UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2021

OR

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

For the transition period from _____ to _____

Commission file number: 001-36544

Sage Therapeutics, Inc.

(Exact name of registrant as specified in its Charter)

Delaware	**27-4486580**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

215 First Street
Cambridge, Massachusetts 02142
(Address of principal executive office) (Zip Code)

Registrant's telephone number, including area code: (617) 299-8380

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	SAGE	The Nasdaq Global Market

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the 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, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer", "accelerated filer", "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

As of October 26, 2021, there were 58,908,485 shares of the registrant's common stock, $0.0001 par value per share, outstanding.

Cautionary Note Regarding Forward-Looking Statements

This Quarterly Report on Form 10-Q, or Quarterly Report, contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Quarterly Report are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may”, “will”, “should”, “expects”, “intends”, “plans”, “anticipates”, “believes”, “estimates”, “predicts”, “potential”, “continue” or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our views as to potential future results of our ongoing commercialization efforts in the U.S. with respect to ZULRESSO® (brexanolone) CIV injection, which is approved in the U.S. for the treatment of postpartum depression, or PPD, in adults;
- our planned clinical and regulatory activities with respect to zuranolone (SAGE-217) for the treatment of major depressive disorder, or MDD, and PPD and related timelines, including: potential regulatory pathways for zuranolone approval; our planned submission of a new drug application, or NDA, for zuranolone to the FDA as a treatment for MDD and an additional filing for zuranolone as a treatment for PPD; the adequacy of the data we plan to submit to support such filings; and the potential for future approval and commercialization of zuranolone in MDD and PPD;
- our view of the potential for zuranolone in the treatment of MDD and PPD, if approved, including the potential product profile and treatment benefit, and the potential for zuranolone to be developed in additional indications;
- our plans for development of our other product candidates for the treatment of brain health diseases and disorders, and potentially for other indications, our plans with respect to other research and development activities, and expected timelines for our planned activities;
- our ability, within the expected time frames, to initiate clinical trials and non-clinical studies of existing or future product candidates, including pivotal clinical trials, and to successfully complete and announce the results of ongoing or future clinical trials;
- our belief as to potential outcomes of our activities;
- our plans and potential outcomes with respect to interactions with regulatory authorities;
- our plans for and the potential costs, benefits and outcomes of our existing collaborations, and our plans for and potential outcomes of any additional business development efforts;
- our plans and expectations with respect to the potential development of any product or product candidate for markets outside the U.S.;
- our estimates regarding the level of expenses we may incur in connection with our activities; use of cash and projected cash on hand at any given timepoint; timing of future cash needs; capital requirements; sources of future financings; and our ability to obtain additional financing when needed to fund future operations;
- our expectations with respect to the availability of supplies of ZULRESSO and our product candidates, and the expected performance of our third-party manufacturers;
- our ability to obtain and maintain intellectual property protection for our proprietary assets and other forms of exclusivity relevant to our business;
- the estimated number of patients with diseases or disorders of interest to us and the potential size of the market for ZULRESSO in PPD and for our product candidates in the indications we are studying or plan to study;
- the potential for our current product and current or future product candidates, if successfully developed and approved, for the indications and in the markets for which they are approved and our ability to serve those markets;

- the potential for success of competing products that are or become available for PPD or MDD or any of the other indications that we are pursuing or may pursue in the future with our products and our product candidates;
- the impact of the COVID-19 pandemic on our activities, business and results of operations, and the potential success of our efforts to address or mitigate such impact; and
- other risks and uncertainties, including those listed under Part II, Item 1A, Risk Factors.

Any forward-looking statements in this Quarterly Report reflect our current views with respect to future events and with respect to our business and future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Part II, Item 1A, Risk Factors and elsewhere in this Quarterly Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

We may from time to time provide estimates, projections and other information concerning, among other things, our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information we provide. Unless otherwise expressly stated, we obtained this industry and business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties; industry, medical and general publications; government data; and similar sources, in some cases applying our own assumptions and analysis that may, in the future, prove not to have been accurate.

Summary of Risks Related to our Business

Our business, prospects, financial condition, and operating results are subject to numerous risks and uncertainties that you should be aware of before making an investment decision, as more fully described under Part II, Item 1A, Risk Factors and elsewhere in this Quarterly Report. These risks may include, but are not limited to, the following:

- Our commercialization efforts in the U.S. with respect to ZULRESSO® (brexanolone) CIV injection may never be successful, and we may never be able to generate meaningful revenues, or revenues at levels or on timing necessary to support our investment and goals.
- Our future business depends heavily on our ability, and that of our collaborators, where applicable, to successfully develop and gain regulatory approval of our current product candidates, including zuranolone (SAGE-217). We cannot be certain that we or our collaborators will be able to complete ongoing clinical trials, initiate new clinical trials or announce results of ongoing or future clinical trials of our product candidates on the timelines we expect or at all, or that the results of our development programs will be positive or sufficient to file for or gain regulatory approval. Decisions or actions of the FDA or other regulatory agencies may adversely affect our plans, progress or results at any stage of development. We cannot be certain that we or our collaborators will be able to successfully file or obtain regulatory approval for, or successfully commercialize, if approved, any of our current or future product candidates, including zuranolone, on the timelines we expect or at all.
- Obtaining regulatory approval to market any of our product candidates is a complex, lengthy, expensive and uncertain process, and the U.S. Food and Drug Administration and regulatory authorities outside of the U.S. may decide not to accept a new drug application or may delay, limit or deny approval of any of our product candidates for many reasons.
- If the affected populations for indications our products and product candidates are targeting, including the addressable markets within such populations, or the number of patients within such markets who are actually

treated with our products, if successful developed and approved, are smaller than we anticipate, our ability to achieve profits from the commercialization of such products at the levels or on the timing we expect could be materially adversely impacted.

- Positive results from non-clinical studies and clinical trials of our product candidates are not necessarily predictive of the results of later non-clinical studies and clinical trials of our product candidates in the same indications or other indications. Interim results from non-clinical studies and clinical trials may not be predictive of results of such non-clinical studies or clinical trials once completed.
- If serious adverse events or other undesirable side effects are identified during the use of any of our marketed products or product candidates, including during commercial use or in clinical trials, such events may adversely affect market acceptance or result in other significant negative consequences for an approved product; delay or prevent further development or regulatory approval with respect to product candidates; or cause regulatory authorities to require labeling statements, such as boxed warnings, or a Risk Evaluation and Mitigation Strategy, on approved products.
- We rely completely on third-party suppliers to manufacture commercial supplies of ZULRESSO and clinical drug supplies for our product candidates and intend to rely on third party manufacturers for commercial supplies of any of our product candidates that is successfully developed and approved for marketing.
- Our current product candidates, if successfully developed and approved, and other future products, if any, may not achieve broad market acceptance or reimbursement at sufficient levels, which may limit the revenue that we generate from sales of such products.
- Competing therapies may exist or could emerge that adversely affect the amount of revenue we are able to generate from the sale of ZULRESSO or any of our current or future product candidates, if successfully developed and approved.
- Our existing collaborations with Biogen MA Inc., Biogen International GmbH, and Shionogi & Co., Ltd., and any future collaborations, may not lead to the successful development or regulatory approval of product candidates or commercialization of products. Our collaborators may have competing priorities, conflicting incentives, or different views than us on key decisions, including appropriate program spending, that may hamper or delay our development and commercialization efforts or increase our costs. Our business may be adversely affected if any of our collaborators fails to perform its obligations or terminates our collaboration.
- We may not be successful in our efforts to identify new targets, generate new compounds, and successfully bring such new compounds through investigational new drug application-enabling non-clinical studies.
- If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our products or product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.
- For certain of our products and product candidates, we are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing certain of our products or product candidates, if approved.
- Existing or future laws, regulations, executive orders or policies aimed at reducing healthcare costs may have a material adverse effect on our business or results of operations.
- We are subject to healthcare laws and regulations, which could expose us to the risk of criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings if we or our employees are alleged or determined not to have complied with such laws and regulations.
- We are a biopharmaceutical company with a limited operating history, and have not generated significant revenue to date. We have incurred significant operating losses since our inception, and anticipate that we will incur losses for the foreseeable future.

- We may need to raise additional funding, which may not be available on acceptable terms, or at all. Raising additional capital, even opportunistically, may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights.
- The COVID-19 pandemic may continue to adversely impact our business, including our sales of ZULRESSO and our initiation, conduct and completion of clinical trials.

Sage Therapeutics, Inc.

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PART I — FINANCIAL INFORMATION

Item 1. Financial Statements

Sage Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Balance Sheets
(in thousands, except share and per share data)
(Unaudited)

	September 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 422,165	$ 1,661,082
Marketable securities	1,421,004	438,467
Prepaid expenses and other current assets	34,343	22,821
Collaboration receivable - related party	24,185	—
Total current assets	1,901,697	2,122,370
Property and equipment, net	2,907	6,755
Restricted cash	1,269	1,716
Right-of-use operating asset	17,432	25,064
Other long-term assets	3,875	3,341
Total assets	$ 1,927,180	$ 2,159,246
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 4,733	$ 3,691
Accrued expenses	66,795	54,851
Operating lease liability, current portion	7,414	8,662
Total current liabilities	78,942	67,204
Operating lease liability, net of current portion	12,481	19,438
Other liabilities	103	270
Total liabilities	91,526	86,912
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Preferred stock, $0.0001 par value per share; 5,000,000 shares authorized at September 30, 2021 and December 31, 2020; no shares issued or outstanding at September 30, 2021 and December 31, 2020	—	—
Common stock, $0.0001 par value per share; 120,000,000 shares authorized at September 30, 2021 and December 31, 2020; 58,835,406 and 58,311,444 shares issued at September 30, 2021 and December 31, 2020; 58,832,373 and 58,308,411 shares outstanding at September 30, 2021 and December 31, 2020	6	6
Treasury stock, at cost, 3,033 shares at September 30, 2021 and December 31, 2020	(400)	(400)
Additional paid-in capital	3,207,028	3,109,807
Accumulated deficit	(1,370,674)	(1,037,494)
Accumulated other comprehensive gain (loss)	(306)	415
Total stockholders' equity	1,835,654	2,072,334
Total liabilities and stockholders' equity	$ 1,927,180	$ 2,159,246

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

Sage Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Product revenue, net	$ 1,440	$ 1,639	$ 4,666	$ 5,014
Operating costs and expenses:				
Cost of goods sold	131	149	466	429
Research and development	83,497	74,078	207,723	211,008
Selling, general and administrative	48,706	35,099	131,899	143,454
Restructuring	—	(529)	—	27,873
Total operating costs and expenses	132,334	108,797	340,088	382,764
Loss from operations	(130,894)	(107,158)	(335,422)	(377,750)
Interest income, net	692	1,347	2,132	8,763
Other income, net	31	76	110	165
Net loss	$ (130,171)	$ (105,735)	$ (333,180)	$ (368,822)
Net loss per share—basic and diluted	$ (2.21)	$ (2.03)	$ (5.69)	$ (7.10)
Weighted average number of common shares outstanding—basic and diluted	58,819,548	51,981,468	58,593,743	51,938,923
Comprehensive loss:				
Net loss	$ (130,171)	$ (105,735)	$ (333,180)	$ (368,822)
Other comprehensive items:				
Unrealized loss on marketable securities	(21)	(763)	(721)	(349)
Total other comprehensive loss	(21)	(763)	(721)	(349)
Total comprehensive loss	$ (130,192)	$ (106,498)	$ (333,901)	$ (369,171)

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

Sage Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Statements of Cash Flows
(in thousands)
(Unaudited)

	Nine Months Ended September 30,	
	2021	2020
Cash flows from operating activities		
Net loss	$ (333,180)	$ (368,822)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	83,981	75,250
Premium on marketable securities	(19,792)	(1,066)
Amortization of premium on marketable securities	8,722	628
Depreciation	3,849	1,981
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(11,522)	(3,647)
Collaboration receivable - related party	(24,185)	—
Other long-term assets	(534)	366
Right-of-use operating asset	3,898	4,914
Operating lease liabilities, current	152	(6)
Operating lease liabilities, non-current	(4,427)	(5,194)
Accounts payable	1,042	(10,913)
Accrued expenses and other liabilities	11,315	(40,182)
Net cash used in operating activities	(280,681)	(346,691)
Cash flows from investing activities		
Proceeds from sales and maturities of marketable securities	699,212	766,339
Purchases of marketable securities	(1,671,399)	(368,829)
Purchases of property and equipment	—	(345)
Net cash provided by (used in) investing activities	(972,187)	397,165
Cash flows from financing activities		
Proceeds from stock option exercises and employee stock purchase plan issuances	14,300	7,091
Payment of employee tax obligations related to vesting of restricted stock units	(796)	—
Net cash provided by financing activities	13,504	7,091
Net increase (decrease) in cash, cash equivalents and restricted cash	(1,239,364)	57,565
Cash, cash equivalents and restricted cash at beginning of period	1,662,798	129,072
Cash, cash equivalents and restricted cash at end of period	$ 423,434	$ 186,637
Supplemental disclosure of non-cash operating and investing activities		
Lease asset de-recognized upon lease cancellation	$ 3,733	$ 2,310

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

Sage Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Statements of Changes in Stockholders' Equity
(in thousands, except share data)
(Unaudited)

