability of the Products manufactured in accordance with this Agreement and conforming to the Specifications or any distribution thereof, (ii) results from a defect in a Component that is not reasonably discoverable by Patheon using the methods set forth in the Specifications or as otherwise provided in this Agreement, (iii) results from a defect in the Active Materials or Client-Supplied Components that is not reasonably discoverable by Patheon using the methods set forth in the Specifications or as otherwise provided in this Agreement, (iv) is caused by actions of Third Parties occurring after the Product is shipped by Patheon under Section 5.4, (v) is due to packaging design or labelling defects or omissions for which neither Patheon nor any of its Affiliates or its or their employees, agents or subcontractors has any responsibility, (vi) is due to any unascertainable reason despite Patheon having performed the Manufacturing Services in accordance with the Quality Agreement, Specifications, cGMPs, Applicable Laws, and the other terms of this Agreement, as determined by an independent laboratory or expert as set forth in Section 6.3(c) above; or (vii) is due to any other breach by Client of its obligations under this Agreement.

6.4 Disposition of Defective or Recalled Products.

Client will not dispose of any damaged, defective, returned, Non-Conforming or Recalled Products for which it intends to assert a claim against Patheon without Patheon's prior written authorization to do so, which will not be unreasonably withheld or delayed. Alternatively, Patheon may instruct Client to return the Products to Patheon. Patheon will bear the cost of disposition (including any applicable storage fees or the cost of destruction) for any damaged, defective, returned or Recalled Products for which it bears responsibility under Section 6.1 or 6.3. In all other circumstances, Client will bear the cost of disposition, including all applicable fees for Manufacturing Services, for any damaged, defective, returned, or Recalled Products.

6.5 Healthcare Provider or Patient Questions and Complaints.

Client will have the sole responsibility for responding to questions and complaints from its customers. Questions or complaints received by Patheon from Client's and its Affiliates' and licensees' customers, healthcare providers or patients will be promptly referred to Client. Patheon will co-operate as reasonably required to allow Client to determine the cause of and resolve any questions and complaints. This assistance will include follow-up investigations, including testing and any other assistance reasonably requested by Client. In addition, Patheon promptly (and in any event within the timelines specified in the Quality Agreement) will give Client all agreed upon information that will enable Client to respond properly to questions or complaints about the Products as set forth in the Quality Agreement.

Client will bear all costs incurred under this Section 6.5, except to the extent the complaint resulted from a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, Applicable Laws, and the other terms of this Agreement, in which case those costs incurred under this Section 6.5 will be borne by Patheon.

6.6 Sole Remedy.

Except for the indemnity set forth in Section 10.3 and subject to the limitations set forth in Sections 10.1 and 10.2, the remedies described in this Article 6 will be Client's sole remedy for any failure by Patheon to supply Products that conform to the Product Warranties.

CO-OPERATION

7.1 Quarterly Review.

Each Party will forthwith upon execution of this Agreement appoint one of its employees to be a relationship manager responsible for liaison between the Parties. The relationship managers will meet not less than Quarterly to review the current status of the business relationship and manage any issues that have arisen.

7.2 Governmental Agencies.

Subject to Section 7.8, Patheon may communicate with any governmental agency, including but not limited to governmental agencies responsible for granting regulatory approval for the Products, regarding the Products only if, in the opinion of Patheon's counsel, the communication is necessary to comply with the terms of this Agreement or the requirements of any Applicable Law and a representative of Client is present for a verbal communication or has reviewed and approved a written communication. Patheon will notify Client immediately upon and in any event within 24 hours after receiving any request from a Regulatory Authority for communication related to a Product.

7.3 Records and Accounting by Patheon.

Patheon will keep records of the manufacture, testing, and shipping of the Products (including evidence on the testing of raw materials, packaging and labeling materials as required by the Quality Agreement), and retain samples of the Products as are necessary to comply with applicable manufacturing regulatory requirements, as well as to assist with resolving Product complaints and other similar investigations. Copies of the records and samples will be retained for five years or one year following the date of Product expiry (whichever is longer), or longer if required by Applicable Laws, at which time Client will be contacted concerning the delivery and destruction of the documents and/or samples of Products at least 45 days prior to the destruction of the documents or samples. Patheon will not store these documents and/or samples beyond the time period set forth above.

7.4 Inspection of Financial Records.

Client or its designee may inspect Patheon reports and records relating to this Agreement during normal business hours and with reasonable advance notice of at least […***…] Business Days, but a Patheon representative must be present during the inspection. In addition, as more fully set forth in Section 4.2, Client will have the right to allow an independent third party auditor to review the information supporting the price adjustments made under Sections 4.2, 4.3 and 4.4.

7.5 Access.

Patheon will give Client reasonable access at agreed times to procedures and documentation relevant to the Product, and to the areas of the Manufacturing Site in which the Products are manufactured, stored, handled, or shipped, to permit Client to verify that the Manufacturing Services are being performed in accordance with the Specifications, cGMPs, Applicable Laws and the Quality Agreement. But, with the exception of "For-Cause" Audits, Client will be limited each Year to one cGMP-type audit, lasting no more than […***…] days, and involving no more than […***…] auditors. Client may request additional cGMP-type audits, additional audit days, or the participation of additional auditors subject to payment to Patheon of a fee of $5,000 for each additional audit day and $1,000 per audit day for each additional auditor. The right of access set forth in this Section 7.5 will not include a right to access or inspect Patheon's financial records. In addition, upon the request of any Regulatory Authority having jurisdiction over the manufacture of Products hereunder, the Regulatory Authority will have access to observe, audit and inspect any Manufacturing Site and Patheon's procedures used for the manufacture, release and stability testing, and/or warehousing of Products and to audit those facilities and procedures for compliance with cGMP and/or other regulatory requirements. Patheon specifically agrees to cooperate with any inspection by a Regulatory Authority, whether prior to or after Regulatory Approval of a Product, and to provide Client a copy of any inspection or audit report resulting from the inspection within three Business Days from receiving the report. Client may be present at the Facility for consultation during any such inspection.

7.6 Notification of Regulatory Inspections.

Patheon will notify Client within one Business Day of any inspection, receipt of notice of any inspection and/or any request for samples by any governmental agency specifically involving the Products. Patheon will also notify Client within three Business Days of receipt of any form 483's or warning letters or any other significant regulatory action or finding which could directly or indirectly impact the regulatory status of the Products or Patheon's ability to perform the Manufacturing Services. Within three Business Days of receipt, Patheon will provide Client with a reasonable description of the notifications and inspections and all supporting documentation, including, as applicable, all form 483's and warning letters or similar warning or objection, responses and all other correspondence and discussions of the applicable Regulatory Authority, which should be redacted to protect the confidential information of Third Parties. Patheon will discuss with Client and consider in good faith any comments provided by Client on the proposed response. Additionally, Patheon will obtain Client's prior approval of any such responses related to Product. Patheon will use commercially reasonable efforts to address and rectify any issues or problems in its manufacturing facility or procedures and any objections or warnings raised by the Regulatory Authority as soon as practicable and to continue to manufacture and supply to Client, in compliance with all Applicable Laws and the terms of this Agreement, the Products ordered by Client. After the filing of a response with the FDA or other Regulatory Authority, Patheon will notify Client of any further contacts with the Regulatory Authority relating to the subject matter of the response.

7.7 Reports.

Patheon will supply on an annual basis all Product data in its control, including release test results, complaint test results, and all investigations (in manufacturing, testing, and storage), that Client reasonably requires in order to complete any filing under any applicable regulatory regime, including any Annual Report that Client is required to file with the FDA or any other Regulatory Authority or other information related to the performance of the Manufacturing Services mandated by a Regulatory Authority. Patheon will promptly provide a copy of the Annual Product Review Report to the Client at no additional cost. Any additional report requested by Client beyond the scope of cGMPs and customary FDA or other Regulatory Authority requirements will be subject to an additional fee to be agreed upon between Patheon and the Client.

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7.8 Regulatory Filings.

(a) Regulatory Authority. Client will have the sole right and responsibility for filing all documents with all Regulatory Authorities and taking any other actions that may be required for the receipt and/or maintenance of Regulatory Authority approval for the manufacture, import, export, distribution, marketing, sale, pricing and/or reimbursement of the Products. Patheon will assist Client, to the extent consistent with Patheon's obligations under this Agreement, to obtain Regulatory Authority approval for the commercial manufacture of all Products as quickly as reasonably possible. Client will provide copies of relevant sections of regulatory filings to Patheon that are necessary for Patheon to ensure compliance of the manufacturing processes to those submitted to Regulatory Authorities.

(b) Verification of Data. Prior to filing any documents with any Regulatory Authority that incorporate data generated by Patheon, Client will give Patheon a copy of the documents incorporating this data to give Patheon the opportunity to verify the accuracy and regulatory validity of those documents as they relate to Patheon generated data. Patheon requires […***…] days to perform this review but the Parties may agree to a shorter time for the review as needed, including as mandated by a Regulatory Authority. These documents will be Confidential Information of Client.

(c) Verification of CMC. Prior to filing with any Regulatory Authority any documentation which is or is equivalent to the FDA's Chemistry and Manufacturing Controls (all such documentation herein referred to as "**CMC**") related to any Marketing Authorization, such as a New Drug Application or Abbreviated New Drug Application, Client will give Patheon a copy of the CMC as well as all supporting documents which have been relied upon to prepare the CMC that directly relate to the Manufacturing Services provided by Patheon. This disclosure will permit Patheon to verify that the CMC accurately describes the work that Patheon has performed and the manufacturing processes that Patheon will perform under this Agreement. Patheon requires […***…] days to perform this review but the Parties may agree to a shorter time for the review as needed. Client will give Patheon copies of all FDA filings at the time of submission to the extent containing CMC information that directly relate to the Manufacturing Services provided by Patheon and may redact this information to protect the Confidential Information of any Third Party.

