

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

FORM 10-Q

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

For the quarterly period ended September 30, 2021

or

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

Commission File Number: 000-50768

ACADIA PHARMACEUTICALS INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware
(State of Incorporation)
12830 El Camino Real, Suite 400
San Diego, California
(Address of Principal Executive Offices)

06-1376651
(I.R.S. Employer Identification No.)

92130
(Zip Code)

(858) 558-2871

(Registrant's Telephone Number, Including Area Code)

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

<u>Title of Each Class</u>	<u>Trading Symbol</u>	<u>Name of Each Exchange on Which Registered</u>
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	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
Emerging growth company	<input type="checkbox"/>		

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 October 25, 2021:

<u>Class</u>	<u>Number of Shares Outstanding</u>
Common Stock, \$0.0001 par value	160,755,971

ACADIA PHARMACEUTICALS INC.

FORM 10-Q

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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)**

	September 30, 2021 (unaudited)	December 31, 2020
Assets		
Cash and cash equivalents	\$ 94,640	\$ 326,028
Investment securities, available-for-sale	445,651	305,930
Accounts receivable, net	60,696	48,247
Interest and other receivables	972	2,035
Inventory	14,336	9,682
Prepaid expenses	24,622	25,694
Total current assets	640,917	717,616
Property and equipment, net	8,581	9,161
Operating lease right-of-use assets	60,032	47,283
Restricted cash	5,770	5,770
Other assets	2,373	2,786
Total assets	<u>\$ 717,673</u>	<u>\$ 782,616</u>
Liabilities and stockholders' equity		
Accounts payable	\$ 7,722	\$ 8,493
Accrued liabilities	80,496	97,474
Total current liabilities	88,218	105,967
Operating lease liabilities	57,677	44,460
Other long-term liabilities	4,823	5,180
Total liabilities	150,718	155,607
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 5,000,000 shares authorized at September 30, 2021 and December 31, 2020; no shares issued and outstanding at September 30, 2021 and December 31, 2020	—	—
Common stock, \$0.0001 par value; 225,000,000 shares authorized at September 30, 2021 and December 31, 2020; 160,690,916 shares and 159,637,771 shares issued and outstanding at September 30, 2021 and December 31, 2020, respectively	16	16
Additional paid-in capital	2,677,422	2,612,663
Accumulated deficit	(2,110,482)	(1,985,706)
Accumulated other comprehensive (loss) income	(1)	36
Total stockholders' equity	566,955	627,009
Total liabilities and stockholders' equity	<u>\$ 717,673</u>	<u>\$ 782,616</u>

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)

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2021</u>	<u>2020</u>	<u>2021</u>	<u>2020</u>
Revenues				
Product sales, net	\$ 131,612	\$ 120,577	\$ 353,387	\$ 320,748
Total revenues	131,612	120,577	353,387	320,748
Operating expenses				
Cost of product sales	3,688	2,005	8,399	7,703
License fees and royalties	2,994	2,796	8,181	7,546
Research and development	58,565	120,083	172,473	257,014
Selling, general and administrative	81,666	81,592	290,116	267,909
Total operating expenses	146,913	206,476	479,169	540,172
Loss from operations	(15,301)	(85,899)	(125,782)	(219,424)
Interest income, net	129	1,242	462	6,056
Other income (expense)	383	(202)	706	(1,262)
Loss before income taxes	(14,789)	(84,859)	(124,614)	(214,630)
Income tax expense	(332)	(199)	162	194
Net loss	\$ (14,457)	\$ (84,660)	\$ (124,776)	\$ (214,824)
Net loss per common share, basic and diluted	\$ (0.09)	\$ (0.54)	\$ (0.78)	\$ (1.37)
Weighted average common shares outstanding, basic and diluted	160,663	158,129	159,651	156,683

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)

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	2021	2020	2021	2020
Net loss	\$ (14,457)	\$ (84,660)	\$ (124,776)	\$ (214,824)
Other comprehensive income:				
Unrealized (loss) gain on investment securities	(41)	(967)	(43)	216
Foreign currency translation adjustments	3	(4)	6	(4)
Comprehensive loss	<u>\$ (14,495)</u>	<u>\$ (85,631)</u>	<u>\$ (124,813)</u>	<u>\$ (214,612)</u>

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)