	Common Stock		Treasury Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balances at December 31, 2019	51,877,194	$ 5	3,033	$ (400)	$ 2,587,322	$ 1,295	$ (1,643,567)	$ 944,655
Issuance of common stock from exercises of stock options	7,196	—	—	—	367	—	—	367
Issuance of common stock under the employee stock purchase plan	33,429	—	—	—	2,793	—	—	2,793
Stock-based compensation expense	—	—	—	—	30,218	—	—	30,218
Unrealized loss on available-for-sale securities	—	—	—	—	—	(2,087)	—	(2,087)
Net loss	—	—	—	—	—	—	(126,740)	(126,740)
Balances at March 31, 2020	51,917,819	$ 5	3,033	$ (400)	$ 2,620,700	$ (792)	$ (1,770,307)	$ 849,206
Issuance of common stock from exercises of stock options	17,160	—	—	—	387	—	—	387
Stock-based compensation expense	—	—	—	—	24,168	—	—	24,168
Unrealized gain on available-for-sale securities	—	—	—	—	—	2,501	—	2,501
Net loss	—	—	—	—	—	—	(136,347)	(136,347)
Balances at June 30, 2020	51,934,979	$ 5	3,033	$ (400)	$ 2,645,255	$ 1,709	$ (1,906,654)	$ 739,915
Issuance of common stock from exercises of stock options	48,560	—	—	—	2,157	—	—	2,157
Issuance of common stock under the employee stock purchase plan	39,290	—	—	—	2,144	—	—	2,144
Stock-based compensation expense	—	—	—	—	19,863	—	—	19,863
Unrealized loss on available-for-sale securities	—	—	—	—	—	(763)	—	(763)
Net loss	—	—	—	—	—	—	(105,735)	(105,735)
Balances at September 30, 2020	52,022,829	$ 5	3,033	$ (400)	$ 2,669,419	$ 946	$ (2,012,389)	$ 657,581
Balances at December 31, 2020	58,308,411	$ 6	3,033	$ (400)	$ 3,109,807	$ 415	$ (1,037,494)	$ 2,072,334
Issuance of common stock from exercises of stock options	80,338	—	—	—	4,687	—	—	4,687
Issuance of common stock under the employee stock purchase plan	18,072	—	—	—	936	—	—	936
Stock-based compensation expense	—	—	—	—	21,734	—	—	21,734
Unrealized loss on available-for-sale securities	—	—	—	—	—	(651)	—	(651)
Net loss	—	—	—	—	—	—	(95,764)	(95,764)
Balances at March 31, 2021	58,406,821	$ 6	3,033	$ (400)	$ 3,137,164	$ (236)	$ (1,133,258)	$ 2,003,276
Issuance of common stock from exercises of stock options	159,070	—	—	—	6,861	—	—	6,861
Stock-based compensation expense	—	—	—	—	27,465	—	—	27,465
Unrealized loss on available-for-sale securities	—	—	—	—	—	(49)	—	(49)
Vesting of restricted stock units, net of employee tax obligations	204,473	—	—	—	(796)	—	—	(796)
Net loss	—	—	—	—	—	—	(107,245)	(107,245)
Balances at June 30, 2021	58,770,364	$ 6	3,033	$ (400)	$ 3,170,694	$ (285)	$ (1,240,503)	$ 1,929,512
Issuance of common stock from exercises of stock options	33,322	—	—	—	430	—	—	430
Issuance of common stock under the employee stock purchase plan	28,687	—	—	—	1,825	—	—	1,825
Stock-based compensation expense	—	—	—	—	34,079	—	—	34,079
Unrealized loss on available-for-sale securities	—	—	—	—	—	(21)	—	(21)
Net loss	—	—	—	—	—	—	(130,171)	(130,171)
Balances at September 30, 2021	58,832,373	$ 6	3,033	$ (400)	$ 3,207,028	$ (306)	$ (1,370,674)	$ 1,835,654

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

1. Nature of the Business

Sage Therapeutics, Inc. ("Sage" or the "Company") is a biopharmaceutical company committed to developing and commercializing novel medicines with the potential to transform the lives of people with debilitating disorders of the brain.

The Company's first product, ZULRESSO® (brexanolone) CIV injection, is approved in the U.S. as a treatment for postpartum depression ("PPD") in adults. The Company launched ZULRESSO commercially in the U.S. in June 2019. The Company has a portfolio of other product candidates with a current focus on modulating two critical central nervous system ("CNS") receptor systems, GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function via activation of $GABA_A$ receptors. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. Dysfunction in these systems is implicated in a broad range of CNS disorders. The Company is currently targeting diseases and disorders of the brain with three key focus areas: depression, neurology and neuropsychiatry.

The Company was incorporated under the laws of the State of Delaware on April 16, 2010, and commenced operations on January 19, 2011 as Sterogen Biopharma, Inc. On September 13, 2011, the Company changed its name to Sage Therapeutics, Inc.

The Company is subject to risks and uncertainties common to companies in the biotechnology and pharmaceutical industries, including, but not limited to, the risks associated with developing product candidates at each stage of non-clinical and clinical development; the challenges associated with gaining regulatory approval of such product candidates; the risks associated with the marketing and sale of pharmaceutical products; the potential for development by third parties of new technological innovations that may compete with the Company's products and product candidates; the dependence on key personnel; the challenges of protecting proprietary technology; the need to comply with government regulations; the high costs of drug development; the uncertainty of being able to secure additional capital when needed to fund operations; and the potential impact of the COVID-19 pandemic on its development activities, operations and financial condition.

Under Accounting Standards Update ("ASU") No. 2014-15, *Presentation of Financial Statements—Going Concern* (Subtopic 205-40), the Company has the responsibility to evaluate whether conditions and/or events raise substantial doubt about its ability to meet its future financial obligations as they become due within one year after the date that the financial statements are issued. The Company has incurred losses and negative cash flows from operations since its inception, except for net income of $606.1 million for the year ended December 31, 2020, reflecting revenue recognized under a collaboration and license agreement with Biogen MA Inc. ("BIMA") and Biogen International GmbH (collectively with BIMA, "Biogen") (the "Biogen Collaboration Agreement"). As of September 30, 2021, the Company had an accumulated deficit of $1.4 billion. From its inception through September 30, 2021, the Company has received aggregate net proceeds of $2.8 billion from the sales of redeemable convertible preferred stock prior to its initial public offering, the issuance of convertible notes, and the sales of common stock in its initial public offering ("IPO") in July 2014, in follow-on public offerings, and to BIMA under a stock purchase agreement executed in connection with the Biogen Collaboration Agreement. The Company has also received $1.0 billion in upfront payments under its collaborations with Biogen and Shionogi & Co., Ltd. ("Shionogi"). Until such time, if ever, as the Company can generate substantial product revenue and achieve profitability, the Company expects to finance its cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other sources of funding. If the Company is unable to raise additional funds through equity or debt financings or other sources of funding when needed, the Company may be required to delay, limit, reduce or terminate product development or future commercialization efforts or grant rights to develop and market products or product candidates that the Company would otherwise prefer to develop and market itself.

The Company expects that, based on its current operating plans, the Company's existing cash, cash equivalents and marketable securities will be sufficient to fund its currently planned operations for at least the next 12 months from the filing date of these unaudited interim condensed consolidated financial statements ("condensed consolidated financial statements"). At some point after that time, the Company anticipates it will require additional financing to fund its future operations. Even if the Company believes it has sufficient funds for its current or future operating plans, the Company may seek to raise additional capital if market conditions are favorable or in light of other strategic considerations.

COVID-19

The ongoing COVID-19 pandemic has caused and may continue to cause major disruptions to businesses and economies worldwide. The rapid spread of COVID-19 in the U.S. resulted in a significant reduction in patient demand for ZULRESSO and in the number of sites available to administer ZULRESSO. This has had a negative impact on the Company's revenue from sales of ZULRESSO. While the Company has not experienced any other material disruptions to date as a result of the COVID-19 pandemic, any prolonged material disruptions to the work of the Company's employees, suppliers, contract manufacturers, or vendors could negatively impact the Company's activities, availability of supplies, or operating results. While we have seen slower recruitment in certain of our clinical trials, due, we believe, to the COVID-19 pandemic, especially with respect to older patients and, in our SKYLARK Study, in patients with PPD, the Company to date has not experienced significant impacts to the Company's development activities as a result of the COVID-19 pandemic. Any material disruption to the Company's development activities may cause delays, increase the Company's costs and impact the Company's operating results. In addition, the COVID-19 pandemic initially caused major volatility in capital markets and a significant global economic downturn, and the Company's ability to access the capital markets in the future could be negatively impacted if current efforts to control the COVID-19 pandemic are not successful.

2. Summary of Significant Accounting Policies

The following is a summary of significant accounting policies followed in the preparation of these condensed consolidated financial statements.

Basis of Presentation

The condensed consolidated financial statements of the Company included herein have been prepared pursuant to the rules and regulations of the Securities and Exchange Commission. Certain information and footnote disclosures normally included in financial statements prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these condensed consolidated financial statements should be read in conjunction with the audited consolidated financial statements as of and for the year ended December 31, 2020, included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

The condensed consolidated financial statements have been prepared on the same basis as the audited consolidated financial statements. In the opinion of the Company's management, the accompanying condensed consolidated financial statements contain all adjustments, consisting of only normal recurring adjustments, necessary for a fair statement of its financial position as of September 30, 2021, its results of operations and comprehensive loss for the three and nine months ended September 30, 2021 and 2020, its cash flows for the nine months ended September 30, 2021 and 2020, and its statements of changes in stockholders' equity for the three and nine months ended September 30, 2021 and 2020. The consolidated balance sheet at December 31, 2020 was derived from audited financial statements, but does not include all disclosures required by GAAP. The results for the three and nine months ended September 30, 2021 are not necessarily indicative of the results for the year ending December 31, 2021, or for any future period.

Principles of Consolidation

The condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries as disclosed in Note 2, *Summary of Significant Accounting Policies*, within the "Notes to Consolidated Financial Statements" accompanying its Annual Report on Form 10-K for the fiscal year ended December 31, 2020. Intercompany accounts and transactions have been eliminated.

Use of Estimates

The preparation of condensed consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the condensed consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. The full extent to which the COVID-19 pandemic may directly or indirectly impact the Company's business, results of operations and financial condition, including sales, expenses, reserves and allowances, manufacturing, clinical trials, research and development costs and employee-related amounts, will depend on future developments that are highly uncertain, including: the scope and duration of the pandemic; the effectiveness of vaccination campaigns, vaccine mandates, and other efforts to control the pandemic; the duration of the vaccines' efficacy against COVID-19 and its variants; the duration and severity of any restrictive measures taken to curb the spread of COVID-19; and the impact of the pandemic on the Company's customers and vendors. The Company has made estimates of the impact of the COVID-19 pandemic within its condensed consolidated financial statements. Due to the evolving nature of the COVID-19 pandemic, and the emergence of highly contagious variants, there may be changes to those estimates in future periods, and actual results could differ from those estimates.

Risks and Uncertainties

The product candidates developed by the Company require approvals from the U.S. Food and Drug Administration ("FDA") or foreign regulatory agencies prior to commercial sales. There can be no assurance that the current and future product candidates of the Company will receive the necessary approvals. If the Company fails to successfully complete clinical development and generate results sufficient to file for regulatory approval or is denied approval or approval is delayed, it may have a material adverse impact on the Company's business and its financial statements.

Research and Development Costs and Accruals

Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries and benefits, overhead costs, depreciation, contract services and other related costs. Research and development costs are expensed to operations as the related obligation is incurred.

The Company has entered into various research and development contracts with research institutions and other companies both inside and outside of the U.S. These agreements are generally cancelable, and related costs are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research and development costs. When billing terms under these contracts do not coincide with the timing of when the work is performed, the Company is required to make estimates of outstanding obligations to those third parties as of the end of the reporting period. Any accrual estimates are based on a number of factors, including the Company's knowledge of the progress towards completion of the research and development activities, invoicing to date under the contracts, communication from the research institution or other companies of any actual costs incurred during the period that have not yet been invoiced, and the costs included in the contracts. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the estimates made by the Company. The historical accrual estimates made by the Company have not been materially different from the actual costs.

Revenue Recognition

The Company generates revenue from the sale of ZULRESSO, which was approved by the FDA in March 2019 and the Company subsequently began selling in June 2019, and from collaboration and supply agreements with the Company's collaborators. To date, revenue from collaboration agreements has come from initial, upfront payments allocated to licenses of intellectual property delivered to the Company's collaborators and from the supply of material for clinical trials under a supply agreement.

Under Accounting Standards Codification ("ASC") Topic 606, *Revenue from Contracts with Customers* ("Topic 606"), an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that

reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right may be accounted for as a contract modification or as a continuation of the contract for accounting purposes.

For contracts determined to be within the scope of Topic 606, the Company assesses whether the goods or services promised within each contract are distinct to identify those that are performance obligations. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract.

The Company allocates the transaction price (the amount of consideration it expects to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognizes the associated revenue when (or as) each performance obligation is satisfied. The Company's estimate of the transaction price for each contract includes all variable consideration to which the Company expects to be entitled.

Collaboration and License Revenue

In assessing whether a promised good or service is distinct in the evaluation of a collaboration or license arrangement subject to Topic 606, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner, and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, the Company is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. In certain circumstances, the Company may apply the residual method to determine the SSP of a good or service if the standalone selling price is considered highly variable or uncertain. The Company validates the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. The Company assessed its arrangements with Shionogi and Biogen and concluded that a significant financing component does not exist for either arrangement. For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is based on the use of an output or input method. Revenue from the Company's collaboration agreement with Shionogi has come from initial, upfront consideration upon execution of the agreement and for the supply of drug product for Shionogi's clinical trials. Revenue from the Company's collaboration agreement with Biogen has come from initial, upfront consideration related to the execution of the Biogen Collaboration Agreement. For additional information, refer to Note 6, *Collaboration Agreements*.

Product Revenue, Net

The Company recognizes product revenues, net of variable consideration related to certain allowances and accruals that are determined using the expected value method, in its condensed consolidated financial statements at the point in time when control transfers to the customer, which is typically when the product has been delivered to the customer's location. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. The Company's only performance obligation identified for ZULRESSO is to deliver the product to the location specified by the customer's order. The Company records shipping and handling costs associated with delivery of product to its customers within selling, general and administrative expenses on its condensed consolidated statements of operations and comprehensive loss. The Company expenses incremental costs of obtaining a contract as incurred if the expected amortization period of the asset would be less than one year. If the Company were to incur incremental costs with an amortization period greater than a year, such costs would be capitalized as contract assets, as they are expected to be recovered, and would be expensed by amortizing on a systematic basis that is consistent with the transfer to the customer of the goods or services to which the asset relates. The Company did not have any contract assets (unbilled receivables) at September 30, 2021, as customer invoicing generally occurs before or at the time of revenue recognition. The Company did not have any contract liabilities at September 30, 2021, as the Company did not receive any payments in advance of satisfying its performance obligations to its customers. Amounts billed or invoiced that are considered trade accounts receivable are included in prepaid expenses and other current assets on the condensed consolidated balance sheets. As of September 30, 2021 and December 31, 2020, the Company had not provided any allowance for bad debts against the trade accounts receivable, and the amount of trade accounts receivable was not significant.