(d) Deficiencies. If, in Patheon's sole discretion, acting reasonably, Patheon determines that any of the information given by Client under clauses (b) and (c) above is inaccurate or deficient in any material respect (the "**Deficiencies**"), Patheon will notify Client in writing of the Deficiencies as promptly as practical and in any case within the time frame set forth in clause (b) or (c), as applicable. The Parties will work together to have the Deficiencies resolved prior to any pre-approval inspection.

(e) Client Responsibility. For clarity, the Parties agree that in reviewing the documents referred to in clause (b) above, Patheon's role will be limited to verifying the accuracy of the description of the work undertaken or to be undertaken by Patheon. Subject to the foregoing, Patheon will not assume any responsibility for the accuracy of any application for receipt of an approval by a Regulatory Authority. The Client is solely responsible for the preparation and filing of the application for approval by the Regulatory Authority and any relevant costs will be borne by the Client.

(f) Inspection by Regulatory Authorities. If Client does not give Patheon the documents requested under clause (b) above within the time specified and if Patheon reasonably believes that Patheon's standing with a Regulatory Authority may be jeopardized, Patheon may, in its sole discretion, delay or postpone any inspection by the Regulatory Authority until Patheon has reviewed the requested documents that directly relate to the Manufacturing Services provided by Patheon and is satisfied with their contents.

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7.9 Quality Agreement.

For clarification, if there is any conflict between the terms and conditions of this Agreement, including this Article 7, and the terms and conditions of the Quality Agreement, the terms and conditions of the Quality Agreement will control with regard to topics directly related to quality and compliance only.

TERM AND TERMINATION

8.1 Initial Term.

This Agreement will become effective as of the Effective Date and will continue until **December 31, 2020** (the "**Initial Term**"), unless terminated earlier by one of the Parties in accordance herewith. This Agreement will automatically renew after the Initial Term for successive terms of two Years each if there is a Product Agreement in effect, unless either Party gives written notice to the other Party of its intention to terminate this Agreement at least 24 months prior to the end of the then current term, subject to earlier termination in accordance with the terms of this Agreement. In any event, the legal terms and conditions of this Agreement will continue to govern any Product Agreement in effect as provided in Section 1.2. Each Product Agreement will have an initial term of five Years from the start of commercial manufacture at the Manufacturing Site for the Product unless the Parties agree to a different number of Years in the applicable Product Agreement (each, an "**Initial Product Term**"), subject to earlier termination in accordance with the terms of this Agreement. Product Agreements will automatically renew after the Initial Product Term for successive terms of two Years each unless either Party gives written notice to the other Party of its intention to terminate the Product Agreement at least 24 months prior to the end of the then current term, subject to earlier termination in accordance with the terms of this Agreement.

8.2 Termination for Cause.

(a) Either Party at its sole option may terminate this Agreement or any Product Agreement upon written notice where the other Party has failed to remedy a material breach of any of its representations, warranties, or other obligations under this Agreement or any Product Agreement within 60 days following receipt of a written notice (the "**Remediation Period**") of the breach that expressly states that it is a notice under this Section 8.2(a) (a "**Breach Notice**"). The aggrieved Party's right to terminate this Agreement or a Product Agreement under this Section 8.2(a) may only be exercised for a period of 60 days following the expiry of the Remediation Period (where the breach has not been remedied) and if the termination right is not exercised during this period then the aggrieved Party will be deemed to have waived the breach of the representation, warranty, or obligation described in the Breach Notice.

(b) Either Party at its sole option may immediately terminate this Agreement or any Product Agreement upon written notice, but without prior advance notice, to the other Party if: (i) the other Party is declared insolvent or bankrupt by a court of competent jurisdiction; (ii) a voluntary petition of bankruptcy is filed in any court of competent jurisdiction by the other Party; or (iii) this Agreement or any Product Agreement is assigned by the other Party for the benefit of creditors.

(c) Client may terminate this Agreement as to any Product and the related Product Agreement upon at least 30 days' prior written notice, if any Authority takes any action, or raises any objection, that prevents Client from importing, exporting, purchasing, or selling the Product, or Client (or its Affiliate or licensee) determines that for safety or efficacy reasons Client is not going to continue to develop or commercialize the Product. But if this occurs, Client must still fulfill all of its obligations under Section 8.4 below and under any Capital Equipment Agreement regarding the Product.

(d) Client may terminate this Agreement or a Product Agreement at any time upon written notice to Patheon, without limiting Client's other rights or remedies under this Agreement, if any Authority takes any enforcement action regarding the Manufacturing Site that relates to the Product or could reasonably be expected to adversely affect the ability of Patheon to supply the Product.

(e) Patheon may terminate this Agreement or a Product Agreement upon 18 months' prior written notice if Client assigns under Section 13.6 any of its rights under this Agreement or a Product Agreement to an assignee that, in the opinion of Patheon acting reasonably is a Patheon Competitor. But this time period will automatically be extended by an additional three months if, at 18 months after the notice, Client is working in good-faith to secure, and/or obtain required approvals for, another supplier.

8.3 Product Discontinuation; Other Causes for Termination by Client.

(a) Client will give at least six months' advance notice if it intends to no longer order Manufacturing Services for a Product due to this Product's discontinuance in the market. Upon expiration of the applicable six-month notice period, this Agreement will terminate with respect to the Product or, if the Product is the only Product subject to this Agreement, this Agreement will terminate in its entirety.

(b) Except for terminations under the other termination provisions of this Agreement (including Sections 8.2, 8.3(a), 9.4 and 13.7), Client will give at least 36 months' advance notice if it intends to no longer order Manufacturing Services for a Product for any other reason. In such case, the Annual Minimum will be reduced by […***…]% beginning one year from the date of notice and each year thereafter. Upon expiration of the applicable 36 month period, at Client's option, this Agreement will terminate with respect to the Product or, if the Product is the only Product subject to this Agreement, the Agreement will terminate in its entirety. Upon receipt of notice, Patheon will provide assistance to Client in a Technology Transfer. Except for a material breach of this Agreement by Patheon, Client will be responsible for all costs associated with the Technology Transfer. If the Technology Transfer is a result of a material breach of the Agreement by Patheon, each Party will be responsible for its own costs associated with the Technology Transfer. In all circumstances, Patheon will use at least commercially reasonable efforts to meet the timeline requested by Client.

8.4 Obligations on Termination.

If a Product Agreement is completed, expires, or is terminated in whole or in part for any reason, then:

(a) Client will take delivery of and pay for all undelivered Products that are manufactured and/or packaged under a Firm Order and in compliance with the terms of this Agreement, at the price in effect at the time the Firm Order was placed;

(b) Client will purchase, at Patheon's actual cost (including all costs incurred by Patheon for the purchase and handling of the Inventory), the Inventory applicable to the Products which was purchased, produced and maintained by Patheon in contemplation of filling Firm Orders or in accordance with Section 5.2;

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(c) Client will reimburse Patheon for the purchase price payable under Patheon's orders with suppliers of Components, if the orders were made by Patheon in reliance on Firm Orders or in accordance with Section 5.2;

(d) Client acknowledges that no Patheon Competitor will be permitted access to the Manufacturing Site; and

(e) Client will make commercially reasonable efforts, at its own expense, to remove from Patheon site(s), within 30 days, all unused Active Material and Client-Supplied Components, all applicable Inventory and Materials (whether current or obsolete), supplies, undelivered Product, chattels, equipment or other moveable property owned by Client, related to the Agreement and located at a Patheon site or that is otherwise under Patheon's care and control ("**Client Property**"). If Client fails to remove the Client Property within 30 days following the completion, termination, or expiration of the Product Agreement, Client will pay Patheon $100.00 per pallet, per month, one pallet minimum (except that Client will pay $200 per pallet, per month, one pallet minimum, for any of the Client Property that contains controlled substances, requires refrigeration or other special storage requirements) thereafter for storing the Client Property and will assume any third party storage charges invoiced to Patheon regarding the Client Property. Patheon will invoice Client for the storage charges as set forth in Section 5.5 of this Agreement.

Any termination or expiration of this Agreement or a Product Agreement will not affect any outstanding obligations or payments due prior to the termination or expiration, nor will it prejudice any other remedies that the Parties may have under this Agreement or a Product Agreement or any related Capital Equipment Agreement. For greater certainty, expiration or termination of this Agreement or of a Product Agreement for any reason will not affect the obligations and responsibilities of the Parties under Articles 10, 11 and 12 and Sections 5.4, 5.6, 6.3, 6.4, 6.5, 6.6, 7.3, 7.4, 8.4, 13.1, 13.2, 13.3, 13.11, 13.15 and 13.16, all of which survive any termination.

REPRESENTATIONS, WARRANTIES AND COVENANTS

9.1 Authority.

Each Party covenants, represents, and warrants to the other Party, as of the Effective Date, that (a) it has the full right and authority to enter into this Agreement and that it is not aware of any impediment that would inhibit its ability to perform its obligations hereunder and has taken all necessary action on its part to authorize the performance of the obligations; (b) the execution and delivery of this Agreement and the performance of the Party's obligations hereunder (i) do not conflict with or violate any requirement of Applicable Laws or regulations and (ii) do not conflict with, or constitute a default or require any consent under, any contractual obligation of the Party; (c) it is duly organized, validly existing and in good standing under the laws of the state or country in which it is organized; and (d) this Agreement has been duly executed and delivered on behalf of the Party, and constitutes a legal, valid, binding obligation, enforceable against the Party in accordance with its terms.