	Nine Months Ended September 30,	
	2021	2020
Cash flows from operating activities		
Net loss	\$ (124,776)	\$ (214,824)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	50,735	63,227
Amortization of premiums and accretion of discounts on investment securities	1,766	821
Amortization of intangible assets	1,108	1,108
(Gain) loss on strategic investment	(706)	1,262
Loss on disposal of assets	—	281
Depreciation	1,701	986
Non-cash in-process research and development	—	44,280
Changes in operating assets and liabilities:		
Accounts receivable, net	(12,449)	(10,563)
Interest and other receivables	1,063	653
Inventory	(4,427)	(1,671)
Prepaid expenses	1,072	(11,403)
Operating lease right-of-use assets	4,794	2,863
Other assets	11	50
Accounts payable	(771)	(3,751)
Accrued liabilities	(17,260)	17,853
Operating lease liabilities	(4,044)	(587)
Long-term liabilities	(357)	737
Net cash used in operating activities	<u>(102,540)</u>	<u>(108,678)</u>
Cash flows from investing activities		
Purchases of investment securities	(453,847)	(100,808)
Maturities of investment securities	312,317	415,863
Purchases of property and equipment	(1,121)	(5,588)
Net cash (used in) provided by investing activities	<u>(142,651)</u>	<u>309,467</u>
Cash flows from financing activities		
Proceeds from issuance of common stock, net of issuance costs	13,797	62,870
Net cash provided by financing activities	<u>13,797</u>	<u>62,870</u>
Effect of exchange rate changes on cash	6	(4)
Net (decrease) increase in cash, cash equivalents and restricted cash	<u>(231,388)</u>	<u>263,655</u>
Cash, cash equivalents and restricted cash		
Beginning of period	331,798	194,467
End of period	<u>\$ 100,410</u>	<u>\$ 458,122</u>
Supplemental disclosure of noncash information:		
Common stock issues in connection with merger agreement	\$ —	\$ 44,280
Property and equipment purchases in accounts payable and accrued liabilities	—	926

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)

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2021</u>	<u>2020</u>	<u>2021</u>	<u>2020</u>
Total stockholders' equity, beginning balances	<u>\$ 564,838</u>	<u>\$ 663,013</u>	<u>\$ 627,009</u>	<u>\$ 699,135</u>
Common stock:				
Beginning balance	16	15	16	15
Issuance of common stock from exercise of stock options and units	—	1	—	1
Ending balance	<u>16</u>	<u>16</u>	<u>16</u>	<u>16</u>
Additional paid-in capital:				
Beginning balance	2,660,809	2,495,804	2,612,663	2,402,945
Issuance of common stock in connection with merger agreement	—	44,280	—	44,280
Issuance of common stock from exercise of stock options and units	1,066	11,714	10,060	58,899
Issuance of common stock pursuant to employee stock purchase plan	—	—	3,737	3,970
Stock-based compensation	15,547	21,490	50,962	63,194
Ending balance	<u>2,677,422</u>	<u>2,573,288</u>	<u>2,677,422</u>	<u>2,573,288</u>
Accumulated deficit:				
Beginning balance	(2,096,025)	(1,834,286)	(1,985,706)	(1,704,122)
Net loss	(14,457)	(84,660)	(124,776)	(214,824)
Ending balance	<u>(2,110,482)</u>	<u>(1,918,946)</u>	<u>(2,110,482)</u>	<u>(1,918,946)</u>
Other comprehensive income (loss):				
Beginning balance	38	1,480	36	297
Other comprehensive (loss) income	(39)	(971)	(37)	212
Ending balance	<u>(1)</u>	<u>509</u>	<u>(1)</u>	<u>509</u>
Total stockholders' equity, ending balances	<u>\$ 566,955</u>	<u>\$ 654,867</u>	<u>\$ 566,955</u>	<u>\$ 654,867</u>

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

ACADIA PHARMACEUTICALS INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
(Unaudited)

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 the Company's business. Sales of NUPLAZID in 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):

	<u>Nine Months Ended September 30, 2021</u>		<u>Nine Months Ended September 30, 2020</u>	
	<u>Beginning of period</u>	<u>End of period</u>	<u>Beginning of period</u>	<u>End of period</u>
Cash and cash equivalents	\$ 326,028	\$ 94,640	\$ 189,680	\$ 452,352
Restricted cash	5,770	5,770	4,787	5,770
Total cash, cash equivalents and restricted cash shown in the statement of cash flows	<u>\$ 331,798</u>	<u>\$ 100,410</u>	<u>\$ 194,467</u>	<u>\$ 458,122</u>

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. The Company has not historically experienced significant credit losses. Based on its assessment, as of September 30, 2021 the Company determined that an allowance for credit loss was not required.

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 and \$1.1 million for each of the three and nine months ended September 30, 2021 and 2020, respectively. As of September 30, 2021, the intangible asset was fully amortized.

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.