The Company records reserves, based on contractual terms, for the following components of variable consideration related to product sold during the reporting period, as well as its estimate of product that remains in the distribution channel inventory of its customers at the end of the reporting period. On a quarterly basis, the Company updates its estimates, if necessary, and records any material adjustments in the period they are identified.

Chargebacks: The Company estimates chargebacks from its customers who directly purchase the product from the Company for discounts resulting from contractual commitments to sell products to eligible healthcare settings at prices lower than the list prices charged to its customers. Customers charge the Company for the difference between what they pay to the Company for the product and the selling price to the eligible healthcare settings. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel inventories at the end of each reporting period that the Company expects will be sold to eligible healthcare settings, and chargebacks that customers have claimed, but for which the Company has not yet issued a credit.

Government Rebates: The Company is subject to discount obligations under government programs, including Medicaid. The Company records reserves for rebates in the same period the related product revenue is recognized, resulting in a reduction of ZULRESSO product revenues and a current liability that is included in accrued expenses on its condensed consolidated balance sheets. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimates of future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

Trade Discounts and Allowances: The Company generally provides customary invoice discounts on ZULRESSO sales to its customers for prompt payment and the Company pays fees for sales order management, data, and distribution services. The Company estimates its customers will earn these discounts and fees and deducts these discounts and fees in full from gross ZULRESSO revenues and accounts receivable at the time the Company recognizes the related revenues.

Financial Assistance: The Company provides voluntary financial assistance programs to patients with commercial insurance that have coverage and reside in states that allow financial assistance. The Company estimates the financial assistance amounts for ZULRESSO and records any such amounts within accrued expenses on its condensed consolidated balance sheets. The calculation of the accrual for financial assistance is based on an estimate of claims and the cost per claim that the Company expects to receive using demographics for patients who have registered and been approved for assistance. Any adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability, which is included as a component of accrued expenses on the condensed consolidated balance sheets.

Product Returns: Consistent with industry practice, the Company offers product return rights to direct customers for damaged, defective or expiring product, provided it is within a specified period around the product expiration date as set forth in the Company's return goods policy. The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as a reserve within accrued expenses on the condensed consolidated balance sheets. Product returns have been immaterial to date and are expected to remain immaterial in the future. The Company will update its estimated refund liability, on at least a quarterly basis, based on actual shipments of ZULRESSO subject to contractual return rights, changes in expectations about the amount of estimated refunds or actual returns.

Collaborative Arrangements

The Company analyzes its collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of ASC Topic 808, *Collaborative Arrangements* ("Topic 808"). This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of Topic 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of Topic 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For those elements of the arrangement that are accounted for pursuant to Topic 606, the Company applies the five-step model described above, and presents the arrangement as collaboration revenue in the condensed consolidated statements of operations and comprehensive loss.

For collaboration arrangements that are within the scope of Topic 808, the Company evaluates the income statement classification for presentation of amounts due from or owed to other participants associated with multiple activities in a collaboration arrangement based on the nature of each separate activity. Payments or reimbursements that are the result of a collaborative relationship instead of a customer relationship, such as co-development and co-commercialization activities, are recorded as research and development expense or selling, general and administrative expense, in the event of a payment to the collaborative partner in a period, or a reduction to these expense line items in the event of a reimbursement from the collaboration partner in a period, as appropriate.

Fair Value Measurements

Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Financial assets and liabilities carried at fair value are classified and disclosed in one of the following three categories:

Level 1 — Quoted market prices in active markets for identical assets or liabilities.

Level 2 — Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company's cash equivalents and marketable securities at September 30, 2021 and December 31, 2020 were carried at fair value, determined according to the fair value hierarchy; see Note 3, *Fair Value Measurements*.

The carrying amounts reflected in the condensed consolidated balance sheets for the collaboration receivable – related party, accounts payable and accrued expenses approximate their fair values due to their short-term maturities at September 30, 2021 and December 31, 2020, respectively.

Recently Issued Accounting Pronouncements

In December 2019, the Financial Accounting Standards Board ("FASB") issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes.* This standard enhances and simplifies various aspects of the income tax accounting guidance in ASC Topic 740, *Income Taxes*, including requirements related to hybrid tax regimes, the tax basis step-up in goodwill obtained in a transaction that is not a business combination, separate financial statements of entities not subject to tax, the intra-period tax allocation exception to the incremental approach, ownership changes in

investments, changes from a subsidiary to an equity method investment, interim-period accounting for enacted changes in tax law, and the year-to-date loss limitation in interim-period tax accounting. The Company adopted the standard on the required effective date of January 1, 2021. This guidance did not have a significant impact on the Company's consolidated financial statements and related disclosures.

Other accounting standards that have been issued or proposed by the FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on the Company's condensed consolidated financial statements upon adoption.

3. Fair Value Measurements

The Company's cash equivalents are classified within Level 1 and Level 2 of the fair value hierarchy. The Company's investments in marketable securities are classified within Level 2 of the fair value hierarchy.

The fair values of the Company's marketable securities are based on prices obtained from independent pricing sources. Consistent with the fair value hierarchy described in Note 2, *Summary of Significant Accounting Policies*, marketable securities with validated quotes from pricing services are reflected within Level 2, as they are primarily based on observable pricing for similar assets or other market observable inputs. Typical inputs used by these pricing services include, but are not limited to, reported trades, benchmark yields, issuer spreads, bids, offers or estimates of cash flow, prepayment spreads and default rates.

The following tables summarize the Company's cash equivalents and marketable securities as of September 30, 2021 and December 31, 2020.

	September 30, 2021			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
	(in thousands)			
Cash equivalents:				
Cash equivalents	$ 422,165	$ 421,570	$ 595	$ —
Total cash equivalents	422,165	421,570	595	—
Marketable securities:				
U.S. government securities	302,022	—	302,022	—
U.S. corporate bonds	560,945	—	560,945	—
International corporate bonds	238,316	—	238,316	—
U.S. commercial paper	120,129	—	120,129	—
International commercial paper	198,592	—	198,592	—
U.S. municipal securities	1,000	—	1,000	—
Total marketable securities	1,421,004	—	1,421,004	—
	$ 1,843,169	$ 421,570	$ 1,421,599	$ —

	December 31, 2020			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
	(in thousands)			
Cash equivalents:				
Cash equivalents	$ 1,661,082	$ 1,637,609	$ 23,473	$ —
Total cash equivalents	1,661,082	1,637,609	23,473	—
Marketable securities:				
U.S. government securities	160,588	—	160,588	—
U.S. corporate bonds	123,107	—	123,107	—
International corporate bonds	57,676	—	57,676	—
U.S. commercial paper	45,963	—	45,963	—
International commercial paper	51,133	—	51,133	—
Total marketable securities	438,467	—	438,467	—
	$ 2,099,549	$ 1,637,609	$ 461,940	$ —

During the nine months ended September 30, 2021 and 2020, there were no transfers among the Level 1, Level 2 and Level 3 categories.

The following tables summarize the gross unrealized gains and losses of the Company's marketable securities as of September 30, 2021 and December 31, 2020:

	September 30, 2021				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Credit Losses	Fair Value
	(in thousands)				
Assets:					
U.S. government securities	$ 302,080	$ 8	$ (66)	$ —	$ 302,022
U.S. corporate bonds	561,120	69	(244)	—	560,945
International corporate bonds	238,376	42	(102)	—	238,316
U.S. commercial paper	120,133	2	(6)	—	120,129
International commercial paper	198,601	2	(11)	—	198,592
U.S. municipal securities	1,000	—	—	—	1,000
	$ 1,421,310	$ 123	$ (429)	$ —	$ 1,421,004

	December 31, 2020				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Credit Losses	Fair Value
	(in thousands)				
Assets:					
U.S. government securities	$ 160,589	$ 11	$ (12)	$ —	$ 160,588
U.S. corporate bonds	122,882	240	(15)	—	123,107
International corporate bonds	57,485	200	(9)	—	57,676
U.S. commercial paper	45,963	—	—	—	45,963
International commercial paper	51,133	—	—	—	51,133
	$ 438,052	$ 451	$ (36)	$ —	$ 438,467

As of September 30, 2021, cash equivalents were comprised of money market funds and U.S. corporate bonds. As of December 31, 2020, cash equivalents were comprised of commercial paper, money market funds and U.S. treasury securities.

As of September 30, 2021, all marketable securities held by the Company had remaining contractual maturities of one year or less, except for U.S. government securities, U.S. corporate bonds, international corporate bonds and a municipal security with a fair value of $486.1 million that had maturities of one to two years.

As of December 31, 2020, all marketable securities held by the Company had remaining contractual maturities of one year or less, except for corporate bonds with a fair value of $5.1 million that had maturities of one to two years.

All marketable securities, including those with remaining contractual maturities of more than one year, are classified as current assets on the balance sheet because they are considered to be “available for sale” and the Company can convert them into cash to fund current operations.

As of September 30, 2021, the marketable securities in a loss position had a maturity of less than one year, except for U.S. government securities, U.S. corporate bonds, and international corporate bonds with a fair value of $383.0 million, that had maturities of one to two years. As of December 31, 2020, the marketable securities in a loss position had a maturity of less than one year.

There have been no impairments of the Company’s assets measured and carried at fair value during the nine months ended September 30, 2021 and the year ended December 31, 2020.

4. Balance Sheet Components

Property and Equipment, net

Property and equipment, net, consists of the following:

	September 30, 2021	December 31, 2020
	(in thousands)	
Computer hardware and software	$ 1,260	$ 2,758
Furniture and equipment	897	1,865
Leasehold improvements	5,799	9,220
	7,956	13,843
Less: Accumulated depreciation	(5,049)	(7,088)
	$ 2,907	$ 6,755

Depreciation expense for the three months ended September 30, 2021 and 2020 was $0.4 million and $0.7 million, respectively. Depreciation expense for the nine months ended September 30, 2021 and 2020 was $3.8 million and $2.0 million, respectively.

During the nine months ended September 30, 2021, the Company removed property and equipment that was fully-depreciated from the condensed consolidated balance sheet, resulting in a decrease of $1.8 million to the gross balance of property and equipment and accumulated depreciation.

During the nine months ended September 30, 2021, the Company wrote off property and equipment related to a multi-tenant building under an operating lease for office space in Cambridge, Massachusetts, in connection with the early termination of the lease by the Company. The gross balance of property and equipment and accumulated depreciation decreased by $3.3 million. Of the decrease to the gross balance, $2.1 million was depreciated immediately upon termination of the lease, and $1.2 million had been depreciated prior to the termination of the lease. Additionally, during the nine months ended September 30, 2021, the Company wrote off property and equipment related to a different multi-tenant building under an operating lease for office space in Cambridge, Massachusetts, in connection with a sublease of a portion of the leased office space. The gross balance of property and equipment and accumulated depreciation decreased by $0.9 million. Of the decrease to the gross balance, $0.5 million was depreciated immediately upon termination of the lease, and $0.4 million had been depreciated prior to the termination of the lease.

The useful life for computer hardware and software is three years, furniture and equipment is five years and leasehold improvements is the lesser of the useful life or the term of the respective lease.

Accrued Expenses

Accrued expenses consist of the following:

	September 30, 2021	December 31, 2020
	(in thousands)	
Accrued research and development costs	$ 44,776	$ 34,398
Employee-related	11,393	14,769
Professional services	9,965	5,184
Other	661	500
	$ 66,795	$ 54,851

5. Leases, Commitments and Contingencies

Operating Leases

The Company leases office space and certain equipment. All of the leases recorded on the condensed consolidated balance sheets are operating leases. The Company's leases have remaining lease terms ranging from less than one year to approximately three years. Some of the leases include options to extend the leases for up to five years. These options were not included for the purpose of determining the right-of-use assets and associated lease liabilities as the Company determined that the renewal of these leases is not reasonably certain so only the original lease term was taken into consideration. The leases do not include any restrictions or covenants that had to be accounted for under the lease guidance.

As of January 1, 2020, the Company leased office space in three multi-tenant buildings in Cambridge, Massachusetts, consisting of 63,017 square feet in the first building, under an operating lease that will expire on August 31, 2024; 40,419 square feet in the second building, under an operating lease that will expire on August 31, 2024; and 15,975 square feet in the third building, under an operating lease that was to expire on February 29, 2024; and in a multi-tenant building in Raleigh, North Carolina, consisting of 15,525 square feet under an operating lease that will expire on November 30, 2024.

During the three months ended March 31, 2021, the Company terminated the operating lease for office space in the third building in Cambridge, Massachusetts and the remaining right-of-use asset of $3.7 million and the associated liabilities related to this lease were de-recognized upon termination of the lease. During the three months ended June 30, 2021, the Company entered into a sublease for a portion of the leased office space in the second building in Cambridge, Massachusetts.

From June 2018 to January 2019, the Company entered into leases for vehicles for field-based employees. These leases were determined to be operating leases and a right-of-use operating asset in the amount of $5.3 million was recorded on the balance sheet upon implementation of the new lease standard on January 1, 2019. The leases were for a term of three years and were to expire on various dates through January 31, 2022. During the three months ended June 30, 2020, these leases were terminated as part of the April 2020 restructuring, and the remaining right-of-use asset of $2.3 million and the associated liabilities related to these leases were de-recognized upon termination of the leases. During the three months ended December 31, 2020, the restricted cash of $0.7 million related to these leases was returned to the Company by the lessor.

License Agreements

CyDex License Agreement

In September 2015, the Company and CyDex Pharmaceuticals, Inc. ("CyDex"), a wholly owned subsidiary of Ligand Pharmaceuticals, Inc., amended and restated their existing commercial license agreement. Under the terms of the commercial license agreement as amended and restated, CyDex has granted to the Company an exclusive license to CyDex's Captisol drug formulation technology and related intellectual property for the manufacture of pharmaceutical products incorporating brexanolone and the Company's compound known as SAGE-689, and the development and commercialization of the resulting products in the treatment, prevention or diagnosis of any disease or symptom in humans or animals other than (i) the ocular treatment of any disease or condition with a formulation, including a hormone; (ii) topical ocular treatment of inflammatory conditions; (iii) treatment and prophylaxis of fungal infections in humans; and (iv) any ocular treatment for retinal degeneration. The Company is required to pay a royalty to CyDex on sales of brexanolone and will be required to pay a royalty on any sales of SAGE-689, if such product candidate is successfully developed in the future. Royalty rates are in the low single digits based on levels of net sales. As of September 30, 2021, the Company has paid to CyDex $1.0 million for licensing fees, which was recorded as research and development expense.