9.2 Client Warranties.

Client covenants, represents, and warrants that:

(a) Non-Infringement.

(i) the Specifications for each of the Products are its or its Affiliate's property and Client may lawfully disclose the Specifications to Patheon;

(ii) any Client Intellectual Property provided by Client for use by Patheon in performing the Manufacturing Services according to the Specifications and the other terms of this Agreement (i) is owned or controlled by Client or its Affiliate, (ii) may be lawfully used by Patheon as directed by Client, and (iii) when used by Patheon according to the Specifications and the other terms of this Agreement does not infringe any Third Party Rights known to Client;

(iii) subject to […***…], the […***…] or the […***…];

as of the Effective Date, there are no actions or other legal proceedings to which the Client is a party or of which Client is aware, concerning the infringement of Third Party Rights related to any of the Specifications, or any of the Active Materials and the Client-Supplied Components, or the sale, use, or other disposition of any Product made in accordance with the Specifications;

(b) Quality and Compliance.

(i) the Specifications for all Products conform to all applicable cGMPs and Applicable Laws;

(ii) once Client has received approval from the FDA to market the Products, the Products, if labelled and manufactured in accordance with the Specifications and in compliance with applicable cGMPs and Applicable Laws (i) may be lawfully sold and distributed in every jurisdiction in which Client markets the Products and (iii) will be safe for human consumption;

(iii) on the date of shipment to the Manufacturing Site, the API will conform to the specifications for the API that Client has given to Patheon, subject to Patheon's obligation to test the API in accordance with the Quality Agreement before beginning manufacture of the Products using the API, and that the API will be adequately contained, packaged, and labelled and will conform to the affirmations of fact on the container.

9.3 Patheon Warranties.

Patheon covenants, represents, and warrants that:

(a) (1) all Products delivered hereunder will (i) conform to the applicable Specifications; (ii) be free and clear of any and all encumbrances, liens, or other third party claims; (iii) be manufactured, packaged, labelled and delivered in compliance with the Quality Agreement and applicable cGMP, all regulatory approvals for the Product, and Applicable Laws and in accordance with manufacturing procedures described in the applicable master Batch records for the Product; (iv) not be adulterated or misbranded within the meaning of the
United States Food, Drug and Cosmetic Act, as amended, and any regulations promulgated thereunder or comparable provisions under the laws and regulations of any other applicable jurisdiction (the **"Act"**); and (v) not be articles that, under the provisions of the Act, may not be introduced into interstate commerce; and (2) Patheon's processes used to perform the Manufacturing Services will not infringe on any Third Party Rights (collectively, the **"Product Warranties"**);

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(b) it will perform the Manufacturing Services in accordance with the Quality Agreement, Specifications, cGMPs, and Applicable Laws;

(c) the Components, Active Materials and the Bill Back Items will at all times be free and clear of any and all encumbrances, liens, or other third party claims; and

(d) any Patheon Intellectual Property used by Patheon to perform the Manufacturing Services (i) is Patheon's or its Affiliate's unencumbered property, (ii) may be lawfully used by Patheon, and (iii) does not infringe and will not infringe any Third Party Rights.

9.4 Debarred Persons.

Patheon covenants that it will not in the performance of its obligations under this Agreement use the services of any person debarred or suspended under 21 U.S.C. §335(a) or (b) or comparable provisions under the laws and regulations of any other applicable jurisdiction. Patheon represents that it does not currently have, and covenants that it will not hire, as an officer or an employee any person who has been convicted of a felony under the laws of the United States for conduct relating to the regulation of any drug product under the Act. If Patheon or any officer, employee or agent of Patheon: (a) becomes debarred; or (b) receives notice of action or threat of action with respect to its debarment, during the term of this Agreement, Patheon agrees to notify Client immediately. If Patheon or any of its officers, employees or agents becomes debarred as set forth in clause (a) above or receives notice of action or threat of action as set forth in clause (b) above, Client will have the right to terminate this Agreement upon written notice to Patheon.

9.5 Permits.

Client will be solely responsible for obtaining or maintaining, on a timely basis, any permits or other regulatory approvals for the Products or the Specifications, including, without limitation, all marketing and post-marketing approvals.

Patheon will maintain at all relevant times all governmental permits, licenses, approval, and authorities required to enable it to lawfully and properly perform the Manufacturing Services.

9.6 No Warranty.

NEITHER PARTY MAKES ANY WARRANTY OR REPRESENTATION OF ANY KIND, EITHER EXPRESSED OR IMPLIED, BY FACT OR LAW, OTHER THAN THOSE EXPRESSLY SET FORTH IN THIS AGREEMENT. WITHOUT LIMITING THE FOREGOING, NEITHER PARTY MAKES ANY WARRANTY OR REPRESENTATION OF FITNESS FOR A PARTICULAR PURPOSE NOR ANY WARRANTY OR REPRESENTATION OF MERCHANTABILITY FOR THE PRODUCTS.

REMEDIES AND INDEMNITIES

10.1 Consequential Damages.

Except for liability for breach by either Party of its obligations of Confidentiality under Article 11, under no circumstances whatsoever will either Party be liable to the other in contract, tort, negligence, breach of statutory duty, or otherwise for (i) any (direct or indirect) loss of profits, of production, of anticipated savings, of business, or goodwill or (ii) for any other liability, damage, costs, or expense of any kind incurred by the other Party of an indirect or consequential nature, regardless of any notice of the possibility of these damages. This Section 10.1 will not be deemed to limit either Party's indemnification obligations under this Article 10.

10.2 Limitation of Liability.

(a) Active Materials. Except as expressly set forth in Section 2.2 and Section 6, under no circumstances will Patheon be responsible for any loss or damage to the Active Materials. Patheon's maximum responsibility per Year for loss or damage to the Active Materials will not exceed the Maximum Credit Value set forth in Schedule D of a Product Agreement.

(b) Maximum Liability. Subject to Section 10.2(c) and excluding Patheon's indemnity obligations arising under Section 10.3, Patheon's maximum liability to Client per Year under this Agreement or the Product Agreement for a single Product for any reason whatsoever, including, without limitation, any liability arising under Article 6 hereof or resulting from any and all breaches of its representations, warranties, or any other obligations under this Agreement or the applicable Product Agreement will not exceed on a per Product basis […***…].

(c) Nothing contained in this Agreement will exclude or limit either Party's liability for personal injury, death or fraudulent misrepresentation.

10.3 Patheon Indemnity.

(a) Patheon agrees to defend and indemnify Client, its Affiliates and licensees, and their respective directors, officers, employees, and agents (**"Client Indemnitees"**) against all losses, damages, costs, judgments, liability, fees and expenses (including reasonable attorneys' fees) (collectively, **"Losses"**) incurred by any Client Indemnitee due to any suit, claim, demand, judgment or action brought by any Third Parties (other than Affiliates) (each, a **"Claim"**), including, without limitation any Claim of personal injury or property damage, to the extent that the injury or damage is the result of (a) a failure by Patheon or any of its Affiliates to perform the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws, (b) Patheon's breach of any of its obligations, representations or warranties under this Agreement, or (c) the negligence or willful misconduct of any Patheon Indemnitee except to the extent that the losses, damages, costs, claims, demands, judgments, and liability are due to the negligence or willful misconduct of any Client Indemnitee.

(b) If a Claim occurs, Client will: (a) promptly notify Patheon of the Claim; (b) use commercially reasonable efforts to mitigate the effects of the Claim; (c) reasonably cooperate with Patheon in the defense of the claim; and (d) permit Patheon to control the defense and settlement of the claim, all at Patheon's cost and expense. Notwithstanding the foregoing, Patheon will not compromise or settle any Claim for which a Client Indemnitee is requesting indemnification for any damages other than monetary damages without Client's prior written consent, which will not be unreasonably withheld.

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10.4 Client Indemnity.

(a) Client agrees to defend and indemnify Patheon and its Affiliates and their respective directors, officers, employees, and agents ("**Patheon Indemnitees**") against all Losses, incurred by any Patheon Indemnitee due to any Claim of infringement or alleged infringement of any Third Party Rights in the Products, or any Claim of personal injury or property damage, in each case, to the extent that the Losses are the result of a breach of this Agreement by Client, including, without limitation, any representation or warranty contained herein, or the negligence or wilful misconduct of any Client Indemnitee, except to the extent that the Losses are due to the negligence or willful misconduct of any Patheon Indemnitee.

(b) If a Claim occurs, Patheon will: (a) promptly notify Client of the Claim; (b) use commercially reasonable efforts to mitigate the effects of the Claim; (c) reasonably cooperate with Client in the defense of the Claim; and (d) permit Client to control the defense and settlement of the Claim, all at Client's cost and expense. Notwithstanding the foregoing, Client will not compromise or settle any Claim for which a Patheon Indemnitee is requesting indemnification for any damages other than monetary damages without Patheon's prior written consent, which will not be unreasonably withheld.

CONFIDENTIALITY

11.1 Confidential Information.

"**Confidential Information**" means any information disclosed by the Disclosing Party to the Recipient (whether disclosed in oral, written, electronic or visual form) that is non-public, confidential or proprietary including, without limitation, information relating to the Disclosing Party's patent and trademark applications, process designs, process models, drawings, plans, designs, data, databases and extracts therefrom, formulae, methods, know-how and other intellectual property, its clients or client confidential information, finances, marketing, products and processes and all price quotations, manufacturing or professional services proposals, information relating to composition, proprietary technology, and all other information relating to manufacturing capabilities and operations. In addition, all analyses, compilations, studies, reports or other documents prepared by any Party's Representatives containing the Confidential Information will be considered Confidential Information. Samples or materials provided hereunder as well as any and all information derived from the approved analysis of the samples or materials will also constitute Confidential Information. For the purposes of this ARTICLE 11, a Party or its Representative receiving Confidential Information under this Agreement is a "**Recipient**," and a Party or its Representative disclosing Confidential Information under this Agreement is the **"Disclosing Party**."