Acquisitions

The Company accounts for acquisitions of an asset or group of similar identifiable assets that do not meet the definition of a business as asset acquisition using the cost accumulation method, whereby the cost of the acquisition, including certain transaction costs, is allocated to the assets acquired on the basis of their relative fair values. No goodwill is recognized in an asset acquisition. Intangible assets acquired in an asset acquisition for use in research and development activities which have no alternative future use are expensed as in-process research and development on the acquisition date. Intangible assets acquired for use in research and development activities which have an alternative future use are capitalized as in-process research and development. Future costs to develop these assets are recorded to research and development expense as they are incurred. Contingent milestone payments associated with asset acquisitions are recognized when probable and estimable. These amounts are expensed to research and development if there is no alternative future use associated with the asset, or capitalized as an intangible asset if alternative future use of the asset exists. The Company includes the costs of asset acquisitions as component of cash flows from operations on the consolidated statements of cash flows.

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 September 30, 2021 and 2020, stock options, employee stock purchase plan rights, restricted stock units, and warrants totaling approximately 18,569,000 shares and 19,704,000 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 September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Cost of product sales	\$ 439	\$ 495	\$ 1,025	\$ 2,087
Research and development	5,176	7,953	17,325	23,645
Selling, general and administrative	9,931	12,924	32,385	37,495
	<u>\$ 15,546</u>	<u>\$ 21,372</u>	<u>\$ 50,735</u>	<u>\$ 63,227</u>

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 the Company's 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 nine months ended September 30, 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 \$6.8 million.

5. Balance Sheet Details

Inventory consisted of the following (in thousands):

	September 30, 2021	December 31, 2020
Finished goods	\$ 1,449	\$ 1,453
Work in process	6,670	6,367
Raw material	6,217	1,862
	<u>\$ 14,336</u>	<u>\$ 9,682</u>

Accrued liabilities consisted of the following (in thousands):

	September 30, 2021	December 31, 2020
Accrued compensation and benefits	\$ 21,783	\$ 25,811
Accrued research and development services	20,930	28,380
Accrued consulting and professional fees	16,866	18,969
Current portion of lease liabilities	8,150	5,087
Accrued sales allowances	8,050	14,115
Current portion of accrued branded prescription drug fees	1,959	1,845
Other	2,758	3,267
	<u>\$ 80,496</u>	<u>\$ 97,474</u>

6. Investments

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

	September 30, 2021			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
U.S. Treasury notes	\$ 179,885	\$ 4	\$ (11)	\$ 179,878
Government sponsored enterprise securities	56,018	—	(6)	56,012
Municipal bonds	19,129	—	(7)	19,122
Commercial paper	190,631	24	(16)	190,639
	<u>\$ 445,663</u>	<u>\$ 28</u>	<u>\$ (40)</u>	<u>\$ 445,651</u>

	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
	<u>\$ 305,899</u>	<u>\$ 74</u>	<u>\$ (43)</u>	<u>\$ 305,930</u>

* 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 September 30, 2021 and December 31, 2020, the Company had 32 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 September 30, 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
September 30, 2021						
U.S. Treasury notes	\$ 105,515	\$ (11)	\$ —	\$ —	\$ 105,515	\$ (11)
Government sponsored enterprise securities	56,012	(6)	—	—	56,012	(6)
Municipal bonds	19,122	(7)	—	—	19,122	(7)
Commercial paper	76,688	(16)	—	—	76,688	(16)
Total	<u>\$ 257,337</u>	<u>\$ (40)</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 257,337</u>	<u>\$ (40)</u>
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	<u>\$ 169,353</u>	<u>\$ (43)</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 169,353</u>	<u>\$ (43)</u>

* 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. The Company has not historically experienced significant losses on its investments. Based on its evaluation, the Company determined its year-to-date credit losses related to its available-for-sale securities were immaterial at September 30, 2021.

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 September 30, 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 September 30, 2021 and December 31, 2020 consisted of the following (in thousands):

	September 30, 2021	Fair Value Measurements at Reporting Date Using		
		Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market fund	\$ 76,248	\$ 76,248	\$ —	\$ —
U.S. Treasury notes	179,878	179,878	—	—
Equity securities	2,015	2,015	—	—
Government sponsored enterprise securities	56,012	—	56,012	—
Municipal bonds	19,122	—	19,122	—
Commercial paper	200,638	—	200,638	—
	<u>\$ 533,913</u>	<u>\$ 258,141</u>	<u>\$ 275,772</u>	<u>\$ —</u>

	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	—
	<u>\$ 632,576</u>	<u>\$ 531,736</u>	<u>\$ 100,840</u>	<u>\$ —</u>

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 terminated in October 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 incurred \$5.0 million in milestone payments for the nine months ended September 30, 2021. As of September 30, 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 development and commercial 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. Defendants' filed a motion to dismiss the third amended complaint on May 31, 2021. The lead plaintiff opposed the motion on July 12, 2021. Defendants' reply in support of its motion is due on August 11, 2021. The motion is set to be heard on November 18, 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 MSN, 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.