Under the amended and restated license agreement with CyDex, the Company agreed to make milestone payments on the achievement of clinical development and regulatory milestones in the amount of up to $0.8 million in clinical milestones and up to $3.8 million in regulatory milestones for each of the first two fields with respect to brexanolone; up to $1.3 million in clinical milestones and up to $8.5 million in regulatory milestones for each of the third and fourth fields with respect to brexanolone; and up to $0.8 million in clinical milestones and up to $1.8 million in regulatory milestones for one field with respect to SAGE-689. As of September 30, 2021, the Company has recorded research and development expense and made cash payments of $3.7 million related to these clinical development and regulatory milestones and has recorded an intangible asset and made a cash payment of $3.0 million related to these regulatory milestones.

For the three and nine months ended September 30, 2021, an additional clinical development milestone was met under the license agreement with CyDex related to SAGE-689, and accordingly, the Company recorded research and development expense and made a cash payment of $0.1 million.

For the nine months ended September 30, 2020, the Company did not record any expense or intangible asset, or make any milestone payments related to clinical development or regulatory milestones for the brexanolone program or SAGE-689 under the license agreement with CyDex.

University of California License Agreements

In October 2013, the Company entered into a non-exclusive license agreement with the Regents of the University of California ("the Regents") under which the Company was granted a non-exclusive license to certain clinical data and clinical material related to brexanolone for use in the development and commercialization of biopharmaceutical products in the licensed field, including status epilepticus and postpartum depression. In May 2014, the license agreement was amended to add the treatment of essential tremor to the licensed field of use, materials and milestone fee provisions of the agreement. The Company paid to the Regents clinical development milestones of $0.1 million, prior to December 31, 2015; no other milestones are outstanding under this non-exclusive license agreement. The Company is required to pay royalties of less than 1% on net sales for a period of fifteen years following the sale of the first product developed using the data and materials. The license will terminate on the earlier to occur of (i) 27 years after the effective date or (ii) 15 years after the last-derived product is first commercially sold.

In June 2015, the Company entered into an exclusive license agreement with the Regents whereby the Company was granted an exclusive license to certain patent rights related to the use of allopregnanolone to treat various diseases. In exchange for such license, the Company paid an upfront payment of $50,000 and will make payments of $15,000 for annual maintenance fees until the calendar year following the first sale, if any, of a licensed product. The Company is obligated to make milestone payments following the achievement of specified regulatory and sales milestones of up to $0.7 million and $2.0 million in the aggregate, respectively. The Company pays royalties at a low single digit percentage of net sales of ZULRESSO, subject to specified minimum annual royalty amounts. Unless terminated by operation of law or by acts of the parties under the terms of the agreement, the license agreement will terminate when the last-to-expire patents or last-to-be abandoned patent applications expire, whichever is later. As of September 30, 2021, the Company has recorded research and development expense and made cash payments of $0.3 million related to these regulatory and sales milestones; and has recorded an intangible asset and made a cash payment of $0.5 million related to these regulatory and sales milestones.

For the nine months ended September 30, 2021 and 2020, the Company did not record any expense or make any milestone payments under the license agreements with the Regents.

Washington University License Agreement

In November 2013, the Company entered into a license agreement with Washington University whereby the Company was granted an exclusive, worldwide license under certain patent and other intellectual property rights related to SAGE-689. In exchange for these rights, the Company paid an upfront, non-refundable payment of $50,000 and, as amended in July 2021, is required to pay an annual license maintenance fee of $25,000 on each subsequent anniversary date until the first commercial sale, if any, of a licensed product. The Company is obligated to make milestone payments to Washington University based on achievement of clinical development and regulatory milestones of up to $0.7 million and $0.5 million, respectively. Additionally, the Company fulfilled its obligation to issue to Washington University 47,619 shares of common stock on December 13, 2013. The fair value of these shares of $0.1 million was recorded as research and development expense in 2013. As of September 30, 2021, the Company has recorded research and development expense and made cash payments of $0.2 million related to these clinical development milestones.

The Company is obligated to pay royalties to Washington University at rates in the low single digits on net sales of licensed products covered under patent rights and royalties at rates in the low single digits on net sales of licensed products not covered under patent rights. Additionally, the Company has the right to sublicense and is required to make payments at varying percentages of sublicensing revenue received, initially in the mid-teens and descending to the mid-single digits over time.

For the three and nine months ended September 30, 2021, an additional clinical development milestone was met under the license agreement with Washington University, and accordingly, the Company recorded research and development expense and made a cash payment of $0.1 million.

For the nine months ended September 30, 2020, the Company did not record any expense or make any milestone payments under the license agreement with Washington University.

6. Collaboration Agreements

Shionogi

In June 2018, the Company entered into a strategic collaboration with Shionogi for the clinical development and commercialization of zuranolone for the treatment of major depressive disorder (“MDD”) and other potential indications in Japan, Taiwan and South Korea (the “Shionogi Territory”). In October 2018, the Company entered into a supply agreement with Shionogi for zuranolone clinical material.

Under the terms of the collaboration agreement, Shionogi is responsible for all clinical development and regulatory filings for zuranolone in MDD and other indications in the Shionogi Territory and would be responsible for commercialization in the Shionogi Territory, if zuranolone is successfully developed and obtains marketing approval in any of the countries within the Shionogi Territory. Shionogi was required to make an upfront payment to the Company of $90.0 million, and the Company will be eligible to receive additional payments of up to $485.0 million if certain regulatory and commercial milestones are achieved by Shionogi. The potential future milestone payments include up to $70.0 million for the achievement of specified regulatory milestones, up to $30.0 million for the achievement of specified commercialization milestones, and up to $385.0 million for the achievement of specified net sales milestones. The Company is eligible to receive tiered royalties on sales of zuranolone in the Shionogi Territory, if development efforts are

successful, with tiers averaging in the low to mid-twenty percent range, subject to other terms of the agreement. Shionogi has also granted to the Company certain rights to co-promote zuranolone in Japan. The Company maintains exclusive rights to develop and commercialize zuranolone outside of the Shionogi Territory. The upfront cash payment and any payments for milestones and royalties are non-refundable and non-creditable. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any milestone payments or any royalty payments from Shionogi.

The Company concluded that Shionogi meets the definition to be accounted for as a customer because the Company is delivering intellectual property and know-how rights for the zuranolone program in support of territories in which the parties are not jointly sharing the risks and rewards. In addition, the Company determined that the Shionogi collaboration met the requirements to be accounted for as a contract, including that it was probable that the Company will collect the consideration to which the Company was entitled in exchange for the goods or services that will be delivered to Shionogi.

In determining the appropriate amount of revenue to be recognized under Topic 606, the Company performed the following steps: (i) identified the promised goods or services in the contract; (ii) determined whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measured the transaction price, including the constraint on variable consideration; (iv) allocated the transaction price to the performance obligations; and (v) recognized revenue when (or as) the Company satisfied each performance obligation.

The Company determined that the performance obligations in the Shionogi collaboration agreement included the license to zuranolone and the supply of certain materials during the clinical development phase, which includes the supply of active pharmaceutical ingredient (“API”). The performance obligation related to the license to zuranolone was determined to be distinct from other performance obligations and therefore was a separate performance obligation for which control was transferred upon signing. The obligation to provide certain clinical materials, including API for use during the development period, was determined to be a separate performance obligation. Given that Shionogi is not obligated to purchase any minimum amount or quantities of commercial API, the supply of API to Shionogi for commercial use was determined to be an option for Shionogi, rather than a performance obligation of the Company at contract inception and will be accounted for if and when exercised. The Company also determined that there was no separate material right in connection with the supply of API for commercial use as the expected pricing was not at a discount. Given this fact pattern, the Company has concluded the agreement has two performance obligations.

Under the clinical supply agreement, the Company will manufacture and supply to Shionogi (i) clinical quantities of API reasonably required by Shionogi for the development of licensed products in the Shionogi territory under the collaboration and license agreement and (ii) quantities of drug product reasonably required for use by Shionogi in Phase 1 clinical trials of zuranolone in the Shionogi territory under the collaboration and license agreement, in the quantities agreed to by the parties. Collaboration revenue from the clinical supply agreement, which excludes the $90.0 million upfront payment, pertains to the clinical material sold under the terms of the clinical supply agreement. The Company records the costs related to the clinical supply agreement in research and development expense on its condensed consolidated statements of operations and comprehensive loss. For the nine months ended September 30, 2021 and 2020, the Company recognized no collaboration revenue from the Company’s agreement with Shionogi.

The Company completed the evaluation of the standalone selling prices of each of the performance obligations and determined that the standalone selling price of the license performance obligation was $90.0 million. The Company recognized the transaction price allocated to the license performance obligation of $90.0 million as revenue during the quarter upon delivery of the license to Shionogi and resulting ability of Shionogi to use and benefit from the license, which was in the three months ended June 30, 2018. The remaining transaction price related to the performance obligation for the supply of certain clinical material is not significant. The potential milestone payments that the Company is eligible to receive were excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of achievement. The Company will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

Biogen

In November 2020, the Company entered into the Biogen Collaboration Agreement to jointly develop and commercialize SAGE-217 products for MDD, PPD and other disorders and SAGE-324 products for essential tremor and other disorders. Concurrently, the Company also entered into a stock purchase agreement with BIMA (the "Biogen Stock Purchase Agreement") to purchase shares of the Company's common stock. The Biogen Collaboration Agreement became effective on December 28, 2020 (the "Effective Date").

Under the terms of the Biogen Collaboration Agreement, the Company granted Biogen co-exclusive licenses to develop and commercialize SAGE-217 products and SAGE-324 products (each, a "Product Class" and together, the "Licensed Products") in the U.S., an exclusive license to develop and commercialize SAGE-217 products in all countries of the world other than the U.S. and the Shionogi Territory, and an exclusive license to develop and commercialize SAGE-324 products in all countries of the world other than the U.S. The Company refers to the territories outside the U.S. to which Biogen has rights under the Biogen Collaboration Agreement with respect to the applicable Licensed Product as the "Biogen Territory".

In connection with the effectiveness of the Biogen Collaboration Agreement and the closing of the sale of shares to BIMA in December 2020, the Company received $1.5 billion in consideration, comprised of an upfront payment of $875.0 million and the $650.0 million purchase price for 6,241,473 newly issued shares of the Company's common stock (the "Biogen Shares"). As a result of the purchase of the Biogen Shares, Biogen has become a related party of the Company.

The Company is eligible to receive additional payments of up to $1.6 billion if certain regulatory and commercial milestones are achieved. The potential future milestone payments for SAGE-217 products include up to $475.0 million for the achievement of specified regulatory and commercial milestones and up to $300.0 million for the achievement of specified net sales milestones. The potential future milestone payments for SAGE-324 products include up to $520.0 million for the achievement of specified regulatory and commercial milestones and up to $300.0 million for the achievement of specified net sales milestones. The Company is also eligible to receive tiered royalties on net sales of SAGE-217 products and SAGE-324 products in the Biogen Territory at percentage rates ranging from the high teens to low twenties.

Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may never receive any milestone payments or any royalty payments under the Biogen Collaboration Agreement.

Development and commercialization activities in the U.S. will be conducted pursuant to plans agreed to by the Company and Biogen and overseen by a joint steering committee that will consist at all times of an equal number of representatives of each party. The Company and Biogen will share equally in the costs for development and commercialization, as well as the profits and losses, in the U.S., subject to the Company's opt-out right described below. Biogen will be solely responsible for all development activities and costs related to any development and commercialization of SAGE-217 products and SAGE-324 products for the Biogen Territory, and the Company will receive royalties on any sales in the Biogen Territory, as mentioned above.

The Company will supply API and bulk drug product for the Biogen Territory and API and final drug product for the U.S. to support development and commercialization activities. Biogen has the right to assume manufacturing responsibilities for API for the Biogen Territory at any time during the term of the agreement and will, within a reasonable period of time after the Effective Date, assume manufacturing responsibility for bulk drug product for the Biogen Territory.

Unless terminated earlier, the Biogen Collaboration Agreement will continue on a Licensed Product-by-Licensed Product and country-by-country basis until the date on which (a) in any country in the Biogen Territory, the royalty term has expired for all Licensed Products in a Product Class in such country, and (b) for the U.S., the parties agree to permanently cease to commercialize all Licensed Products in a Product Class. Biogen also has the right to terminate the Biogen Collaboration Agreement for convenience in its entirety, on a Product Class-by-Product Class basis or as to a particular region, upon advance written notice. The Company has an opt-out right to convert the co-exclusive licenses in the U.S. to an exclusive license to Biogen on a Product Class-by-Product Class basis. Following the exercise of the opt-out right, the Company would no longer share equally in the profits and losses in the U.S. and would be entitled to receive certain royalty payments at percentage rates ranging from the high teens to low twenties and additional sales milestones.

The Company concluded that the Biogen Collaboration Agreement and the Biogen Stock Purchase Agreement should be combined and treated as a single arrangement for accounting purposes as the agreements were entered into contemporaneously and in contemplation of one another. The Company determined that the combined agreements had elements that were within the scope of Topic 606 and Topic 808.

As of the Effective Date, the Company identified the following promises in the Biogen Collaboration Agreement that were evaluated under the scope of Topic 606: delivery of (i) a co-exclusive license for SAGE-217 products in the U.S.; (ii) an exclusive license for SAGE-217 products in the Biogen Territory; (iii) a co-exclusive license for SAGE-324 products in the U.S.; (iv) an exclusive license for SAGE-324 products in the Biogen Territory; (v) the clinical manufacturing supply of API and bulk drug product for SAGE-217 products in the Biogen Territory; and (vi) the clinical manufacturing supply of API and bulk drug product for SAGE-324 products in the Biogen Territory.

The Company also evaluated whether certain options outlined within the Biogen Collaboration Agreement represented material rights that would give rise to a performance obligation and concluded that none of the options convey a material right to Biogen and therefore are not considered separate performance obligations within the Biogen Collaboration Agreement.