11.2 Use of Confidential Information.

The Recipient will use the Confidential Information solely for the purpose of meeting its obligations under this Agreement. The Recipient will keep the Confidential Information strictly confidential and will not disclose the Confidential Information in any manner whatsoever, in whole or in part, other than to those of its Representatives who (i) have a need to know the Confidential Information for the purpose of this Agreement; (ii) have been advised of the confidential nature of the Confidential Information and (iii) have obligations of confidentiality and non-use to the Recipient no less restrictive than those of this Agreement. Additionally, Client will have the right to disclose Confidential Information

to sublicensees and/or other strategic partners or in connection with financings or similar transactions provided that the parties to whom Client discloses this information are bound by obligations of confidentiality and non-use no less restrictive than those of this Agreement. Recipient will protect the Confidential Information disclosed to it by using all reasonable precautions to prevent the unauthorized disclosure, dissemination or use of the Confidential Information, which precautions will in no event be less than those exercised by Recipient with respect to its own confidential or proprietary Confidential Information of a similar nature. The obligations of confidentiality and non-use set forth in this Article 11 will remain in effect for a period of seven years following the termination of this Agreement.

11.3 Exclusions.

The obligations of confidentiality will not apply to the extent that the information:

(a) is or becomes publicly known through no breach of this Agreement or fault of the Recipient or its Representatives;

(b) is in the Recipient's possession at the time of disclosure by the Disclosing Party other than as a result of the Recipient's breach of any legal obligation;

(c) is or becomes known to the Recipient on a non-confidential basis through disclosure by sources, other than the Disclosing Party, having the legal right to disclose the Confidential Information, provided that the other source is not known by the Recipient to be bound by any obligations (contractual, legal, fiduciary, or otherwise) of confidentiality to the Disclosing Party with respect to the Confidential Information;

(d) is independently developed by the Recipient without use of or reference to the Disclosing Party's Confidential Information as evidenced by Recipient’s written records; or

(e) is expressly authorized for release by the written authorization of the Disclosing Party.

Any combination of information which comprises part of the Confidential Information are not exempt from the obligations of confidentiality merely because individual parts of that Confidential Information were publicly known, in the Recipient’s possession, or received by the Recipient, unless the combination itself was publicly known, in the Recipient’s possession, or received by the Recipient.

11.4 Photographs and Recordings.

Neither Party will take any photographs or videos of the other Party’s facilities, equipment or processes, nor use any other audio or visual recording equipment (such as camera phones) while at the other Party’s facilities, without that Party’s express written consent.

11.5 Permitted Disclosure.

Notwithstanding any other provision of this Agreement, the Recipient may disclose Confidential Information of the Disclosing Party to the extent required, as advised by counsel, in response to a valid order of a court or other governmental body or as required by law, regulation or stock exchange rule. But the Recipient will advise the Disclosing Party in advance of the disclosure to the extent practicable and permissible by the order, law, regulation or stock exchange rule and any other applicable law, will reasonably cooperate with the Disclosing Party, if required, in seeking an appropriate protective order or other remedy, and will otherwise continue to perform its obligations of confidentiality set out

herein. If any public disclosure is required by law, the Parties will consult concerning the form of announcement prior to the public disclosure being made.

11.6 Marking.

The Disclosing Party agrees to use reasonable efforts to summarize in writing the content of any oral disclosure or other non-tangible disclosure of Confidential Information within 30 days of the disclosure, but failure to provide this summary will not affect the nature of the Confidential Information disclosed if the Confidential Information was identified as confidential or proprietary when disclosed orally or in any other non-tangible form.

11.7 Return of Confidential Information.

Upon the written request of the Disclosing Party, the Recipient will promptly return the Confidential Information to the Disclosing Party or, if the Disclosing Party directs, destroy all Confidential Information disclosed in or reduced to tangible form including any copies thereof and any summaries, compilations, analyses or other notes derived from the Confidential Information except for one copy which may be maintained by the Recipient for its records. The retained copy will remain subject to all confidentiality provisions contained in this Agreement.

11.8 Remedies.

The Parties acknowledge that monetary damages may not be sufficient to remedy a breach by either Party of this Agreement and agree that the non-breaching Party will be entitled to seek specific performance, injunctive and/or other equitable relief to prevent breaches of this Agreement and to specifically enforce the provisions hereof in addition to any other remedies available at law or in equity. These remedies will not be the exclusive remedies for breach of this Agreement but will be in addition to any and all other remedies available at law or in equity.

DISPUTE RESOLUTION

12.1 Commercial Disputes.

If any dispute arises out of this Agreement or any Product Agreement (other than a dispute under Section 6.1(b) or a Technical Dispute, as defined herein), the Parties will first try to resolve it amicably. In that regard, any Party may send a notice of dispute to the other, and each Party will appoint, within […***…] Business Days from receipt of the notice of dispute, a single representative having full power and authority to resolve the dispute. The representatives will meet as necessary in order to resolve the dispute. If the representatives fail to resolve the matter within […***…] from their appointment, or if a Party fails to appoint a representative within the […***…] Business Day period set forth above, the dispute will immediately be referred to the Chief Operating Officer (or another officer as he/she may designate) of Patheon and the Chief Executive Officer of Client each Party who will meet and discuss as necessary to try to resolve the dispute amicably. Should the Parties fail to reach a resolution under this Section 12.1, the dispute will be referred to a court of competent jurisdiction in accordance with Section 13.16.

12.2 Technical Dispute Resolution.

If a dispute arises (other than disputes under Sections 6.1(b) or 12.1) between the Parties that is exclusively related to technical aspects of the manufacturing, packaging, labelling, quality control testing, handling, storage, or other activities under this Agreement (a "**Technical Dispute**"), the Parties will make all reasonable efforts to resolve the dispute by amicable negotiations. In that regard, senior representatives of each Party will, as soon as possible and in any event no later than […***…] Business Days after a written request from either Party to the other, meet in good faith to resolve any Technical Dispute. If, despite this meeting, the Parties are unable to resolve a Technical Dispute within a reasonable time, and in any event within […***…] Business Days of the written request, the Technical Dispute will, at the request of either Party, be referred for determination to an expert in accordance with Exhibit A. If the Parties cannot agree that a dispute is a Technical Dispute, Section 12.1 will prevail. For greater clarity, the Parties agree that the release of the Products for sale or distribution under the applicable marketing approval for the Products will not by itself indicate compliance by Patheon with its obligations for the Manufacturing Services and further that nothing in this Agreement (including Exhibit A) will remove or limit the authority of the relevant qualified person (as specified by the Quality Agreement) to determine whether the Products are to be released for sale or distribution.

MISCELLANEOUS

13.1 Inventions.

(a) For the term of this Agreement, Client hereby grants to Patheon a non-exclusive, paid-up, royalty-free, non-transferable license under Client's Intellectual Property solely to the extent necessary for Patheon to perform the Manufacturing Services in accordance with this Agreement, and not for any other purpose.

(b) All Inventions generated or derived by Patheon while performing the Manufacturing Services, to the extent relating specifically to the development, manufacture, use or sale of any Product that is the subject of the Manufacturing Services, and all Client Intellectual Property, will be the exclusive property of Client. Patheon hereby assigns, and agrees to assign, all of its right, title and interest in and to all such Inventions and Client Intellectual Property to Client and agrees to take all further acts reasonably required to evidence and/or perfect such assignment to Client, at Client's expense. Patheon will notify Client in writing, as promptly as practicable, of all Inventions and Client Intellectual Property made, created, discovered, generated or derived by Patheon in the course of performing the Manufacturing Services. Patheon may retain one copy of records relating to Client Intellectual Property to the extent required under Applicable Laws.

(c) All Patheon Intellectual Property will be the exclusive property of Patheon. Patheon hereby grants to Client a perpetual, irrevocable, non-exclusive, paid-up, royalty-free, transferable license, with the right to sublicense through multiple tiers, to use the Patheon Intellectual Property used by Patheon to perform the Manufacturing Services to enable Client to manufacture the Product(s).

(d) Each Party will be solely responsible for the costs of filing, prosecution, and maintenance of patents and patent applications on its own Inventions.

*****Confidential Treatment Requested**
*****Confidential Treatment Requested**

13.2 Intellectual Property.

All Client Intellectual Property will be owned by Client and all Patheon Intellectual Property will be owned by Patheon. Neither Party has, nor will it acquire, any interest in any of the other Party's Intellectual Property unless otherwise expressly agreed to in writing or expressly set forth in this Agreement. Neither Party will use any Intellectual Property of the other Party, except as specifically authorized by the other Party or as required for the performance of its obligations under this Agreement.

13.3 Insurance.

Each Party will maintain commercial general liability insurance, including blanket contractual liability insurance covering the obligations of that Party under this Agreement through the term of this Agreement and for a period of three years thereafter. This insurance will have policy limits of not less than (i) $[…***…] for each occurrence for personal injury or property damage liability; and (ii) $[…***…] in the aggregate per annum for product and completed operations liability. If requested each Party will give the other a certificate of insurance evidencing the above and showing the name of the issuing company, the policy number, the effective date, the expiration date, and the limits of liability. Each Party will further provide the other Party a minimum of 30 days' written notice of a cancellation of, or material change in, the insurance. If a Party is unable to maintain the insurance policies required under this Agreement through no fault of its own, then the Party will forthwith notify the other Party in writing and the Parties will in good faith negotiate appropriate amendments to the insurance provision of this Agreement in order to provide adequate assurances.