On April 22, 2021, Aurobindo filed its answer, affirmative defenses, and counterclaims to the Company's first amended complaint, seeking declaratory judgments of noninfringement and invalidity. On May 11, 2021, the Company filed its answer to MSN's counterclaims. On May 12, the Company filed its answer to Teva's counterclaims. On May 13, the Company filed its answer to Zydus's counterclaims and its answer to Aurobindo's counterclaims. 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 supplemental New Drug Application (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 was unlikely to approve the sNDA in its current form. The complaint seeks unspecified monetary damages and other relief. On June 21, 2021, five motions for lead plaintiff and lead counsel were filed. Thereafter, four of the five movants either withdrew their motions or filed statements of non-opposition. On September 29, 2021, the Court issued an order designating lead plaintiff and lead counsel.

Management currently believes that none of the foregoing claims or actions pending against the Company as of September 30, 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 0.3 years to 9.7 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):

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2021</u>	<u>2020</u>	<u>2021</u>	<u>2020</u>
Operating lease cost	\$ 2,014	\$ 1,835	\$ 7,016	\$ 4,750

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

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2021</u>	<u>2020</u>	<u>2021</u>	<u>2020</u>
Cash paid for amounts included in the measurement of lease liabilities:				
Operating cash flows from operating leases	\$ 1,713	\$ 1,128	\$ 3,423	\$ 3,710
Right-of-use assets obtained in exchange for operating lease obligations:	166	41,190	17,543	41,571

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

	<u>September 30,</u>	<u>December 31,</u>
	<u>2021</u>	<u>2020</u>
Operating lease liabilities		
Current portion included in accrued liabilities	\$ 8,150	\$ 5,087
Operating lease liabilities	57,677	44,460
Total operating lease liabilities	<u>\$ 65,827</u>	<u>\$ 49,547</u>

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

	<u>Operating Leases</u>
Remainder of 2021	\$ 1,848
Years ending December 31,	
2022	8,701
2023	8,482
2024	8,275
2025	8,355
Thereafter	44,275
Total lease payments	79,936
Less:	
Imputed interest	(14,109)
Total operating lease liabilities	<u>\$ 65,827</u>

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 September 30, 2021, the weighted average remaining lease term was 9.2 years and the weighted average discount rate used to determine the operating lease liability was 4.3%.

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. In the first quarter of 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. We continue to access our customers both in person and virtually. 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 being conducted both in person and 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 reducing 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 2021, sales of NUPLAZID have been negatively impacted by ongoing conditions related to the pandemic, including a reduction in patient office visits, continuing reduced occupancy rates at long-term care facilities, and reduced access to healthcare professionals. While we observed incremental improvements in some of these factors during the later part of the year, the levels are still meaningfully below where they were pre-pandemic. It remains difficult to predict the duration of the pandemic’s impact and the pace of recovery, and no assurances can be given that the pandemic will not continue to have additional negative 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 and in July 2021, the New England Journal of Medicine published the results from the Phase 3 HARMONY study. 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 an sNDA for NUPLAZID for the treatment of hallucinations and delusions associated with DRP. In July 2020 the FDA notified us of its 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 in the HARMONY study, as well as insufficient numbers of patients with certain less common dementia subtypes as lack of substantial evidence of effectiveness to support approval. The FDA also stated in the CRL that it considers Alzheimer's disease psychosis study -019 to not be adequate and well controlled, citing that it was a single center study with no type I error control of secondary endpoints in which certain protocol deviations occurred. We conducted a Type A, end of review, meeting at which the FDA reiterated its stated position in the CRL, that pimavanserin should be studied by individual subgroups of DRP, and advised us that the best path forward is to conduct an additional clinical study in each of the subgroups for which we seek approval. However, the FDA was also open to reviewing additional analyses from the HARMONY and -019 studies in support of a potential resubmission for individual subgroups without additional clinical studies. We have scheduled a follow-up meeting with the FDA to further discuss later this year. 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 pimavanserin 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. We completed enrollment in our LAVENDER study and expect results 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 non-opioid, first in class, Redox Modulator in development for treatment of acute and chronic pain. The mechanism of action is believed to modulate redox pathways involved in pain signaling by removing increased levels of reactive oxygen and nitrogen species caused by tissue injury, inflammation, and disease. 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. We now anticipate results from this study in the first quarter of 2022. This slight delay is due to slower than expected enrollment with the postponement of many elective surgeries during the summer surge of the COVID-19 delta variant. In June 2021, we initiated an additional Phase 2 study evaluating ACP-044 for the treatment of pain associated with osteoarthritis.