The Company assessed the above promises and determined that the co-exclusive licenses for SAGE-217 products and SAGE-324 products in the U.S. are reflective of a vendor-customer relationship and therefore represent performance obligations within the scope of Topic 606. The co-exclusive license for SAGE-217 products and SAGE-324 products in the U.S. are considered functional intellectual property and distinct from other promises under the contract. The exclusive licenses for SAGE-217 products and SAGE-324 products in the Biogen Territory are considered functional licenses that are distinct in the context of the Biogen Collaboration Agreement as Biogen can benefit from the licenses on its own or together with other readily available resources. As the co-exclusive licenses in the U.S. and the exclusive licenses in the Biogen Territory are delivered at the same time, they are considered one performance obligation at contract inception. The clinical manufacturing supply of API and bulk drug product for SAGE-217 products and SAGE-324 products for the Biogen Territory are considered distinct in the context of the Biogen Collaboration Agreement as Biogen can benefit from the manufacturing services together with the licenses transferred by the Company at the inception of the agreement. Therefore, each represents a separate performance obligation within a contract with a customer under the scope of Topic 606 at contract inception.

The Company considers the collaborative activities associated with the co-development, co-commercialization, and co-manufacturing of SAGE-217 products and SAGE-324 products in the U.S. to be separate units of account within the scope of Topic 808 as the Company and Biogen are both active participants in the development and commercialization activities and are exposed to significant risks and rewards that are dependent on the development and commercial success of the activities in the arrangement. The Company has determined that the supply of API and bulk drug product for the Biogen Territory and API and final drug product for the U.S. to Biogen will be classified as collaboration revenue in the condensed consolidated statements of operations and comprehensive loss. During the nine months ended September 30, 2021, there were no collaboration revenues recognized related to the Biogen Collaboration Agreement.

Payments to or reimbursements from Biogen related to the co-development, co-commercialization, and co-manufacturing activities and the agreement of the parties to share equally the cost of these activities will be accounted for as an increase to or reduction of research and development expenses or selling, general and administrative expenses, depending on the nature of the activity.

During the three and nine months ended September 30, 2021, the Company recorded a net reimbursement of $24.2 million and $72.6 million, respectively, for the amount due from Biogen as a reduction of the related operating expense categories in the condensed consolidated statement of operations and comprehensive loss. As of September 30, 2021, the Company recorded a Collaboration Receivable – Related Party of $24.2 million in the condensed consolidated balance sheet. During the three and nine months ended September 30, 2021, no payments were made to Biogen and the Company received $48.4 million from Biogen for the amounts due for the six months ended June 30, 2021.

The following table summarizes expenses related to the Biogen Collaboration Agreement that were incurred by the Company and the related reimbursement from Biogen, reflected by category of operating expenses:

	Three Months Ended September 30, 2021	Nine Months Ended September 30, 2021
	(in thousands)	
Expenses related to the Biogen Collaboration Agreement incurred by Sage	$ 50,950	$ 149,653
Net reimbursement from Biogen reflected in the condensed consolidated statement of operations and comprehensive loss:		
Research and development expenses	(21,634)	(63,843)
Selling, general and administrative expenses	(2,551)	(8,780)
Total net expenses related to the Biogen Collaboration Agreement in the condensed consolidated statement of operations and comprehensive loss	$ 26,765	$ 77,030

The Company determined the transaction price under Topic 606 at the inception of the Biogen Collaboration Agreement to be $1.1 billion, consisting of the upfront payment of $875.0 million plus $232.5 million in excess proceeds from the equity investment under the Biogen Stock Purchase Agreement, when measured at fair value, plus future variable consideration for manufacturing supply of clinical API and bulk drug product for the Biogen Territory. The amount of variable consideration related to the future manufacturing services was not material. The Company determined that any variable consideration related to clinical development and regulatory milestones is deemed to be fully constrained and therefore excluded from the transaction price due to the high degree of uncertainty and risk associated with these potential payments, as the Company determined that it could not assert that it was probable that a significant reversal in the amount of cumulative revenue recognized will not occur. The Company also determined that royalties and sales milestones relate solely to the licenses of intellectual property and are therefore excluded from the transaction price under the sales- or usage-based royalty exception of Topic 606. Revenue related to these royalties and sales milestones will only be recognized when the associated sales occur, and relevant thresholds are met.

As noted above, the Company identified three performance obligations in the Biogen Collaboration Agreement: (i) the delivery of the co-exclusive licenses for SAGE-217 products and SAGE-324 products in the U.S. and the exclusive licenses for SAGE-217 products and SAGE-324 products in the Biogen Territory; (ii) the clinical manufacturing supply of API and bulk drug product for SAGE-217 products in the Biogen Territory; and (iii) the clinical manufacturing supply of the API and bulk drug product for SAGE-324 products in the Biogen Territory. The selling price of each performance obligation in the Biogen Collaboration Agreement was determined based on the Company's SSP with the objective of determining the price at which it would sell such an item if it were to be sold regularly on a standalone basis. The Company allocated the variable consideration related to the manufacturing obligations to the future clinical supply of SAGE-217 products and SAGE 324 products in the Biogen Territory and the remaining fixed consideration to the license obligation. The variable consideration related to the manufacturing obligations was not material. As such, the entirety of the $1.1 billion fixed consideration of the transaction price has been allocated to the transfer of the co-exclusive licenses for SAGE-217 products and SAGE-324 products in the U.S. and the exclusive licenses for SAGE-217 products and SAGE-324 products in the Biogen Territory. The Company recognizes revenue for the license performance obligations at a point in time, that is upon transfer of the licenses to Biogen. As control of these licenses was transferred on the Effective Date and Biogen could begin to use and benefit from the licenses, the Company recognized $1.1 billion of license revenue during the year ended December 31, 2020 under the Biogen Collaboration Agreement. The Company will recognize revenue for the clinical manufacturing supply obligations at a point in time, that is upon the delivery of the supply to Biogen.

Accounting for the Biogen Stock Purchase Agreement

In connection with the execution of the Biogen Collaboration Agreement, the Company and BIMA entered into the Biogen Stock Purchase Agreement. Pursuant to the Biogen Stock Purchase Agreement, the Company sold the Biogen Shares to BIMA at a price of approximately $104.14 per share, which represented a 40 percent premium over the 30-day volume-weighted average share price as of the last trading day prior to the date the Biogen Collaboration Agreement and Biogen Stock Purchase Agreement were executed in November 2020, for aggregate consideration of $650.0 million. The sale of the shares to BIMA closed on December 31, 2020.

The Biogen Stock Purchase Agreement includes certain standstill provisions, lock-up restrictions, and a voting agreement with respect to the Biogen Shares. Pursuant to the terms of the Biogen Stock Purchase Agreement, BIMA has agreed not to, and to cause its affiliates not to, directly or indirectly acquire the Company's securities, seek or propose a tender or exchange offer or merger between the Company and Biogen, solicit proxies or consents with respect to any matter, or undertake other specified actions, in each case subject to specified conditions. The standstill restrictions terminate on the earliest of (i) a specified regulatory milestone under the Biogen Collaboration Agreement, (ii) the date one year following the termination of the Biogen Collaboration Agreement and (iii) the seventh anniversary of the Effective Date. BIMA has also agreed not to, and to cause its affiliates not to, sell or transfer any of the Biogen Shares for a period of eighteen months from the closing of the sale of the Biogen Shares and to limit sales and transfers of the Biogen Shares for an additional eighteen-month period, in each case subject to specified conditions and exceptions.

The Company determined the fair value of the common shares issued using an option pricing valuation model to take into consideration the holding period restrictions. The fair value of the Company's common stock was considered a level 2 fair value measurement within the fair value hierarchy. The most significant assumptions within the model are the Company's stock price, the term of the restrictions and the stock price volatility, which is based upon a blend of historical and implied volatility of the Company's stock. Based on the fair value adjustments made by management, the fair value of the shares issued was determined to be $417.5 million, which was $232.5 million less than the proceeds received from BIMA for the issuance of the Company's common stock under the Biogen Stock Purchase Agreement. As such, the $232.5 million in excess proceeds has been included in the $1.1 billion transaction price of the Biogen Collaboration Agreement determined above.

7. Common Stock

On December 31, 2020, the Company completed the sale of 6,241,473 shares of its common stock in a private placement to BIMA at a price of approximately $104.14 per share, resulting in aggregate gross proceeds to the Company of $650.0 million. For additional information, refer to Note 6, *Collaboration Agreements*.

8. Stock-Based Compensation

Equity Plans

On July 2, 2014, the stockholders of the Company approved the 2014 Stock Option and Incentive Plan (the "2014 Plan"), which became effective immediately prior to the completion of the Company's IPO. The 2014 Plan provides for the grant of restricted stock awards, restricted stock units, incentive stock options and non-statutory stock options. The 2014 Plan replaced the Company's 2011 Stock Option and Grant Plan (the "2011 Plan"). The Company no longer grants stock options or other awards under its 2011 Plan, but any stock options outstanding under the 2011 Plan remain outstanding and effective in accordance with their terms.

The 2014 Plan provides for an annual increase, to be added on the first day of each fiscal year, by up to 4% of the Company's outstanding shares of common stock as of the last day of the prior year. On January 1, 2021, 2,332,336 shares of common stock, representing 4% of the Company's outstanding shares of common stock as of December 31, 2020, were added to the 2014 Plan.

On December 15, 2016, the Board of Directors of the Company (the "Board") approved the 2016 Inducement Equity Plan (as amended and restated, the "2016 Plan"). The 2016 Plan provides for the grant of equity awards to individuals who have not previously been an employee or a non-employee director of the Company to induce them to accept employment and to provide them with a proprietary interest in the Company. On September 20, 2018, the Board amended the 2016 Plan to increase the total number of shares reserved for issuance by 1,200,000 shares.

Terms of equity grants, including vesting requirements, are determined by the Board or the Compensation Committee of the Board, subject to the provisions of the applicable plan. Stock options granted by the Company that are not performance-based are considered time-based because they generally vest based on the continued service of the grantee with the Company during a specified period following grant. These awards, when granted to employees, generally vest ratably over four years, with 25% cliff vesting at the one-year anniversary. All stock option awards expire 10 years after the date of grant.

As of September 30, 2021, the total number of shares underlying outstanding awards under all equity plans was 8,644,442 and the total number of shares available for future issuance under all equity plans was 5,687,262 shares.

Restricted Stock Units

The table below summarizes activity relating to time-based restricted stock units and performance restricted stock units:

	Shares
Outstanding as of December 31, 2020	957,695
Granted	420,161
Vested	(218,017)
Forfeited	(153,121)
Outstanding as of September 30, 2021	1,006,718

During the three months ended June 30, 2020, the Company granted 550,890 time-based restricted stock units to certain employees of the Company. These time-based restricted stock units will vest over two years, with 25% vesting at the one-year anniversary of the grant date and 75% vesting at the two-year anniversary of the grant date, which was in

April 2021 and will be in April 2022, respectively. During the three months ended June 30, 2021, 113,941 time-based restricted stock units vested, and the fair value of the restricted stock units that vested was $8.8 million.

During the nine months ended September 30, 2021, the Company granted no time-based restricted stock units.

During the three months ended September 30, 2021 and 2020, the Company granted 47,040 and 11,800 performance restricted stock units to employees of the Company, respectively; and during the nine months ended September 30, 2021 and 2020, the Company granted 420,161 and 444,616 performance restricted stock units to employees of the Company, respectively. The performance restricted stock units granted during the nine months ended September 30, 2021 are related to the achievement of a certain regulatory development milestone related to product candidates and commercial milestones. The performance restricted stock units granted during the nine months ended September 30, 2020 are related to the achievement of certain clinical development milestones related to product candidates and commercial milestones.

Recognition of stock-based compensation expense associated with performance restricted stock units commences when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

During the three months ended June 30, 2021, one milestone for outstanding performance restricted stock units was achieved. The fair value of the performance restricted stock units that vested upon achievement was $6.1 million and the Company recognized stock-based compensation expense related to this milestone of $3.8 million. 39% of the performance restricted stock units that were granted during the year ended December 31, 2020 included this milestone as a vesting condition.

During the three months ended September 30, 2021, the Company considered probable the achievement of a specific clinical milestone which was the criteria for vesting of certain performance restricted stock units but which had not been met as of September 30, 2021. Therefore, $12.6 million of stock-based compensation expense was recognized related to these awards for the three months ended September 30, 2021. Performance restricted stock units with this milestone were granted during the years ended December 31, 2020 and 2019.

No performance restricted stock units vested during the three months ended September 30, 2021 and the nine months ended September 30, 2020.

At September 30, 2021, 1,006,718 time-based restricted stock units and performance restricted stock units were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was $64.7 million. Of that amount, $12.6 million was recognized during the three months ended September 30, 2021 for the milestone that was considered probable.

Stock Option Rollforward

The table below summarizes activity related to time-based and performance-based stock options:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2020	7,157,830	$ 91.41	6.91	$ 167,242
Granted	1,967,133	$ 82.14		
Exercised	(271,430)	$ 43.95		
Forfeited	(1,215,809)	$ 121.85		
Outstanding as of September 30, 2021	7,637,724	$ 85.86	6.90	$ 20,583
Exercisable as of September 30, 2021	4,344,625	$ 84.79	5.58	$ 19,215

At September 30, 2021, the Company had unrecognized stock-based compensation expense related to its unvested time-based stock option awards of $115.8 million, which is expected to be recognized over the remaining weighted average vesting period of 2.25 years.

The intrinsic value of stock options exercised during the nine months ended September 30, 2021 and 2020 was $8.0 million and $0.9 million, respectively.

Performance-Based Stock Options

Recognition of stock-based compensation expense associated with performance-based stock options commences when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

During the three months ended March 31, 2021, in connection with the hiring of its chief executive officer, the Company granted to its chief executive officer 650,000 stock options to purchase shares of common stock that contain performance-based vesting criteria which will vest upon the achievement of certain regulatory and commercial milestones.

During the year ended December 31, 2020, the Company granted no stock options to employees to purchase shares of common stock that contained performance-based vesting criteria.

As of September 30, 2021 and 2020, for performance-based stock option grants that were outstanding, the achievement of the milestones that had not been met that are the criteria for vesting of performance-based stock options was considered not probable, and therefore no expense has been recognized related to these awards in the nine months ended September 30, 2021 and 2020, respectively.

As of September 30, 2021, 908,726 performance-based stock options were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was $26.2 million.