13.4 Independent Contractors.

The Parties are independent contractors and this Agreement and any Product Agreement will not be construed to create between Patheon and Client any other relationship such as, by way of example only, that of employer-employee, principal agent, joint-venturer, co-partners, or any similar relationship, the existence of which is expressly denied by the Parties.

13.5 No Waiver.

Either Party's failure to require the other Party to comply with any provision of this Agreement or any Product Agreement will not be deemed a waiver of the provision or any other provision of this Agreement or any Product Agreement.

13.6 Assignment.

(a) Patheon may not assign this Agreement or any Product Agreement or any of its associated rights or obligations, or subcontract any of its rights or obligations, hereunder without the written consent of Client, this consent not to be unreasonably withheld. But Patheon may arrange for subcontractors to perform specific testing services arising under any Product Agreement without the consent of Client to the extent the subcontractors are specifically named and agreed in the Quality Agreement, provided that Patheon remains primarily liable to the Client for performance by Patheon's subcontractors. Further it is specifically agreed that Patheon may subcontract any part of the Services under a Product Agreement to any of its Affiliates to the extent the Affiliates are specifically named and agreed in the applicable Product Agreement and in the Quality Agreement, provided that Patheon remains primarily liable to the Client for performance by Patheon's Affiliates.

(b) Subject to Section 8.2(e), Client may assign this Agreement or any Product Agreement or any of its associated rights or obligations without approval from Patheon. Client will give Patheon prior
written notice of any assignment, any assignee will covenant in writing with Patheon to be bound by the terms of this Agreement or the Product Agreement and Client will remain liable hereunder. If Client only assigns a portion of this Agreement or a Product Agreement to a Third Party, the partial assignment will be subject to Patheon's cost review of the assigned Products and Patheon may terminate this Agreement or the Product Agreement or any assigned part thereof, on 18 months' prior written notice to Client and the assignee if good faith discussions do not lead to agreement on amended Manufacturing Service fees within a reasonable time. But this time period will automatically be extended by an additional three months if, at 18 months after the notice, Client is working in good-faith to secure, and/or obtain required approvals for, another supplier.

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(c) Despite the foregoing provisions of this Section 13.6, either Party may assign this Agreement or any Product Agreement to any of its Affiliates or to a successor to or purchaser of all or substantially all of its business to which this Agreement relates, but the assignee must execute an agreement with the non-assigning Party whereby it agrees to be bound hereunder.

13.7 Force Majeure.

Neither Party will be liable for the failure to perform its obligations under this Agreement or any Product Agreement if the failure is caused by an event beyond that Party's reasonable control, including, but not limited to, strikes or other labor disturbances, lockouts, riots, quarantines, communicable disease outbreaks, wars, acts of terrorism, fires, floods, storms, interruption of or delay in transportation, lack of or inability to obtain fuel, power or compliance with any order or regulation of any government entity acting within colour of right (a "**Force Majeure Event**"). A Party claiming a right to excused performance under this Section 13.7 will immediately notify the other Party in writing of the extent of its inability to perform, which notice will specify the event beyond its reasonable control that prevents the performance. Neither Party will be entitled to rely on a Force Majeure Event to relieve it from an obligation to pay money (including any interest for delayed payment) which would otherwise be due and payable under this Agreement or any Product Agreement. If the performance of any obligation under this Agreement is delayed due to a Force Majeure Event for a continuous period of more than 60 days, the other Party may terminate this Agreement without penalty upon written notice to the other Party under such event. All Annual Minimums will be suspended for the period of a Force Majeure Event but will be re-instated if the Force Majeure Event is cured. If this Agreement or any Product Agreement is terminated due to a Force Majeure Event lasting longer than 60 days as set forth above, Client may request Patheon to reasonably assist in the transfer of the technology required to manufacture the Product to a third party supplier designated by Client. If so requested, Patheon will promptly initiate and complete the technology transfer at Client's cost.

13.8 Additional Product.

Additional Products may be added to, or existing Products deleted from, any Product Agreement by amendments to the Product Agreement including Schedules A, B, C, and D as applicable.

13.9 Notices.

Unless otherwise agreed in a Product Agreement, any notice, approval, instruction or other written communication required or permitted hereunder will be sufficient if made or given to the other Party by personal delivery, by telecopy, facsimile communication, or confirmed receipt email or by sending the same by first class mail, postage prepaid to the respective addresses, telecopy or facsimile numbers or electronic mail addresses set forth below:

If to Client:

ACADIA Pharmaceuticals Inc.
3611 Valley Centre Drive, Suite 300
San Diego, CA 92130
Attention: […***…]
Telecopier No.: […***…]
Email address: […***…]

With a copy to:

ACADIA Pharmaceuticals Inc.
3611 Valley Centre Drive, Suite 300
San Diego, CA 92130
Attention: […***…]
Telecopier No.: […***…]
Email address: […***…]

If to Patheon:

Patheon Pharmaceuticals Inc.
2110 East Galbraith Road
Cincinnati, OH 45237-1625
Attention: […***…]
Telecopier No.: […***…]
Email address: […***…]

With a copy to:

Patheon Inc.
Canterbury Place
4815 Emperor Boulevard
Research Triangle Park,
NC 27703
Attention: […***…]
Telecopier No.: […***…]

or to any other addresses, telecopy or facsimile numbers or electronic mail addresses given to the other Party in accordance with the terms of this Section 13.9. Notices or written communications made or given by personal delivery, telecopy, facsimile, or electronic mail will be deemed to have been sufficiently made or given when sent (receipt acknowledged), or if mailed, five days after being deposited in the United States, Canada, or European Union mail, postage prepaid or upon receipt, whichever is sooner, or one Business Day after being sent by overnight courier.

*****Confidential Treatment Requested**

13.10 Severability.

If any provision of this Agreement or any Product Agreement is determined by a court of competent jurisdiction to be invalid, illegal, or unenforceable in any respect, that determination will not impair or affect the validity, legality, or enforceability of the remaining provisions, because each provision is separate, severable, and distinct.

13.11 Entire Agreement.

This Agreement, and all Schedules hereto, together with the applicable Product Agreement and Quality Agreement, constitutes the full, complete, final and integrated agreement between the Parties relating to the subject matter hereof and supersedes all previous written or oral negotiations, commitments, agreements, transactions, or understandings concerning the subject matter hereof. Any modification, amendment, or supplement to this Agreement or any Product Agreement must be in writing and signed by authorized representatives of the Parties. In case of conflict, the prevailing order of documents will be this Agreement, the Product Agreement, and the Quality Agreement.

13.12 Other Terms.

No terms, provisions or conditions of any purchase order or other business form or written authorization used by Client or Patheon will have any effect on the rights, duties, or obligations of the Parties under or otherwise modify this Agreement or any Product Agreement, regardless of any failure of Client or Patheon to object to the terms, provisions, or conditions unless the document specifically refers to this Agreement or the applicable Product Agreement and is signed by the Parties.

13.13 No Third Party Benefit or Right.

For greater clarity, nothing in this Agreement or any Product Agreement will confer or be construed as conferring on any third party any benefit or the right to enforce any express or implied term of this Agreement or any Product Agreement.

13.14 Execution in Counterparts.

This Agreement and any Product Agreement may be executed in two or more counterparts, by original or facsimile signature, each of which will be deemed an original, but all of which together will constitute one and the same instrument.

13.15 Use of Client Name.

Patheon will not make any use of Client's name, trademarks or logo or any variations thereof, alone or with any other word or words, without the prior written consent of Client, which consent will not be unreasonably withheld. Despite this, Client agrees that Patheon may include Client's name and logo in customer lists or related marketing and promotional material for the purpose of identifying users of Patheon's Manufacturing Services.

13.16 Governing Law.

This Agreement and any Product Agreement will be construed and enforced in accordance with the laws of the State of New York and the laws of the United States of America applicable therein and subject to the exclusive jurisdiction of the courts thereof. The UN Convention on Contracts for the International Sale of Goods will not apply to this Agreement or any Product Agreement.

IN WITNESS WHEREOF, the duly authorized representatives of the Parties have executed this Agreement as of the date first written above.

PATHEON PHARMACEUTICALS INC.

By: /s/ Francis P. McCune

Name: Francis P. McCune

Title: Secretary

ACADIA PHARMACEUTICALS INC.

By: /s/ Steve Davis

Name: Steve Davis

Title: Interim CEO

APPENDIX 1

FORM OF PRODUCT AGREEMENT

(Includes Schedules A to D)

PRODUCT AGREEMENT

This Product Agreement (this "**Product Agreement**") is issued under the Master Manufacturing Services Agreement dated August 3, 2015 between **Patheon Pharmaceuticals Inc.**, and **ACADIA Pharmaceuticals Inc.** (the "**Master Agreement**"), and is entered into **[insert effective date]** (the "**Effective Date**"), between Patheon Pharmaceuticals Inc., **[or applicable Patheon Affiliate]**, a corporation existing under the laws of the State of Delaware **[or applicable founding jurisdiction for Patheon Affiliate]**, having a principal place of business at 2110 East Galbraith Road, Cincinnati, OH 45237-1625 **[or Patheon Affiliate address]** ("**Patheon**") and **[insert Client name, legal entity, founding jurisdiction and address]** ("**Client**").

The terms and conditions of the Master Agreement are incorporated herein except to the extent this Product Agreement expressly references the specific provision in the Master Agreement to be modified by this Product Agreement. All capitalized terms that are used but not defined in this Product Agreement will have the respective meanings given to them in the Master Agreement.

The Schedules to this Product Agreement are incorporated into and will be construed in accordance with the terms of this Product Agreement.