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 preclinical 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 September 30, 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. This obligation terminated in October 2021.

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 the potential costs for additional clinical studies that may be required 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 and nine months ended September 30, 2021 and 2020 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Costs of external service providers:				
NUPLAZID (pimavanserin)	\$ 20,542	\$ 23,182	\$ 53,945	\$ 79,685
Trofinetide	6,883	17,179	23,979	38,299
Early stage programs	8,163	5,204	23,577	10,443
Upfront and milestone payments*	5,999	52,749	10,999	62,749
Subtotal	41,587	98,314	112,500	191,176
Internal costs	11,802	13,816	42,648	42,193
Stock-based compensation	5,176	7,953	17,325	23,645
Total research and development	\$ 58,565	\$ 120,083	\$ 172,473	\$ 257,014

* 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 September 30, 2021 and 2020

Product Sales, Net

Net product sales, comprised of NUPLAZID, were \$131.6 million and \$120.6 million for the three months ended September 30, 2021 and 2020, respectively. The increase in net product sales of \$11.0 million was due to growth in NUPLAZID unit sales of approximately 3% in the three months ended September 30, 2021 as compared to the same period in 2020, as well as a higher average gross selling price of NUPLAZID in 2021 compared to 2020.

Cost of Product Sales

Cost of product sales was \$3.7 million and \$2.0 million for the three months ended September 30, 2021 and 2020, respectively, or approximately 3% and 2% of net product sales, respectively. The cost of product sales as a percentage of net sales increased during the three months ended September 30, 2021 as compared to the same period in 2020 due primarily to charges of \$1.0 million in the three months ended September 30, 2021 to reduce certain finished goods inventory to its net realizable value as inventory related to potential DRP launch is no longer usable.

License Fees and Royalties

License fees and royalties were \$3.0 million and \$2.8 million for the three months ended September 30, 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 September 30, 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 \$58.6 million for the three months ended September 30, 2021, including \$5.2 million in stock-based compensation expense, from \$120.1 million for the three months ended September 30, 2020, including \$8.0 million in stock-based compensation expense. The decrease in research and development expenses was mainly due to decreased costs associated with the upfront consideration and transaction costs paid for acquisition compared to the same period in the prior year, as well as reduced development costs for trofinetide and the cessation of development of pimavanserin for major depressive disorder (MDD), partially offset by increased costs of our development activities for ACP-044.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased to \$81.7 million for the three months ended September 30, 2021, including \$9.9 million in stock-based compensation expense, from \$81.6 million for the three months ended September 30, 2020, including \$12.9 million in stock-based compensation expense. The increase in selling, general and administrative expenses was primarily due to increased charitable contributions during the three months ended September 30, 2021 as compared to the same period in 2020, offset by the decreased costs of stock-based compensation resulted from a change in estimate related to the achievement of certain performance-based criteria for performance-based stock awards.

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

Product Sales, Net

Net product sales, comprised of NUPLAZID, were \$353.4 million and \$320.7 million for the nine months ended September 30, 2021 and 2020, respectively. The increase in net product sales of \$32.7 million was due to growth in NUPLAZID unit sales of approximately 4% in the nine months ended September 30, 2021 as compared to the same period in 2020, as well as 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 nine months ended September 30, 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	51,705	1,384	34,056	87,145
Credits/payments for current period sales	(44,857)	(1,073)	(27,778)	(73,708)
Credits/payments for prior period sales	(4,221)	152	(12,344)	(16,413)
Balance as of September 30, 2021	<u>\$ 6,848</u>	<u>\$ 311</u>	<u>\$ 8,050</u>	<u>\$ 15,209</u>

Cost of Product Sales

Cost of product sales was \$8.4 million and \$7.7 million for the nine months ended September 30, 2021 and 2020, respectively, or approximately 2% of net product sales, respectively. The cost of product sales as a percentage of net sales stayed flat during the nine months ended September 30, 2021 as compared to the same period in 2020.