Stock-Based Compensation Expense

Stock-based compensation expense recognized during the three and nine months ended September 30, 2021 and 2020 was as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands)			
Research and development	$ 17,864	$ 9,927	$ 40,598	$ 32,270
Selling, general and administrative	16,478	10,181	43,383	41,192
Restructuring	—	—	—	1,788
	$ 34,342	$ 20,108	$ 83,981	$ 75,250

Stock-based compensation expense recognized during the three and nine months ended September 30, 2021 and 2020 by award type was as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
	(in thousands)			
Stock options	$ 19,516	$ 18,797	$ 60,740	$ 72,434
Restricted stock units	14,563	1,066	22,538	1,815
Employee stock purchase plan	263	245	703	1,001
	$ 34,342	$ 20,108	$ 83,981	$ 75,250

The stock-based compensation expense recorded for the restructuring in the nine months ended September 30, 2020 is the incremental amount related to modifying the exercise period for outstanding, vested option grants that had been made to employees whose employment was terminated in the restructuring.

The weighted average grant date fair value per share of stock options granted under the Company's stock option plans during the nine months ended September 30, 2021 and 2020 was $53.42 and $37.04, respectively.

9. Net Loss Per Share

Basic and diluted net loss per share was calculated as follows for the three and nine months ended September 30, 2021 and 2020:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Basic net loss per share:				
Numerator:				
Net loss (in thousands)	$ (130,171)	$ (105,735)	$ (333,180)	$ (368,822)
Denominator:				
Weighted average common stock outstanding —basic	58,819,548	51,981,468	58,593,743	51,938,923
Dilutive effect of shares of common stock equivalents resulting from common stock options and restricted stock units	—	—	—	—
Weighted average common stock outstanding —diluted	58,819,548	51,981,468	58,593,743	51,938,923
Net loss per share—basic and diluted	$ (2.21)	$ (2.03)	$ (5.69)	$ (7.10)

The following common stock equivalents outstanding as of September 30, 2021 and 2020 were excluded from the calculation of diluted net loss per share for the periods presented because including them would have been anti-dilutive:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Stock options	6,728,998	6,945,435	6,728,998	6,945,435
Restricted stock units	310,418	489,495	310,418	489,495
Employee stock purchase plan	15,437	16,396	15,437	16,396
	7,054,853	7,451,326	7,054,853	7,451,326

Stock options and restricted stock units that are outstanding and contain performance-based vesting criteria for which the performance conditions have not been met are excluded from the calculation of common stock equivalents outstanding.

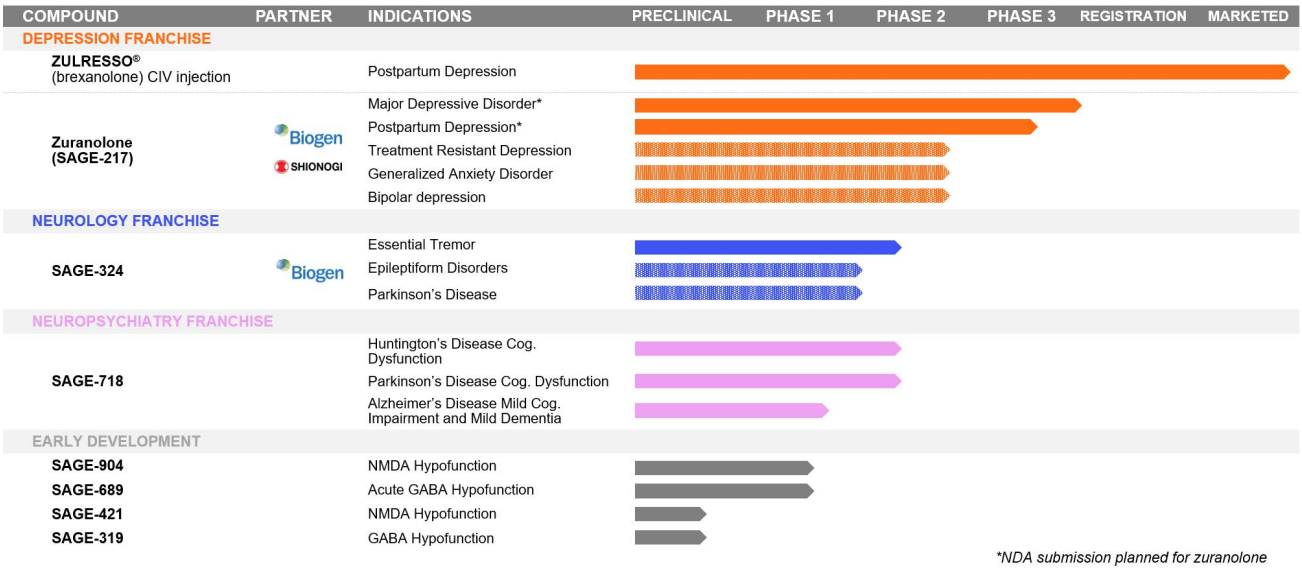
Item 2.Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with our condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q, or Quarterly Report, and the audited financial statements and related notes contained in our Annual Report on Form 10-K for the year ended December 31, 2020, or Annual Report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. We caution you that forward-looking statements are not guarantees of future performance, and that our actual results of operations, financial condition and liquidity, and the developments in our business and the industry in which we operate, may differ materially from the results discussed or projected in the forward-looking statements contained in this Quarterly Report. We discuss risks and other factors that we believe could cause or contribute to these potential differences elsewhere in this report, including under Part II, Item 1A, "Risk Factors" and under "Cautionary Note Regarding Forward-Looking Statements" in this Quarterly Report. In addition, even if our results of operations, financial condition and liquidity, and the developments in our business and the industry in which we operate are consistent with the forward-looking statements contained in this Quarterly Report, they may not be predictive of results or developments in future periods. We caution readers not to place undue reliance on any forward-looking statements made by us, as such statements speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the Securities and Exchange Commission, or SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Overview

We are a biopharmaceutical company committed to developing and commercializing novel medicines with the potential to transform the lives of people with debilitating disorders of the brain. Our first product, ZULRESSO® (brexanolone) CIV injection, is approved in the U.S. for the treatment of postpartum depression, or PPD, in adults. We have a portfolio of other product candidates with a current focus on modulating two critical central nervous system, or CNS, receptor systems, GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function via activation of $GABA_A$ receptors. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. Dysfunction in these systems is implicated in a broad range of CNS disorders. We are currently targeting diseases and disorders of the brain with three key focus areas: depression, neurology and neuropsychiatry.

The following table summarizes the status of our product and product candidate portfolio as of the filing date of this Quarterly Report.



Our first product, ZULRESSO, is a proprietary intravenous formulation of brexanolone, approved in the U.S. as a treatment for PPD in adults. Brexanolone is chemically identical to allopregnanolone, a naturally occurring neuroactive steroid that acts as a positive allosteric modulator of GABAA receptors. We launched ZULRESSO commercially in the U.S. for the treatment of PPD in June 2019. We plan to initiate an open-label clinical trial designed to demonstrate the safe-use administration of ZULRESSO in a patient's home in the treatment of PPD, which is expected to enroll an estimated 50 patients and is anticipated to be completed in 2022.

Our next most advanced product candidate is zuranolone (SAGE-217), a novel oral compound being developed for certain affective disorders, including major depressive disorder, or MDD, and PPD. Zuranolone is a neuroactive steroid that, like brexanolone, is a positive allosteric modulator of GABAA receptors, targeting both synaptic and extrasynaptic GABAA receptors. To date, we have completed four pivotal clinical trials of zuranolone, three in MDD and one in PPD. The completed pivotal trial evaluating zuranolone in the treatment of PPD and two of the three completed pivotal trials evaluating zuranolone in the treatment of MDD met their primary endpoints, including the WATERFALL Study, a pivotal, Phase 3, double-blind, randomized, placebo-controlled study evaluating the efficacy and safety of zuranolone 50 mg in adults 18 to 64 years with MDD, for which we announced results in June 2021. We plan to submit a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, in the second half of 2022 seeking approval of zuranolone in the treatment of MDD. An additional filing seeking approval of zuranolone for PPD is anticipated in the first half of 2023, after the completion of the ongoing SKYLARK Study in PPD.

Two Phase 3 placebo-controlled clinical trials of zuranolone 50 mg, the CORAL Study, designed to demonstrate a rapid onset of depression relief when zuranolone is co-initiated with a standard antidepressant therapy in MDD, and the SKYLARK Study, a placebo-controlled trial evaluating a two-week course of zuranolone in women with PPD, with additional short-term follow-up, are ongoing. The CORAL Study is fully enrolled and closed to further screening, with topline data expected in early 2022. We expect to report topline results from the SKYLARK Study in mid-2022. An open-label Phase 3 clinical trial of zuranolone in MDD, known as the SHORELINE Study, is also ongoing. In March 2021, we reported topline 12-month data from the completed 30 mg cohort and interim topline data from the 50 mg cohort of the SHORELINE Study, which is designed to evaluate the safety and tolerability of zuranolone in adults for up to one year. We expect to report a data cut from the 50 mg cohort of the SHORELINE Study in late 2021.

We are jointly developing zuranolone and another of our late-stage compounds, SAGE-324, in the U.S. with Biogen MA Inc., or BIMA, and Biogen International GmbH, or, together with BIMA, Biogen, under a collaboration and license agreement, or the Biogen Collaboration Agreement, that became effective in December 2020. Under the Biogen Collaboration Agreement, we will also jointly commercialize products containing zuranolone, which we refer to as Licensed 217 Products, and products containing SAGE-324, which we refer to as Licensed 324 Products, with Biogen in the U.S. if our development efforts are successful. We refer to the Licensed 217 Products and Licensed 324 Products collectively as the Licensed Products. In addition, we have granted Biogen sole rights to develop and commercialize the Licensed Products outside the U.S., other than in Japan, Taiwan and South Korea, or the Shionogi Territory, with respect to zuranolone, where we have granted such rights to Shionogi & Co., Ltd., or Shionogi. Shionogi recently completed a Phase 2 clinical trial of zuranolone for the treatment of patients with moderate to severe MDD in Japan. We refer to the territories outside the U.S. to which Biogen has rights under the Biogen Collaboration Agreement with respect to the applicable Licensed Product as the Biogen Territory.

In addition to zuranolone, we have a portfolio of other novel compounds that target GABAA receptors, including SAGE-324. SAGE-324 is a novel GABAA receptor positive allosteric modulator intended for chronic oral dosing. In April 2021, we announced that our placebo-controlled Phase 2 KINETIC Study evaluating SAGE-324 in the treatment of adults with essential tremor had achieved its primary endpoint. We intend to initiate a Phase 2 dose-ranging clinical trial of SAGE-324 in patients with essential tremor in late 2021. Additional development plans for SAGE-324 will be determined as part of our strategic collaboration with Biogen. We believe SAGE-324 also has potential for the treatment of a number of other neurological conditions, including epilepsy and Parkinson's disease.

Our second area of focus for development is novel compounds that target the NMDA receptor. The lead product candidate selected in this area is SAGE-718, an oxysterol-based positive allosteric modulator of the NMDA receptor, which we are exploring in certain cognition-related disorders associated with NMDA receptor dysfunction, including cognition dysfunction associated with diseases such as Huntington's disease, Parkinson's disease and Alzheimer's disease. In September 2021, the FDA granted SAGE-718 Fast Track designation as a potential treatment for Huntington's disease. We plan to initiate a placebo-controlled Phase 2 clinical trial with SAGE-718 in patients with early to moderate Huntington's disease in late 2021.

In May 2021, we announced results from the first part of a Phase 2a open-label study of SAGE-718 evaluating patients with Parkinson's disease cognitive dysfunction, known as the PARADIGM Study. A 4-week dosing cohort in the PARADIGM Study is ongoing to gather additional data in the Parkinson's disease patient population. In this cohort, up to 20 additional patients aged 50 to 75 years old with mild cognitive impairment due to Parkinson's disease will receive 3 mg of SAGE-718 for four weeks, and will continue to be assessed for a period of time after treatment is complete. We plan to initiate a placebo-controlled Phase 2 clinical trial with SAGE-718 in patients with Parkinson's disease cognitive impairment in 2022. We are also conducting a Phase 2a open-label clinical trial of SAGE-718 in patients with Alzheimer's disease mild cognitive impairment and mild dementia, known as the LUMINARY Study. We expect to report topline data from the LUMINARY Study in late 2021.

We have other programs at earlier stages of development with a focus on both acute and chronic brain health disorders. Our early-stage GABAA modulators include SAGE-689, for which we have initiated Phase 1 development as a potential intramuscular therapy for disorders associated with acute GABA hypofunction, and SAGE-319, intended to be studied as an oral therapy for potential use in disorders of social interaction and for which the IND-enabling work has begun. Our early-stage NMDA modulators include SAGE-904, in Phase 1 development as a potential oral therapy for disorders associated with NMDA hypofunction, and SAGE-421, intended to be studied as a potential oral therapy for certain neurodevelopmental disorders and cognitive recovery and rehabilitation. We expect to complete ongoing Phase 1 single ascending dose clinical trials of SAGE-689 and SAGE-904 in late 2021. Results from Phase 1 studies will inform further development of these programs. We expect to continue our work on allosteric modulation of the GABAA and NMDA receptor systems in the brain. The GABAA and NMDA receptor systems are broadly accepted as impacting many psychiatric and neurological disorders, spanning disorders of mood, seizure, cognition, anxiety, sleep, pain, and movement, among others. We believe that we may have the opportunity to develop molecules from our internal portfolio with the goal of addressing a number of these disorders in the future. We believe that we may also have the opportunity to use our scientific approach to explore targets beyond the GABAA and NMDA receptor systems and to develop compounds in areas of unmet need outside of brain health.

We began to generate revenue from product sales in the second quarter of 2019 in conjunction with the launch of our first product, ZULRESSO, in June 2019.

We have incurred net losses in each year since our inception, except for net income of $606.1 million for the year ended December 31, 2020, reflecting revenue recognized under the Biogen Collaboration Agreement, and we had an accumulated deficit of $1.4 billion as of September 30, 2021. Our net loss was $333.2 million for the nine months ended September 30, 2021. These losses have resulted principally from costs incurred in connection with research and development activities and selling, general and administrative costs associated with our operations and our commercial build. We expect to incur significant expenses and increasing operating losses for the foreseeable future.