1. **Product List and Specifications** (See Schedule A attached hereto)

2. **Minimum Order Quantity, Annual Volume, and Price** (See Schedule B attached hereto)

3. **Annual Stability Testing and Validation Activities (if applicable)** (See Schedule C attached hereto)

4. **Active Materials, Active Materials Credit Value, and Maximum Credit Value** (See Schedule D attached hereto)

5. **Yearly Forecasted Volume:** (insert for sterile products if applicable under Section 4.2.1 of the Master Agreement)

6. **Territory**: (insert the description of the Territory here)

7. **Manufacturing Site**: (insert address of Patheon Manufacturing Site where the Manufacturing Services will be performed)

8. **Governing Law**: (if applicable under Section 13.16 of the Master Agreement)

9. **Inflation Index:** (if applicable under Section 4.2(a) of the Master Agreement for Products manufactured outside of the Unites States or Puerto Rico)

10. **Currency**: (if applicable under Section 1.4 of the Master Agreement)

11. **Initial Set Exchange Rate**: (if applicable under Section 4.2(d) of the Master Agreement)

12. **Initial Product Term:** (if applicable under Section 8.1 of the Master Agreement)

13. **Notices**: (if applicable under Section 13.9 of the Master Agreement)

14. **Other Modifications to the Master Agreement**: (if applicable under Section 1.2 of the Master Agreement)

_____

IN WITNESS WHEREOF, the duly authorized representatives of the Parties have executed this Product Agreement as of the Effective Date set forth above.

PATHEON PHARMACEUTICALS INC. [or applicable Patheon Affiliate]

By: _____

Name: _____

Title: _____

ACADIA PHARMACEUTICALS INC. [or applicable Client Affiliate]

By: _____

Name: _____

Title: _____

SCHEDULE A

PRODUCT LIST AND SPECIFICATIONS

Product List

[insert product list]

Specifications

Prior to the start of commercial manufacturing of Product under this Agreement Client will give Patheon the originally executed copies of the Specifications as approved by the applicable Regulatory Authority or as most recently filed with such Regulatory Authority. If the Specifications received are subsequently amended, then Client will give Patheon the revised and originally executed copies of the revised Specifications. Upon acceptance of the revised Specifications, Patheon will give Client a signed and dated receipt indicating Patheon's receipt of the revised Specifications.

SCHEDULE B

MINIMUM ORDER QUANTITY, ANNUAL VOLUME, AND PRICE

[Insert Price Table]

Manufacturing Assumptions:

Packaging Assumptions:

Testing Assumptions:

Costs Included in Unit Pricing

[…***…]

Costs Not Included in Unit Pricing

[…***…]

*****Confidential Treatment Requested**

[…***…]

*****Confidential Treatment Requested**

SCHEDULE C

ANNUAL STABILITY TESTING

Patheon and Client will agree in writing on any stability testing to be performed by Patheon on the Products. This agreement will specify the commercial and Product stability protocols applicable to the stability testing and the fees payable by Client for this testing.

[NTD: Schedule C should clearly indicate when and/or under what conditions Patheon's responsibility to perform stability testing will end]

*****Confidential Treatment Requested**

SCHEDULE D

ACTIVE MATERIALS

Active Materials	Supplier
l	l
l	l

ACTIVE MATERIALS CREDIT VALUE

The Active Materials Credit Value will be as follows:

PRODUCT	ACTIVE MATERIALS	ACTIVE MATERIALS CREDIT VALUE
		Client's actual cost for Active Materials not to exceed $_____per kilogram

MAXIMUM CREDIT VALUE

Patheon's liability for Active Materials calculated in accordance with Section 2.2 of the Master Agreement **[for any Product]** in a Year will not exceed, in the aggregate, the maximum credit value set forth below:

PRODUCT	MAXIMUM CREDIT VALUE
	[…***…]

[End of Product Agreement]

*****Confidential Treatment Requested**

EXHIBIT A

TECHNICAL DISPUTE RESOLUTION

Technical Disputes which cannot be resolved by negotiation as provided in Section 12.2 will be resolved in the following manner:

1. **Appointment of Expert**. Within […***…] Business Days after a Party requests under Section 12.2 that an expert be appointed to resolve a Technical Dispute, the Parties will jointly appoint a mutually acceptable expert with experience and expertise in the subject matter of the dispute. If the Parties are unable to so agree within the […***…] Business Day period, or in the event of disclosure of a conflict by an expert under Paragraph 2 hereof which results in the Parties not confirming the appointment of the expert, then an expert (willing to act in that capacity hereunder) will be appointed by an experienced arbitrator on the roster of the American Arbitration Association.

2. **Conflicts of Interest**. Any person appointed as an expert will be entitled to act and continue to act as an expert even if at the time of his appointment or at any time before he gives his determination, he has or may have some interest or duty which conflicts or may conflict with his appointment if before accepting the appointment (or as soon as practicable after he becomes aware of the conflict or potential conflict) he fully discloses the interest or duty and the Parties will, after the disclosure, have confirmed his appointment.

3. **Not Arbitrator**. No expert will be deemed to be an arbitrator and the provisions of the American Arbitration Act or of any other applicable statute (foreign or domestic) and the law relating to arbitration will not apply to the expert or the expert's determination or the procedure by which the expert reaches his determination under this Exhibit A.

4. **Procedure**. Where an expert is appointed:

   (a) Timing. The expert will be so appointed on condition that (i) he promptly fixes a reasonable time and place for receiving representations, submissions or information from the Parties and that he issues the authorizations to the Parties and any relevant third party for the proper conduct of his determination and any hearing and (ii) he renders his decision (with full reasons) within […***…] Business Days (or another other date as the Parties and the expert may agree) after receipt of all information requested by him under Paragraph 4(b) hereof.

   (b) Disclosure of Evidence. The Parties undertake one to the other to give to any expert all the evidence and information within their respective possession or control as the expert may reasonably consider necessary for determining the matter before him which they will disclose promptly and in any event within […***…] Business Days of a written request from the relevant expert to do so.

   (c) Advisors. Each Party may appoint any counsel, consultants and advisors as it feels appropriate to assist the expert in his determination and so as to present their respective cases so that at all times the Parties will co-operate and seek to narrow and limit the issues to be determined.

   (d) Appointment of New Expert. If within the time specified in Paragraph 4(a) above the expert will not have rendered a decision in accordance with his appointment, a new expert may (at the request of either Party) be appointed and the appointment of the existing expert will thereupon cease for the purposes of determining the matter at issue between the Parties save this if the existing expert renders his decision with full reasons
   prior to the appointment of the new expert, then this decision will have effect and the proposed appointment of the new expert will be withdrawn.

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(e) Final and Binding. The determination of the expert will, except for fraud or manifest error, be final and binding upon the Parties.

(f) Costs. Each Party will bear its own costs for any matter referred to an expert hereunder and, in the absence of express provision in the Agreement to the contrary, the costs and expenses of the expert will be shared equally by the Parties.

For greater certainty, the release of the Products for sale or distribution under the applicable marketing approval for the Products will not by itself indicate compliance by Patheon with its obligations for the Manufacturing Services and further that nothing in this Agreement (including this Exhibit A) will remove or limit the authority of the relevant qualified person (as specified by the Quality Agreement) to determine whether the Products are to be released for sale or distribution.

EXHIBIT B

MONTHLY ACTIVE MATERIALS INVENTORY REPORT

TO: ACADIA PHARMACEUTICALS INC.

FROM: PATHEON PHARMACEUTICALS INC. [or applicable Patheon Affiliate]

RE: Active Materials monthly inventory report under Section 2.2(a) of the Master Manufacturing Services Agreement dated August 3, 2015 (the "**Agreement**")

Reporting month:

Active Materials on hand
at beginning of month: kg (A)

Active Materials on hand
at end of month: kg (B)

Quantity Received during month: kg (C)

Quantity Dispensed during month: 26 kg
(A + C – B)

Quantity Converted during month: kg
(total Active Materials in Products produced
and not rejected, recalled or returned)

Capitalized terms used in this report have the meanings given to the terms in the Agreement.

PATHEON PHARMACEUTICALS INC. DATE:
[or applicable Patheon Affiliate]

Per:
Name:
Title:

1 Excludes any (i) Active Materials that must be retained by Patheon as samples, (ii) Active Materials contained in Product that must be retained as samples, (iii) Active Materials used in testing (if applicable), and (iv) Active Materials received or consumed in technical transfer activities or development activities, including, without limitation, any regulatory, stability, validation, or test Batches manufactured during the month.

EXHIBIT C

REPORT OF ANNUAL ACTIVE MATERIALS INVENTORY RECONCILIATION

AND CALCULATION OF ACTUAL ANNUAL YIELD

TO: ACADIA PHARMACEUTICALS INC.

FROM: PATHEON PHARMACEUTICALS INC. [or applicable Patheon Affiliate]

RE: Active Materials annual inventory reconciliation report and calculation of Actual Annual Yield under Section 2.2(a) of the Master Manufacturing Services Agreement dated August 3, 2015 (the "**Agreement**")

Reporting Year ending:

Active Materials on hand
at beginning of Year:kg (A)

Active Materials on hand
at end of Year:kg (B)

Quantity Received during Year:kg (C)

Quantity Dispensed during Year:[2] kg (D)
(A + C - B)

Quantity Converted during Year:kg (E)
(total Active Materials in Products produced
and not rejected, recalled or returned)

Active Materials Credit Value:$ / kg(F)

Target Yield:%(G)

Actual Annual Yield:%(H)

2 Excludes any (i) Active Materials that must be retained by Patheon as samples, (ii) Active Materials contained in Product that must be retained as samples, (iii) Active Materials used in testing (if applicable), and (iv) Active Materials received or consumed in technical transfer activities or development activities, including, without limitation, any regulatory, stability, validation, or test Batches manufactured during the Year.