License Fees and Royalties

License fees and royalties were \$8.2 million and \$7.5 million for the nine months ended September 30, 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 nine months ended September 30, 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 \$172.5 million for the nine months ended September 30, 2021, including \$17.3 million in stock-based compensation expense, from \$257.0 million for the nine months ended September 30, 2020, including \$23.6 million in stock-based compensation expense. The decrease in research and development expenses was mainly due to decreased costs associated with the upfront consideration and transaction costs paid for acquisition compared to the same period in the prior year, as well as reduced development costs for trofinetide and the cessation of development of pimavanserin for MDD, partially offset by increased costs of our development activities for ACP-044.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased to \$290.1 million for the nine months ended September 30, 2021, including \$32.4 million in stock-based compensation expense, from \$267.9 million for the nine months ended September 30, 2020, including \$37.5 million in stock-based compensation expense. The increase in selling, general and administrative expenses was primarily due to increased costs associated with advertising, promotion and charitable contributions, as well as increased personnel and related costs, partially offset by decreased 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 September 30, 2021, we had \$540.3 million in cash, cash equivalents, and investment securities, compared to \$632.0 million at December 31, 2020. This \$91.7 million decrease was primarily due to cash used in operating activities. Net cash used in operating activities decreased to \$102.5 million for the nine months ended September 30, 2021 compared to \$108.7 million for the nine months ended September 30, 2020. This decrease in cash used in operations was primarily due to an increase in our net revenues as well as decreased research and development costs.

Net cash used in investing activities totaled \$142.7 million for the nine months ended September 30, 2021 compared to net cash provided by investing activities totaled \$309.5 million for the nine months ended September 30, 2020. The decrease in net cash provided by investing activities for the nine months ended September 30, 2021 compared to the nine months ended September 30, 2020 was primarily due to decreased net maturities of investment securities.

Net cash provided by financing activities decreased to \$13.8 million for the nine months ended September 30, 2021 compared to \$62.9 million for the nine months ended September 30, 2020. This decrease in net cash provided by financing activities for the nine months ended September 30, 2021 was attributable primarily to a decrease 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 year. 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 September 30, 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 (our principal executive and financial officer), 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 September 30, 2021, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive 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 concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of September 30, 2021.

An evaluation was also performed under the supervision and with the participation of our management, including our Chief Executive 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

The information required to be set forth under this Item 1 is incorporated by reference to the section titled “Legal Proceedings” in Note 9 to the condensed consolidated financial statements included in this Quarterly Report.

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 2021, sales of NUPLAZID were negatively impacted by ongoing conditions related to the pandemic, including a reduction in patient office visits and a continuing reduced occupancy rates at long-term care facilities. While we observed incremental improvements in some of these factors during the later part of the year, the levels are still meaningfully below where they were pre-pandemic. It remains difficult to predict the duration of the pandemic's impact and the pace of recovery, and no assurances can be given that the pandemic will not continue to have additional negative 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 in the HARMONY study, as well as insufficient numbers of patients with certain less common dementia subtypes as lack of substantial evidence of effectiveness to support approval. The FDA also stated in the CRL that it considers Alzheimer's disease psychosis study -019 to not be adequate and well controlled, citing that it was a single center study with no type I error control of secondary endpoints in which certain protocol deviations occurred. We conducted a Type A, end of review, meeting at which the FDA reiterated its stated position in the CRL, that pimavanserin should be studied by individual subgroups of DRP, and advised us that the best path forward is to conduct an additional clinical study in each of the subgroups for which we seek approval. However, the FDA was also open to reviewing additional analyses from the HARMONY and -019 studies in support of a potential resubmission for individual subgroups without additional clinical studies. We have scheduled a follow-up meeting with the FDA to further discuss later this year. 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 preclinical 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 to date in 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. Moreover, there can be no assurance that a positive study outcome will ultimately result in approval by the FDA.

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 in the HARMONY study, as well as insufficient numbers of patients with certain less common dementia subtypes as lack of substantial evidence of effectiveness to support approval. The FDA also stated in the CRL that it considers Alzheimer's disease psychosis study -019 to not be adequate and well controlled, citing that it was a single center study with no type I error control of secondary endpoints in which certain protocol deviations occurred. We conducted a Type A meeting at which the FDA reiterated its stated position in the CRL, that pimavanserin should be studied by individual subgroups of DRP, and advised us that the best path forward is to conduct an additional clinical study in each of the subgroups for which we seek approval. However, the FDA was also open to reviewing additional analyses from the HARMONY and -019 studies in support of a potential resubmission for individual subgroups without additional clinical studies. We have scheduled a follow-up meeting with the FDA to further discuss later this year. At this point, 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;
- SAEs 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.

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 September 30, 2021, we employed approximately 570 employees. 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, and integrate additional employees and retain existing 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. 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 September 30, 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 \$540.3 million at September 30, 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, legislation enacted in 2017, informally titled 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 Coronavirus Aid, Relief, and Economic Security Act (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, the CARES 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.