We expect that our expenses will increase significantly in the foreseeable future in connection with our ongoing activities, if and as we:

- complete ongoing Phase 3 clinical trials of zuranolone in MDD and PPD; advance our regulatory, pre-launch and launch readiness activities with respect to zuranolone, including activities focused on the planned filing of an NDA for zuranolone in MDD in the U.S. in the second half of 2022, and the planned additional filing for zuranolone in PPD in the U.S. in the first half of 2023; and potentially advance development of zuranolone in additional indications as part of our strategic collaboration with Biogen;
- continue our commercialization efforts with respect to ZULRESSO in the treatment of PPD in the U.S., with a primary focus on geographies that have existing, active ZULRESSO treating sites;
- initiate additional development activities with SAGE-324, including the planned dose-ranging Phase 2 clinical trial with SAGE-324 in essential tremor, with potential future development in epilepsy, Parkinson's disease, and other neurological conditions, as part of our strategic collaboration with Biogen;
- initiate planned placebo-controlled Phase 2 clinical trials of SAGE-718 in patients with early to moderate Huntington's disease and in patients with Parkinson's disease cognitive impairment; and complete the Phase 2a open-label LUMINARY Study of SAGE-718 in patients with Alzheimer's disease mild cognitive impairment and mild dementia;
- support our collaboration with Biogen with respect to zuranolone and SAGE-324 in the U.S., and support Biogen's development of zuranolone and SAGE-324 in Biogen's licensed territories outside the U.S. and Shionogi's development of zuranolone in the Shionogi Territory;
- advance SAGE-689 and SAGE-904 in Phase 1 clinical development;
- continue our research and development efforts to evaluate the potential for our existing product candidates in the treatment of additional indications or in new formulations;
- identify new targets, and generate and test new compounds and product candidates, with a focus on indications where we believe we can make well-informed, rapid go/no-go decisions, with the goal of developing a diversified portfolio of assets with differentiated features;
- prepare and file new drug applications with the U.S. Food and Drug Administration, or FDA, and conduct pre-launch activities with respect to any of our other product candidates that we believe have been successfully developed;
- prepare to commercialize, and ultimately commercialize, any product candidates for which we obtain regulatory approval, including the manufacture of commercial supplies;
- as our development efforts progress, add personnel, including personnel to support product development and ongoing and future commercialization efforts;
- evaluate the market potential and regulatory pathways for our product candidates beyond zuranolone and SAGE-324 in the European Union and other countries outside the U.S., and determine how best to move forward where and when it may make business and strategic sense;

- continue to build, maintain, defend, leverage, and expand our intellectual property portfolio, including by utilizing the strengths of our proprietary chemistry platform and scientific know-how to expand our portfolio of new chemical entities to lessen our long-term reliance on the success of any one program and to facilitate long-term growth; and
- continue to explore opportunities to establish agreements or alliances with other pharmaceutical companies, at the appropriate time, where we believe a collaboration will add significant value to our efforts, including through capabilities, infrastructure, speed or financial contributions, or to acquire new compounds, product candidates or products if we believe such opportunities will help us achieve our goals or meet other strategic objectives.

Until such time that we can generate significant revenue from product sales, if ever, we expect to finance our operations primarily through a combination of revenue, equity or debt financings and other sources, including our collaborations with Biogen and Shionogi and potential future collaborations. We may not be successful in our commercialization of ZULRESSO or any other product, and may not generate meaningful revenue or revenue at the levels or on the timing necessary to support our investment and goals. We may never successfully complete development of any of our current or future product candidates, file for or obtain necessary regulatory approval for such product candidates, or achieve commercial viability for any resulting approved product. We may not obtain or maintain adequate patent protection or other exclusivity for our products or product candidates. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital if and when needed would have a negative impact on our financial condition and on our ability to pursue our business strategy. Arrangements with our existing collaborators have required us to relinquish rights to certain of our technologies or product candidates, and any future collaborations may require us to relinquish additional rights. We will need to generate significant revenue to achieve profitability, and we may never do so.

We expect that our existing cash, cash equivalents and marketable securities as of September 30, 2021, will enable us to fund our operating expenses and capital expenditure requirements, based on our current operating plan, for at least the next 12 months from the filing date of this Quarterly Report. See “—Liquidity and Capital Resources”.

Financial Operations Overview

Revenue

We began to generate revenue from product sales in the second quarter of 2019 in conjunction with the launch of our first product, ZULRESSO, in June 2019.

Our revenue from sales of ZULRESSO has been negatively impacted by significant barriers arising from the complex requirements for treatment, and, more recently, by the spread of COVID-19 in the U.S. ZULRESSO is administered as a continuous infusion given over two and a half days. Because of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness during the ZULRESSO infusion, ZULRESSO must be administered only in a medically-supervised healthcare setting that has been certified under a Risk Evaluation and Mitigation Strategies, or REMS, program and meets the other requirements of the REMS program, including requirements related to monitoring of the patient during the infusion. The actions required for a healthcare setting to be ready and willing to treat women with PPD are complex and time-consuming. These actions include: becoming REMS-certified; achieving formulary approvals; establishing protocols for administering ZULRESSO; and securing satisfactory reimbursement. Sites must often negotiate reimbursement on a payor-by-payor basis under commercial coverage. These requirements have created significant barriers to treatment, and are expected to continue to limit future revenue growth. These barriers have been compounded by the COVID-19 pandemic. The spread of COVID-19 in the U.S. resulted in a significant number of sites of care pausing treatment of new patients with ZULRESSO and potential new sites of care pausing site activation activities for a period of time. We believe concerns about exposure to the virus or its variants have also caused a significant reduction in the number of women with PPD seeking treatment with ZULRESSO and in physicians willing to prescribe it. Given continuing concerns about the COVID-19 pandemic across the country, including as a result of the spread of variants and “breakthrough” cases among fully-vaccinated people, we expect the significant adverse impact of the pandemic on ZULRESSO revenues to continue for the foreseeable future. The scope and timing of the expected negative impact will depend on, among other factors, the scope and duration of the pandemic; the effectiveness of vaccination campaigns, vaccine mandates, and other efforts to control the pandemic; the duration of the vaccines’ efficacy

against COVID-19 and its variants; the duration and severity of any restrictive measures taken to curb the spread of COVID-19; and the impact of the pandemic on our customers and vendors.

In April 2020, we implemented a workforce reduction that primarily affected the ZULRESSO commercial operation and related support functions, including eliminating the entirety of our salesforce at that time. While we remain committed to working with healthcare providers and women with PPD seeking access to ZULRESSO and plan to continue to evaluate opportunities to raise awareness and help reduce hurdles to appropriate treatment, our ongoing commercial efforts, including our small account management field-based team and a small number of sales representatives now in place, are primarily focused on geographies that have existing, active ZULRESSO treating sites. We expect that this approach to our commercial efforts may continue to substantially limit the revenue opportunity for ZULRESSO.

We expect that ZULRESSO revenues are likely to fluctuate quarter to quarter. We will not generate revenue from other products unless and until we or any of our collaborators successfully develop, obtain regulatory approval of, and commercialize one of our current or future product candidates. If we enter into additional collaboration agreements with third parties for our product candidates, we may generate revenue from those collaborations. We expect that revenue, if any, that we may generate under our existing or future collaboration agreements will fluctuate from quarter to quarter as a result of the timing and amount of license fees, payments for clinical materials or manufacturing services, milestone payments, royalties paid to us and our share of collaboration profits or losses resulting from sales of any commercialized products, and other payments.

In June 2018, we entered into a strategic collaboration with Shionogi for the clinical development and commercialization of zuranolone for the treatment of MDD and other potential indications in the Shionogi Territory. Under the terms of the agreement, Shionogi is responsible for all clinical development, regulatory filings and commercialization and manufacturing of zuranolone for MDD, and potentially other indications, in the Shionogi Territory. In October 2018, we also entered into a supply agreement with Shionogi for zuranolone clinical material. To date, revenue from our collaboration with Shionogi has come from an initial, upfront license fee upon execution of the collaboration agreement of $90.0 million, which was recorded as collaboration revenue in the year ended December 31, 2018, and for the supply of active pharmaceutical agreement, or API, for Shionogi's clinical trials.

In November 2020, we entered into the Biogen Collaboration Agreement with Biogen for the development, manufacture and commercialization of the Licensed Products. In connection with the execution of the Biogen Collaboration Agreement, we also entered into a stock purchase agreement for the sale and issuance to BIMA of 6,241,473 shares of our common stock. The Biogen Collaboration Agreement became effective on December 28, 2020, and the sale of the common stock under the stock purchase agreement closed on December 31, 2020. As a result of this purchase of common stock by BIMA, Biogen has become a related party of ours. Under the terms of the Biogen Collaboration Agreement, we will jointly develop and, if successful, commercialize the Licensed Products in the U.S., and Biogen solely will develop and commercialize the Licensed Products in the Biogen Territory. We and Biogen have agreed to share equally all costs for activities under the Biogen Collaboration Agreement solely for the U.S. Biogen is solely responsible for all costs for activities under the Biogen Collaboration Agreement in the Biogen Territory. In the year ended December 31, 2020, we recorded collaboration revenue of $1.1 billion, consisting of an upfront payment of $875.0 million plus $232.5 million in excess proceeds from the equity investment under the stock purchase agreement, when measured at fair value. For further discussion regarding the accounting for the Biogen Collaboration Agreement, please refer to Note 6, *Collaboration Agreements*, in the accompanying Notes to Condensed Consolidated Financial Statements appearing in Part I, Item 1 of this Quarterly Report.

Collaborative Arrangements

We analyze our collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of Accounting Standards Codification, or ASC, Topic 808, *Collaborative Arrangements*, or Topic 808. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of Topic 808 that contain multiple elements, we first determine which elements of the collaboration are deemed to be within the scope of Topic 808 and which elements of the collaboration are more reflective

of a vendor-customer relationship and therefore within the scope of ASC Topic 606, *Revenue from Contracts with Customers*, or Topic 606. For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For those elements of the arrangement that are accounted for pursuant to Topic 606, we apply the five-step model and present the arrangement as collaboration revenue in the condensed consolidated statements of operations and comprehensive loss. For further discussion regarding the accounting for the Biogen Collaboration Agreement, please refer to Note 6, *Collaboration Agreements*, in the accompanying Notes to Condensed Consolidated Financial Statements appearing in Part I, Item 1 of this Quarterly Report.

For collaboration arrangements that are within the scope of Topic 808, we evaluate the income statement classification for presentation of amounts due from or owed to other participants associated with multiple activities in a collaboration arrangement based on the nature of each separate activity. Payments or reimbursements that are the result of a collaborative relationship, instead of a customer relationship, such as co-development and co-commercialization activities, are recorded as research and development expense or selling, general and administrative expense in the event of a payment to the collaborative partner in a period, or a reduction to these expense line items in the event of a reimbursement from the collaboration partner in a period, as appropriate.

Cost of Goods Sold

Cost of goods sold includes direct and indirect costs related to the manufacturing and distribution of ZULRESSO, including third-party manufacturing costs, packaging services, freight, third-party royalties payable on our net product revenues and amortization of intangible assets associated with ZULRESSO. We estimate that our cost of goods sold as a percentage of net product revenue will remain in the mid-single digit percentage range for the foreseeable future. We expect to utilize zero-cost inventory with respect to ZULRESSO for an extended period of time.

Operating Expenses

Our operating expenses since inception have consisted primarily of costs associated with research and development activities and selling, general and administrative activities.

Research and Development Expenses

Research and development expenses, which consist primarily of costs associated with our product research and development efforts, are expensed as incurred. Research and development expenses consist primarily of:

- personnel costs, including salaries, benefits, stock-based compensation and travel expenses, for employees engaged in research and development functions;
- expenses incurred under agreements with contract research organizations, or CROs, and sites that conduct our non-clinical studies and clinical trials;
- expenses associated with manufacturing materials for use in non-clinical studies and clinical trials and developing external manufacturing capabilities;
- costs of outside consultants engaged in research and development activities, including their fees and travel expenses;
- other expenses related to our non-clinical studies and clinical trials and expenses related to our regulatory activities, including the planned submission of NDAs to the FDA for zuranolone in 2022 and 2023;
- payments made under our third-party license agreements; and
- a portion of our information technology, facilities and other related expenses, including rent, depreciation, maintenance of facilities, insurance and supplies.

We consider the collaborative activities associated with the co-development, co-commercialization, and co-manufacturing of Licensed Products in the U.S. to be separate units of account within the scope of Topic 808 as we and Biogen are both active participants in the development and commercialization activities and are exposed to significant risks and rewards that are dependent on the development and commercial success of the activities in the arrangement. Payments to or reimbursements from Biogen related to the co-development and co-manufacturing activities are accounted for as an increase to or reduction of research and development expense. During the three and nine months ended September 30, 2021, research and development expense was reduced by $21.6 million and $63.8 million, respectively, related to this net reimbursement.

Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We have been developing our product candidates and focusing on other research and development programs, including exploratory efforts to identify new compounds, target validation for identified compounds and lead optimization for our earlier-validated programs. Our direct research and development expenses are tracked on a program-by-program basis, and consist primarily of external costs, such as fees paid to investigators, central laboratories, CROs and contract manufacturing organizations, in connection with our non-clinical studies and clinical trials; third-party license fees related to our product candidates; and fees paid to outside consultants who perform work on our programs. We do not allocate employee-related costs and other indirect costs to specific research and development programs because these costs are deployed across multiple product programs under research and development and, as such, are separately classified as unallocated or stock-based compensation in research and development expenses.

Research and development activities are central to our business. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase in the foreseeable future as we continue or initiate clinical trials and non-clinical studies for certain product candidates and pursue later stages of clinical development of our product candidates.

We cannot determine with certainty the duration and costs of the current or future clinical trials of our product candidates. The duration, costs, and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope, size, rate of progress, and expense of our ongoing as well as any additional clinical trials, non-clinical studies, and other research and development activities;
- future results of ongoing, planned or future clinical trials and non-clinical studies;
- decisions by regulatory authorities related to our product candidates;
- uncertainties in clinical trial enrollment rate or design;
- significant and changing government regulation; and
- the receipt and timing of regulatory approvals, if any.