((E / D) * 100)

Shortfall: $(I)
(((G – […***…]) - H) / 100) * F * D(if a negative number, insert zero)

Based on the foregoing reimbursement calculation Patheon will reimburse Client the amount of $.

Capitalized terms used in this report have the meanings given to the terms in the Agreement.

DATE:

PATHEON PHARMACEUTICALS INC.
[or applicable Patheon Affiliate]

Per:
Name:
Title:

EXHIBIT D

*****Confidential Treatment Requested**

EXAMPLE OF PRICE ADJUSTMENT DUE TO CURRENCY FLUCTUATION

Section 4.2(d)

Time period: 10/01/11 to 09/30/12.

Average (365 days):

0.998

-- "Set Exchange Rate"

SAMPLE EXCHANGE CALCULATION

Initial Exchange Rate:

1.000

CAD/USD

Set Exchange Rate:

0.998

CAD/USD

Initial Price:

3.59

Revised Price (FX):

3.70

(Material price and PPI adjustments)

Calculation:

[Revised Price (After FX)] = [Revised Price (Before FX)] X [Initial Exchange Rate] / [Set Exchange Rate]

= 3.70 X [1.000 / 0.998]

= 3.71

PRODUCT AGREEMENT

This Product Agreement (this "**Product Agreement**") is issued under the Master Manufacturing Services Agreement dated August 3, 2015 between **Patheon Pharmaceuticals Inc.**, and **ACADIA Pharmaceuticals Inc.** (the "**Master Agreement**"), and is entered into as of August 3, 2015 (the "**Effective Date**"), between Patheon Pharmaceuticals Inc., a corporation existing under the laws of the State of Delaware, having a principal place of business at 2110 East Galbraith Road, Cincinnati, OH 45237-1625 ("**Patheon**") and ACADIA Pharmaceuticals Inc., a corporation existing under the laws of the State of Delaware, having a principal place of business at 3611 Valley Centre Drive, Ste. 300, San Diego, CA 92130 ("**Client**").

The terms and conditions of the Master Agreement are incorporated herein except to the extent this Product Agreement expressly references the specific provision in the Master Agreement to be modified by this Product Agreement. All capitalized terms that are used but not defined in this Product Agreement will have the respective meanings given to them in the Master Agreement.

The Schedules to this Product Agreement are incorporated into and will be construed in accordance with the terms of this Product Agreement.

3. **Product List and Specifications** (See Schedule A attached hereto)

4. **Minimum Order Quantity, Annual Volume, and Price** (See Schedule B attached hereto)

3. **Annual Stability Testing and Validation Activities (if applicable)** (See Schedule C attached hereto)

4. **Active Materials, Active Materials Credit Value, and Maximum Credit Value** (See Schedule D attached hereto)

5. **Yearly Forecasted Volume:** (insert for sterile products if applicable under Section 4.2.1 of the Master Agreement)

6. **Territory**: (insert the description of the Territory here)

7. **Manufacturing Site**: (insert address of Patheon Manufacturing Site where the Manufacturing Services will be performed)

8. **Governing Law**: (if applicable under Section 13.16 of the Master Agreement)

9. **Inflation Index:** (if applicable under Section 4.2(a) of the Master Agreement for Products manufactured outside of the Unites States or Puerto Rico)

10. **Currency**: (if applicable under Section 1.4 of the Master Agreement)

11. **Initial Set Exchange Rate**: (if applicable under Section 4.2(d) of the Master Agreement)

12. **Initial Product Term:** (if applicable under Section 8.1 of the Master Agreement)

13. **Notices**: (if applicable under Section 13.9 of the Master Agreement)

14. **Other Modifications to the Master Agreement**: (if applicable under Section 1.2 of the Master Agreement)

_____

IN WITNESS WHEREOF, the duly authorized representatives of the Parties have executed this Product Agreement as of the Effective Date set forth above.

PATHEON PHARMACEUTICALS INC.

By: /s/ Francis P. McCune

Name: Francis P. McCune

Title: Secretary

ACADIA PHARMACEUTICALS INC.

By: /s/ Steve Davis

Name: Steve Davis

Title: Interim CEO

SCHEDULE A

PRODUCT LIST AND SPECIFICATIONS

Product List

Pimavanserin Tablets 17 mg strength (the "**Product**")

Specifications

Prior to the start of commercial manufacturing of Product under this Agreement Client will give Patheon the originally executed copies of the Specifications as approved by the applicable Regulatory Authority or as most recently filed with such Regulatory Authority. If the Specifications received are subsequently amended, then Client will give Patheon the revised and originally executed copies of the revised Specifications. Upon acceptance of the revised Specifications, Patheon will give Client a signed and dated receipt indicating Patheon's receipt of the revised Specifications.

SCHEDULE B

MINIMUM ORDER QUANTITY, ANNUAL VOLUME, AND PRICE

Annual Volume Forecasts

Patheon is presenting pricing based on the following volume.

Product	# of Batches [...***...]
Pimavanserin Tablets	[...***...]

Pricing Table

Pricing includes the cost of labor, overhead, raw materials, packaging components and QC testing and such additional items noted as being included in the price as described below.

[…***…**]**

Costs Included in Unit Pricing

[…***…]

Costs Not Included in Unit Pricing

[…***…]

*****Confidential Treatment Requested**

Key Technical Assumptions

Below are listed the main assumptions that were utilized by Patheon for quoting this Product. Should any of the assumptions change, then the prices will be revised accordingly as agreed by the Parties.

Manufacturing Assumptions

- The manufacturing process at Patheon will follow the master Batch Product record approved by the Parties.

- The core tablet weights and manufacturing batch sizes for each strength are summarized in the following table.

[…***…]

- The following manufacturing equipment train is used for the Product.

[…***…**]**

*****Confidential Treatment Requested**

***Confidential Treatment Requested

Packaging Assumptions

The Product will be packaged into the configurations listed in the tables below.

[…***…]

Testing Assumptions

- Testing for raw materials, excipients, packaging components and finished Product are based on information provided by Client.
- Full release testing of API is included.
- It is assumed that QC test methods are fully validated and robust.
- Micro testing has been included on the finished Product.
- Testing labor may be subject to change after the final agreement on testing specifications and requirements.

Supply Chain Assumptions

- The quoted raw materials and packaging components (other than Client-Supplied Components) are assumed to be supplied from standard Patheon suppliers. This will need to be reviewed upon the detailed specifications of these materials. Patheon will procure components (raw materials and primary packaging materials) for the manufacture of the Product from Patheon qualified suppliers. Should Client require Patheon to source any materials from specified suppliers other than Patheon qualified suppliers or those otherwise agreed upon in the Master Agreement, as applicable, then these suppliers will remain under the quality audit control of Client unless it is agreed that Patheon will take on this responsibility. Components and excipients to be supplied by Patheon in accordance with Client's specifications. Patheon will issue formal Patheon specifications for each component following Client component requirements. Each lot of incoming components will be sampled and tested according to the agreed specifications. If different component specifications for primary packaging are required, these will be subject to a further evaluation and assessment by Patheon.

*****Confidential Treatment Requested**

***Confidential Treatment Requested

SCHEDULE C

ANNUAL STABILITY TESTING

Patheon and Client will agree in writing on any stability testing to be performed by Patheon on the Products. This agreement will specify the commercial and Product stability protocols applicable to the stability testing and the fees payable by Client for this testing. Release testing will be used for time zero testing as long as batches are placed on stability within […***…] days of completion of release testing. Patheon will be responsible for retest of time zero if delay of placing batches are due to Patheon. Client will be responsible for $[…***…] per sample for any batch delayed more than […***…] days from release testing due to Client.

[…***…]

SCHEDULE D

ACTIVE MATERIALS

Active Materials	Supplier
Pimavanserin tartrate	BASF Pharma (Evionnaz) SA and/or its affiliates

ACTIVE MATERIALS CREDIT VALUE

The Active Materials Credit Value will be as follows:

PRODUCT	ACTIVE MATERIALS	ACTIVE MATERIALS CREDIT VALUE
Pimavanserin tablets 17 mg strength	Pimavanserin tartrate	Client's actual cost for Active Materials not to exceed $[…***…] per kilogram

MAXIMUM CREDIT VALUE

Patheon's liability for Active Materials calculated in accordance with Section 2.2 of the Master Agreement for Product in a Year will not exceed, in the aggregate, the maximum credit value set forth below:

PRODUCT	MAXIMUM CREDIT VALUE
Pimavanserin tablets 17 mg strength	[…***…]

Exhibit 10.2

First Amendment to Product Agreement
between Patheon Pharmaceuticals Inc. and ACADIA Pharmaceuticals Inc.

This First Amendment to Product Agreement (the "**Amendment**"), dated April 25, 2016 (the "**Amendment Date**"), is made by and between Patheon Pharmaceuticals Inc. ("**Patheon**") and ACADIA Pharmaceuticals Inc. ("**ACADIA**").

WHEREAS, Patheon and ACADIA have entered into that certain Master Manufacturing Services Agreement, dated August 3, 2015 (the "**MSA**") and that certain Product Agreement under the MSA, dated August 3, 2015 (the "**Product Agreement**"); and

WHEREAS, Patheon and ACADIA now wish to amend the Product Agreement as set forth in this Amendment. All capitalized terms used but not defined in this Amendment shall have the respective meanings set forth in the MSA or Product Agreement, as applicable.

NOW THEREFORE in consideration of the premises hereof and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by the parties, the parties agree as follows:

1. **Amendment to Schedule B.** The Product pricing tables on Schedule B of the Product Agreement are hereby amended and replaced with the pricing tables set forth on Exhibit 1 of this Amendment. For clarity, the pricing set forth in the updated pricing tables applies with respect to Product purchases beginning retroactively as of January 1, 2016.