Portions 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 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. We continue to closely monitor the COVID-19 situation and will reopen our offices to allow employees to return when appropriate. We may face several challenges or disruptions upon a return back to the workplace, including re-integration challenges by our employees and distractions to management related to such transition. 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 2021, sales of NUPLAZID were negatively impacted by ongoing conditions related to the pandemic, including a reduction in patient office visits and a continuing reduced occupancy rates at long-term care facilities. While we observed incremental improvements in some of these factors during the later part of the year, the levels are still meaningfully below where they were pre-pandemic. It remains difficult to predict the duration of the pandemic’s impact and the pace of, and no assurances can be given that the pandemic will not continue to have additional negative 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. In response, we have filed complaints against these companies alleging infringement of certain of our Orange Book-listed patents covering NUPLAZID. For a more detailed description of these matters, the section titled “Legal Proceedings” in Note 8 to the condensed consolidated financial statements included in this Quarterly Report. 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, 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. Furthermore, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Moreover, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order also instructed 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 possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and other 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. In addition, Congress is considering additional health reform measures as part of the budget reconciliation process.

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. presidential executive orders, 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, 2023. 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. As a result of litigation challenging the Most Favored Nation model, on August 10, 2021, CMS published a proposed rule that seeks to rescind the Most Favored Nation model interim final rule. Further, in July 2021, the Biden administration released an executive order that included multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform. The plan sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. 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 current or potential future collaborators, partners or service providers are or may become subject to data privacy and security regulation by both the U.S. federal government and the states in which we conduct our business, including laws and regulations that apply to our processing of personal data or the processing of personal data on our behalf. 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 chiropractors under 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 personal data protection, such as 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 European Economic Area (EEA); 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 as potential fines for noncompliant companies of are up to the greater of €20 million or 4% of annual global revenue and potential penalties include a prohibition on use of personal data subject to the GDPR, which could impact our operations and ability to develop our products and provide our services, including interrupting or ending EEA clinical trials. Compliance with the GDPR and the laws and regulations of applicable EU Member States and similar data protection laws in domestic and other foreign jurisdictions (such as Switzerland and the United Kingdom) 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 activities.

In addition, certain jurisdictions have enacted data localization laws and laws regulating or restricting cross-border personal data transfers. For example, European data protection laws, including the GDPR, generally restrict the transfer of personal data from Europe, including the EEA, United Kingdom and Switzerland, to the United States and most other countries unless the parties to the transfer have implemented specific safeguards to protect the transferred personal data. A decision by the Court of Justice of the European Union (the “Schrems II” ruling), however, invalidated the EU-U.S. Privacy Shield Framework, which was one of the primary mechanisms used by U.S. companies to import personal data 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 opined that the Swiss-U.S. Privacy Shield is inadequate for transfers of personal 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. In June 2021, the European Commission released a set of “Standard Contractual Clauses” that are designed to be a valid mechanism by which entities can transfer personal data out of the EEA to jurisdictions that the European Commission has not found to provide an adequate level of protection. Currently, these Standard Contractual Clauses are a valid mechanism to transfer personal data outside of the EEA. The Standard Contractual Clauses, however, require parties that rely upon them to comply with additional obligations, such as conducting transfer impact assessments to determine whether additional security measures are necessary to protect the at-issue personal data. Moreover, due to potential legal challenges, there exists some uncertainty regarding whether the Standard Contractual Clauses will remain a valid mechanism for transfers of personal data out of the EEA. If we are unable to implement a valid compliance mechanism for cross-border personal data transfers, we may face increased exposure to regulatory actions, substantial fines and injunctions against processing or transferring personal data. For example, inability to import personal data from Europe to the United States may limit our ability to conduct clinical trial activities in Europe, limit our ability to collaborate with contract research organizations, service providers, contractors and other entities subject to European data protection laws, adversely impact our operations, product development and ability to provide our products, and require us to increase our data processing capabilities in Europe at significant expense.

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 data protections of the GDPR continued to apply to United Kingdom-related processing of personal data in substantially unvaried form under the so-called “UK GDPR.” However, going forward, there will be increasing potential for divergence in the application and interpretation of the data protection laws as between the United Kingdom and the EEA. Furthermore, the relationship between the United Kingdom and the EEA in relation to certain aspects of data protection law remains somewhat uncertain. On June 28, 2021, the European Commission issued an adequacy decision under the GDPR which allows personal data transfers (other than those carried out for the purposes of United Kingdom immigration control) from the EEA to the United Kingdom to continue without restriction for four years (ending June 27, 2025). After that period, the adequacy decision may be renewed, however, only if the United Kingdom continues to ensure an adequate level of data protection. During these four years, the European Commission will continue to monitor the situation in the United Kingdom and could intervene at any point if the United Kingdom deviates from the level of data protection in place at the time of the issuance of the adequacy decision. If the adequacy decision is withdrawn or not renewed, transfers of personal data from the EEA to the United Kingdom will require a valid ‘transfer mechanism’ and we may be required to implement new processes and put new agreements in place, such as SCCs, to enable transfers of personal data from the EEA to the United Kingdom to continue.