2. **Amendment to Schedule C.** The stability pricing table on Schedule C of the Product Agreement is hereby amended and replaced with the stability pricing tables set forth on Exhibit 2 of this Amendment.

3. **No Other Modifications**. Except as specifically modified by this Amendment, the terms and conditions of the Product Agreement including, without limitation, all other terms and conditions included in each of the amended Schedules, and the MSA, shall remain unchanged.

IN WITNESS WHEREOF, the parties have caused this Amendment to be duly executed by their authorized representatives, effective as of the Amendment Date.

Patheon Pharmaceuticals Inc.	**ACADIA Pharmaceuticals Inc.**
By: /s/ Francis P. McCune	By: /s/ James Nash
Name: Francis P. McCune	Name: James Nash
Title: Secretary	Title: SVP, Technology Development & Operations

Exhibit 1

Updated Pricing Tables

[…*…]**

Exhibit 2

Updated Stability Pricing

[…***…]

[…***…]

Exhibit 10.3

Second Amendment to Product Agreement
between Patheon Pharmaceuticals Inc. and ACADIA Pharmaceuticals Inc.

This Second Amendment to Product Agreement (the "**Amendment**"), dated October 6, 2016 (the "**Amendment Date**"), is made by and between Patheon Pharmaceuticals Inc. ("**Patheon**") and ACADIA Pharmaceuticals Inc. ("**ACADIA**").

WHEREAS, Patheon and ACADIA have entered into that certain Master Manufacturing Services Agreement, dated August 3, 2015 (the "**MSA**") and that certain Product Agreement under the MSA, dated August 3, 2015, as amended on April 25, 2016 (the "**Product Agreement**"); and

WHEREAS, Patheon and ACADIA now wish to amend the Product Agreement as set forth in this Amendment. All capitalized terms used but not defined in this Amendment shall have the respective meanings set forth in the MSA or Product Agreement, as applicable.

NOW THEREFORE in consideration of the premises hereof and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by the parties, the parties agree as follows:

1. **Amendment to Schedule C.** The stability pricing table on Schedule C of the Product Agreement is hereby amended and replaced with the stability pricing tables set forth on Exhibit 1 of this Amendment.

2. Side Letter Agreements. The parties hereby agree that any future changes to stability testing set forth in Schedule C of the Product Agreement, and any annual adjustments to Product pricing set forth in Schedule B of the Product Agreement pursuant to Section 4.2 of the MSA, may be documented via separate side letter agreement between Patheon and ACADIA.

3. No Other Modifications. Except as specifically modified by this Amendment, the terms and conditions of the Product Agreement including, without limitation, all other terms and conditions included in each of the amended Schedules, and the MSA, shall remain unchanged.

IN WITNESS WHEREOF, the parties have caused this Amendment to be duly executed by their authorized representatives, effective as of the Amendment Date.

Patheon Pharmaceuticals Inc.	**ACADIA Pharmaceuticals Inc.**
By: /s/ Nicholas M. Buschur	By: /s/ James Nash
Name: Nicholas M. Buschur	Name: James Nash
Title: Executive Director & GM	Title: SVP, Technology Development &

Exhibit 1

Updated Stability Pricing

[…*…]**

[…*…]**

[…*…]**

[…*…]**

[…*…]**

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) IS THE TYPE THAT ACADIA PHARMACEUTICALS, INC. TREATS AS PRIVATE OR CONFIDENTIAL

Exhibit 10.4

Third Amendment to Product Agreement
between Patheon Pharmaceuticals Inc. and ACADIA Pharmaceuticals Inc.

This Third Amendment to Product Agreement (this "**Amendment**"), dated December 11, 2017 (the "**Amendment Date**"), is made by and between Patheon Pharmaceuticals Inc. ("**Patheon**") and ACADIA Pharmaceuticals Inc. ("**ACADIA**").

WHEREAS, Patheon and ACADIA have entered into that certain Master Manufacturing Services Agreement, dated August 3, 2015 (the "**MSA**") and that certain Product Agreement under the MSA, dated August 3, 2015, as amended on April 25, 2016 and October 6, 2016 (the "**Product Agreement**"); and

WHEREAS, Patheon and ACADIA now wish to amend Schedules A, B, C, and D to the Product Agreement to add Nuplazid 10 mg tablets as a Product as set forth in this Amendment. All capitalized terms used but not defined in this Amendment will have the respective meanings set forth in the MSA or Product Agreement, as applicable.

NOW THEREFORE in consideration of the premises hereof and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by the parties, the parties agree as follows:

1. **Amendment to Schedules A, B, C, and D.**

(a) **Schedule A** is revised to add to the Product List an additional and separate Product as follows: "**Pimavanserin Tablets 10mg Strength**." The language regarding Specifications shall remain as currently drafted, and is applicable to both Products.

(b) **Schedule B** is revised to add information for Pimavanserin Tablets 10mg Strength as set forth in **Exhibit 1**.

(c) **Schedule C** is revised to add information for Pimavanserin Tablets 10mg Strength as set forth in **Exhibit 2**.

(d) **Schedule D, Active Materials Credit Value, and Maximum Credit Value, Product,** are revised to add "**Pimavanserin Tablets 10mg Strength**" in the Product column of each table.

(e) For clarity, the term of the Product Agreement as set forth on the cover page of the Product Agreement shall remain unchanged.

2. **Side Letter Agreements**. For clarity, the language in Section 2 of the Second Amendment to the Product Agreement, dated April 25, 2016, regarding side letter agreements to document

future changes to stability testing and annual adjustments to pricing pursuant to Section 4.2 of the MSA, shall continue to apply to both Products covered by the Product Agreement.

3. No Other Modifications. Except as specifically modified by this Amendment, the terms and conditions of the Product Agreement including, without limitation, all other terms and conditions included in each of the amended Schedules, and the MSA, remain unchanged.

[signature page to follow]

IN WITNESS WHEREOF, the parties have caused this Amendment to be duly executed by their authorized representatives, effective as of the Amendment Date.

Patheon Pharmaceuticals Inc.	**ACADIA Pharmaceuticals Inc.**
By: /s/ Amanda Bosse	By: /s/ James Nash
Name: Amanda Bosse	Name: James Nash
Title: VP and GM Cincinnati Regional Ops	Title: SVP, Technology Development & Operations

Exhibit 1

SCHEDULE B

MINIMUM ORDER QUANTITY, ANNUAL VOLUME AND PRICE
(Pimavanserin Tablets 10mg Strength)

Annual Volume Forecast

[…***…]

Pricing Tables

Pricing includes the cost of labor, overhead, raw materials, packaging components and QC testing and such additional items noted as being included in the price as described below. For clarity, both commercial and validation batches of Pimavanserin Tablets 10mg Strength are subject to this Product Agreement as described below.

[…***…]

Costs Included in Unit Price

[…***…]

Costs Not Included in Unit Price

[…***…]

Key Technical Assumptions

The following technical parameters apply to the production of Pimavanserin Tablets 10mg Strength and the materials used therein. […***…]

Manufacturing Assumptions

[…***…]

Packaging Assumptions

- **Packaging Components:**

[…***…]

Testing Assumptions

[…***…]

Supply Chain Assumptions

[…***…]

For clarity, the foregoing shall not amend the Pricing provisions of the MSA that are applicable to all Products and Product Agreements as set forth in the MSA.

Exhibit 2

SCHEDULE C

ANNUAL STABLITY TESTING
(Pimavanserin Tablets 10mg Strength)

ACTIVITY	*PRICE*
[…***…]	

Exhibit 31.1

CERTIFICATION
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Stephen Davis, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Acadia Pharmaceuticals Inc.

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

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

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

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

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

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

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

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

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

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

Date: May 5, 2021

/S/ STEPHEN DAVIS

Stephen Davis
Chief Executive Officer
(Registrant's Principal Executive Officer)

Exhibit 31.2

CERTIFICATION
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Elena Ridloff, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Acadia Pharmaceuticals Inc.

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

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

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

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

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

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

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

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

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

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

Date: May 5, 2021

/s/ ElenA Ridloff

Elena Ridloff
Executive Vice President and Chief Financial Officer
(Registrant's Principal Financial Officer)

Exhibit 32.1

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

In connection with the quarterly report of Acadia Pharmaceuticals Inc. (the "Company") on Form 10-Q for the quarterly period ended March 31, 2021, as filed with the Securities and Exchange Commission on or about the date hereof (the "Report"), I, Stephen Davis, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

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

(2) the information contained in the Report fairly presents, in all material respects, the financial condition of the Company at the end of the period covered by the Report and results of operations of the Company for the period covered by the Report.

Date: May 5, 2021

/S/ STEPHEN DAVIS

Stephen Davis
Chief Executive Officer
(Registrant's Principal Executive Officer)

This certification shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of Section 18 of the Exchange Act. Such certification shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent that the Company specifically incorporates it by reference.

Exhibit 32.2

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

In connection with the quarterly report of Acadia Pharmaceuticals Inc. (the "Company") on Form 10-Q for the quarterly period ended March 31, 2021, as filed with the Securities and Exchange Commission on or about the date hereof (the "Report"), I, Elena Ridloff, Executive Vice President and Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

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

(2) the information contained in the Report fairly presents, in all material respects, the financial condition of the Company at the end of the period covered by the Report and results of operations of the Company for the period covered by the Report.

Date: May 5, 2021

/S/ ELENA RIDLOFF

Elena Ridloff
Executive Vice President and Chief Financial Officer
(Registrant's Principal Financial Officer)

This certification shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of Section 18 of the Exchange Act. Such certification shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent that the Company specifically incorporates it by reference.