Moreover, states in the U.S. 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 called 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. The CCPA authorizes private lawsuits to recover statutory damages for data breaches that is expected to increase data breach litigation. The CCPA also allows for statutory fines for noncompliance (up to \$7,500 per violation). Although the CCPA exempts some personal information processed in the context of clinical trials, the CCPA, to the extent applicable to our business and operations, may increase our potential liability with respect to other personal information we maintain about California residents. In addition, it is anticipated that the California Privacy Rights Act of 2020 (CPRA), effective January 1, 2023, will expand the CCPA. For example, the CPRA establishes a new California Privacy Protection Agency to enforce the CCPA (as amended), which could increase the risk of an enforcement action. Moreover, other states have enacted data privacy laws. For example, Virginia passed the Consumer Data Protection Act and Colorado passed the Colorado Privacy Act, both of which differ from the CPRA and become effective in 2023.

Compliance with U.S. and foreign 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 personal data, or in some cases, impact our ability to operate in certain jurisdictions. Data protection laws worldwide are, and are 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 and other 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 obligations. Actual or perceived failure to comply with our protection obligations could result in government enforcement actions (which could include civil or criminal penalties), investigations, private litigation, other liabilities and/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.

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.

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 (AMP), 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 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 obligations, loss of customers or sales, interruption of our clinical trials, or users curtailing or ceasing their use of our products.*

We are dependent upon our own and 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), personnel theft or misuse, denial-of-service attacks (such as credential stuffing), phishing attacks, sophisticated nation-state and nation-state supported actors now engage in attacks (including advanced persistent threat intrusions). Ransomware attacks are becoming increasingly prevalent and severe and can lead to significant interruptions, delays, or outages in our operations, disruption of clinical trials, loss of data (including data related to clinical trials), loss of income, significant extra expenses to restore data or systems, reputational loss and the diversion of funds. To alleviate the financial, operational and reputational impact of a ransomware attack, ransomware attack victims may prefer to make payment demands, but if we were to be a victim of such an attack, we may be unwilling or unable to do so (including, for example, if applicable laws or regulations prohibit such payments). Similarly, supply chain attacks have increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach or disruption of our systems and networks or the systems or networks of third parties that support us. Despite the security controls we have in place, such attacks are difficult to avoid. 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. For example, due to the COVID-19 pandemic and the potential that our personnel may work remotely, there may exist an increased risk to our information technology assets and data. 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.

We may be required to expend significant resources, fundamentally change our business activities and practices (including our clinical trials) 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/ trial participant 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 our data protection obligations, any of which could disrupt our business and/or result in increased costs or loss of revenue. Further, a security breach could result in temporary or permanent bans on all or some processing of personal data, which could impact our clinical trials or other development of our products. Moreover, security incidents can result in the diversion of funds, and interruptions, delays or outages in our operations. Failures or significant downtimes of or information technology or telecommunication systems or those used by the third parties upon whom we rely could cause significant interruptions in our operations and could adversely impact the confidentiality, integrity, and availability of sensitive information, including preventing us from conducting clinical trials, tests or research and development activities and preventing us from managing the administrative aspects of our business. 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. 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 66²/₃% 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	<u>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).</u>
3.2	<u>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).</u>
3.3	<u>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).</u>
4.1	<u>Form of common stock certificate of the Registrant (incorporated by reference to Exhibit 4.1 to Registration Statement No. 333-52492).</u>
4.2	<u>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).</u>
31.1	<u>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.</u>
32.1	<u>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.</u>
101	The following financial statements from the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, filed on November 8, 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)

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: November 8, 2021

By: /s/ Stephen R. Davis

Stephen R. Davis

Chief Executive Officer

(on behalf of the registrant and as the registrant's Principal Financial Officer)

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: November 8, 2021

/s/ STEPHEN DAVIS

Stephen Davis
Chief Executive Officer
(Registrant's Principal Executive and Financial Officer)

**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 September 30, 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: November 8, 2021

/s/ STEPHEN DAVIS

Stephen Davis
Chief Executive Officer
(Registrant's Principal Executive and 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.