In addition, the ongoing COVID-19 pandemic may also negatively impact our ongoing and planned development activities and increase our research and development costs. Concerns, precautions and restrictions arising from the COVID-19 pandemic may substantially slow clinical site recruitment and initiation and enrollment in our clinical trials, may impair the conduct, auditing, monitoring, or completion of our trials, may impair or impede the timeliness and completion of our data collection and analysis efforts or the integrity of our data, or may cause us to pause trials, in each case which may significantly impact our ability to meet our expected timelines or cause us to change our plans and may significantly increase our research and development costs. For example, we have seen some slower recruitment in certain of our clinical trials, especially with respect to older patients, and, in our SKYLARK Study in patients with PPD, which caused us to revise our expected timeline for reporting topline data from that study.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate or for regulatory approval, or if we experience significant delays in enrollment in any of our clinical trials or need to enroll additional patients, we could be required to expend significant additional financial resources and time on the completion of clinical development.

Any failure to complete any stage of the development of any potential product candidates in a timely manner could have a material adverse effect on our operations, financial position and liquidity. A discussion of some of the risks and uncertainties associated with not completing our programs on schedule, or at all, and the potential consequences of failing to do so, are set forth in Part II, Item 1A of this Quarterly Report under the heading “Risk Factors”.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of personnel costs, including salaries, benefits and travel expenses for our executive, finance, business, commercial, corporate development and other administrative functions, and stock-based compensation expense. Selling, general and administrative expenses also include professional fees for expenses incurred under agreements with third parties relating to the commercialization of ZULRESSO; pre-launch and launch readiness activities related to zuranolone; public relations, audit, tax and legal services, including legal expenses to pursue patent protection of our intellectual property; and a portion of our information technology, facilities and other related expenses, including rent, depreciation, maintenance of facilities, insurance and supplies.

In April 2020, we implemented a workforce reduction that primarily affected the ZULRESSO commercial operation and related support functions, including eliminating the entirety of our salesforce at that time. While we remain committed to working with healthcare providers and women with PPD seeking access to ZULRESSO and plan to continue to evaluate opportunities to raise awareness and help reduce hurdles to appropriate treatment, our ongoing commercial efforts, including our small account management field-based team and a small number of sales representatives now in place, are primarily focused on geographies that have existing, active ZULRESSO treating sites. We expect to continue to incur significant commercialization expenses, including payroll and related expenses, to support our ongoing commercial activities associated with ZULRESSO. We expect that selling, general and administrative expenses will increase in the future as we progress development efforts and prepare for potential commercialization of our zuranolone and our other current or future product candidates, if successfully developed and approved. We expect to continue to incur significant expenses associated with general operations, including costs related to accounting and legal services, director and officer insurance premiums, facilities and other corporate infrastructure and office-related costs, such as information technology costs.

We consider the collaborative activities associated with the co-development, co-commercialization, and co-manufacturing of SAGE-217 products and SAGE-324 products in the U.S. to be separate units of account within the scope of Topic 808 as we and Biogen are both active participants in the development and commercialization activities and are exposed to significant risks and rewards that are dependent on the development and commercial success of the activities in the arrangement. Payments to or reimbursements from Biogen related to the co-commercialization activities are accounted for as an increase to or reduction of selling, general and administrative expense. During the three and nine months ended September 30, 2021, selling, general and administrative expense was reduced by $2.6 million and $8.8 million, respectively, related to this net reimbursement.

Results of Operations

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

The following table summarizes our results of operations for the three months ended September 30, 2021 and 2020:

	Three Months Ended September 30,		Increase (Decrease)
	2021	2020	
	(in thousands)		
Product revenue, net	$ 1,440	$ 1,639	$ (199)
Operating costs and expenses:			
Cost of goods sold	131	149	(18)
Research and development	83,497	74,078	9,419
Selling, general and administrative	48,706	35,099	13,607
Restructuring	—	(529)	529
Total operating costs and expenses	132,334	108,797	23,537
Loss from operations	(130,894)	(107,158)	(23,736)
Interest income, net	692	1,347	(655)
Other income, net	31	76	(45)
Net loss	$ (130,171)	$ (105,735)	$ (24,436)

Product Revenue, Net

During the three months ended September 30, 2021 and 2020, we recognized $1.4 million and $1.6 million, respectively, of net product revenues related to sales of ZULRESSO. Sales allowances and accruals consisted of patient financial assistance, distribution fees, discounts and chargebacks.

Collaboration Revenue

During the three months ended September 30, 2021 and 2020, we recognized no collaboration revenue from our agreements with Shionogi and Biogen. We expect that revenue, if any, that we may generate under our collaboration agreements will fluctuate from quarter to quarter as a result of the timing and amount of license fees, payments for clinical materials or manufacturing services, milestone payments, royalties paid to us and our share of collaboration profits or losses resulting from sales of any commercialized products, and other payments. For further discussion regarding our collaboration agreements with Shionogi and Biogen and the accounting for revenue from collaboration agreements, please refer to Note 6, *Collaboration Agreements*, in the accompanying Notes to Condensed Consolidated Financial Statements appearing in Part I, Item 1 of this Quarterly Report.

Cost of Goods Sold

During the three months ended September 30, 2021 and 2020, cost of goods sold was $0.1 million and $0.1 million, respectively, and is made up of a low-single digit royalty paid to CyDex Pharmaceuticals, Inc. (“CyDex”) and The Regents of the University of California (“The Regents”) on net product revenue from sales of ZULRESSO, the amortization of intangible assets associated with ZULRESSO, and third-party manufacturing and distribution costs associated with labeling, packaging, and shipping of ZULRESSO. Prior to receiving initial FDA approval for ZULRESSO on March 19, 2019, we manufactured ZULRESSO inventory to be sold upon commercialization and recorded approximately $8.9 million related to this inventory build-up as research and development expense. As a result, the manufacturing costs related to the ZULRESSO inventory build-up incurred before FDA approval were already expensed in a prior period and are therefore excluded from the cost of goods sold for the three months ended September 30, 2021 and 2020. We estimate that our cost of goods sold as a percentage of net product revenue will remain in the mid-single digit percentage range for the foreseeable future. We expect to utilize zero-cost inventory with respect to ZULRESSO for an extended period of time.

Research and Development Expenses

	Three Months Ended September 30,		Increase
	2021	2020	(Decrease)
	(in thousands)		
zuranolone (SAGE-217)	$ 18,525	$ 31,343	$ (12,818)
SAGE-324	858	5,509	(4,651)
SAGE-718	8,606	2,126	6,480
Other research and development programs	18,416	8,888	9,528
Unallocated expenses	19,228	16,285	2,943
Stock-based compensation	17,864	9,927	7,937
Total research and development expenses	$ 83,497	$ 74,078	$ 9,419

Research and development expenses for the three months ended September 30, 2021 were $83.5 million, compared to $74.1 million for the three months ended September 30, 2020. The increase of $9.4 million was primarily due to the following:

- a decrease of $12.8 million in expenses for development of zuranolone. The amount for the three months ended September 30, 2021 reflects an increase in expenses of $5.7 million offset by a reduction in expenses of $18.5 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. The primary reason for the increase in expenses was manufacturing-related activities, including process validation and production of zuranolone for clinical and commercial use, if approved for commercial sale;
- a decrease of $4.7 million in expenses for development of SAGE-324. The amount for the three months ended September 30, 2021 reflects a decrease in expenses of $3.8 million and a reduction in expenses of $0.9 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. The primary reason for the decrease in expenses was the timing of Phase 2 clinical trials;
- an increase of $6.5 million in expenses for development of SAGE-718. The increase in expenses was primarily attributable to the initiation of a Phase 2 clinical trial and clinical pharmacology studies that were initiated during 2021;
- an increase of $9.5 million in expenses for other research and development programs. The increase in expenses was primarily due to ongoing Phase 1 clinical trials of SAGE-689 and SAGE-904 and increased work on early-stage research programs;
- an increase of $2.9 million in unallocated expenses. The amount for the three months ended September 30, 2021 reflects an increase in expenses of $5.2 million partially offset by a reduction in expenses of $2.2 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. The primary reason for the increase in expenses was an increase in the hiring of employees; and
- an increase of $7.9 million in non-cash stock-based compensation expense. The increase in non-cash stock-based compensation expense was primarily due to the determination that achievement of a milestone for certain outstanding performance restricted stock units was probable as of September 30, 2021, resulting in the recognition of $7.9 million of expense during the three months ended September 30, 2021. There was no non-cash stock-based compensation expense recognized related to the achievement of performance-based vesting criteria during the three months ended September 30, 2020.

Selling, General and Administrative Expenses

	Three Months Ended September 30, 2021	2020	Increase (Decrease)
	(in thousands)		
Personnel-related	$ 12,237	$ 8,487	$ 3,750
Stock-based compensation	16,478	10,181	6,297
Professional fees	10,075	8,612	1,463
Other	9,916	7,819	2,097
Total selling, general and administrative expenses	$ 48,706	$ 35,099	$ 13,607

Selling, general and administrative expenses for the three months ended September 30, 2021 were $48.7 million, compared to $35.1 million for the three months ended September 30, 2020. The increase of $13.6 million was primarily due to the following:

- an increase of $3.8 million in personnel-related costs. The amount for the three months ended September 30, 2021 reflects an increase in expenses of $4.5 million partially offset by a reduction in expenses of $0.8 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. The primary reason for the increase in expenses was an increase in the hiring of employees;
- an increase of $6.3 million in non-cash stock-based compensation expense. The increase in non-cash stock-based compensation expense was primarily due to the determination that achievement of a milestone for certain outstanding performance restricted stock units was probable as of September 30, 2021, resulting in the recognition of $4.7 million of expense during the three months ended September 30, 2021. There was no non-cash stock-based compensation expense recognized related to the achievement of performance-based vesting criteria during the three months ended September 30, 2020;
- an increase of $1.5 million in professional fees. The amount for the three months ended September 30, 2021 reflects an increase in expenses of $2.7 million partially offset by a reduction in expenses of $1.2 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. The primary reasons for the increase in expenses were an increase in activities focused on disease awareness and increased launch readiness activities for a potential product launch, if our zuranolone development and regulatory efforts are successful, and general infrastructure-related costs; and
- an increase of $2.1 million in other costs. The amount for the three months ended September 30, 2021 reflects an increase in expenses of $2.9 million partially offset by a reduction in expenses of $0.8 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. The primary reason for the increase in expenses was corporate infrastructure costs, such as information technology costs.

Interest Income, Net and Other Income, Net

Interest income, net, and other expense, net, for the three months ended September 30, 2021 and 2020 were $0.7 million and $1.4 million, respectively. The primary reason for the decrease was the reduction in interest rates that started in early 2020.

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

The following table summarizes our results of operations for the nine months ended September 30, 2021 and 2020:

	Nine Months Ended September 30,		Increase (Decrease)
	2021	2020	
	(in thousands)		
Product revenue, net	$ 4,666	$ 5,014	$ (348)
Operating costs and expenses:			
Cost of goods sold	466	429	37
Research and development	207,723	211,008	(3,285)
Selling, general and administrative	131,899	143,454	(11,555)
Restructuring	—	27,873	(27,873)
Total operating costs and expenses	340,088	382,764	(42,676)
Loss from operations	(335,422)	(377,750)	42,328
Interest income, net	2,132	8,763	(6,631)
Other income, net	110	165	(55)
Net loss	$ (333,180)	$ (368,822)	$ 35,642

Product Revenue, Net

During the nine months ended September 30, 2021 and 2020, we recognized $4.7 million and $5.0 million, respectively, of net product revenues related to sales of ZULRESSO. Sales allowances and accruals consisted of patient financial assistance, distribution fees, discounts and chargebacks.

Collaboration Revenue

During the nine months ended September 30, 2021 and 2020, we recognized no collaboration revenue from our agreements with Shionogi and Biogen. We expect that revenue, if any, that we may generate under our collaboration agreements will fluctuate from quarter to quarter as a result of the timing and amount of license fees, payments for clinical materials or manufacturing services, milestone payments, royalties paid to us and our share of collaboration profits or losses resulting from sales of any commercialized products, and other payments. For further discussion regarding our collaboration agreements with Shionogi and Biogen and the accounting for revenue from collaboration agreements, please refer to Note 6, *Collaboration Agreements*, in the accompanying Notes to Condensed Consolidated Financial Statements appearing in Part I, Item 1 of this Quarterly Report.

Cost of Goods Sold

During the nine months ended September 30, 2021 and 2020, cost of goods sold was $0.5 million and $0.4 million, respectively, and is made up of a low-single digit royalty paid to CyDex and The Regents on net product revenue from sales of ZULRESSO, the amortization of intangible assets associated with ZULRESSO and third-party manufacturing and distribution costs associated with labeling, packaging, and shipping of ZULRESSO. Prior to receiving initial FDA approval for ZULRESSO on March 19, 2019, we manufactured ZULRESSO inventory to be sold upon commercialization and recorded approximately $8.9 million related to this inventory build-up as research and development expense. As a result, the manufacturing costs related to the ZULRESSO inventory build-up incurred before FDA approval were already expensed in a prior period and are therefore excluded from the cost of goods sold for the nine months ended September 30, 2021 and 2020. We estimate that our cost of goods sold as a percentage of net product revenue will remain in the mid-single digit percentage range for the foreseeable future. We expect to utilize zero-cost inventory with respect to ZULRESSO for an extended period of time.

Research and Development Expenses

	Nine Months Ended September 30,		Increase (Decrease)
	2021	2020	
	(in thousands)		
zuranolone (SAGE-217)	$ 50,410	$ 83,402	$ (32,992)
SAGE-324	6,161	12,664	(6,503)
SAGE-718	17,615	4,296	13,319
Other research and development programs	37,635	25,432	12,203
Unallocated expenses	55,304	52,944	2,360
Stock-based compensation	40,598	32,270	8,328
Total research and development expenses	$ 207,723	$ 211,008	$ (3,285)

Research and development expenses for the nine months ended September 30, 2021 were $207.7 million, compared to $211.0 million for the nine months ended September 30, 2020. The decrease of $3.3 million was primarily due to the following:

- a decrease of $33.0 million in expenses for development of zuranolone. The amount for the nine months ended September 30, 2021 reflects an increase in expenses of $17.4 million offset by a reduction in expenses of $50.4 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. The primary reasons for the increase in expenses was spending on the WATERFALL Study and manufacturing-related activities, including process validation and production of zuranolone for clinical and commercial use, if approved for commercial sale;
- a decrease of $6.5 million in expenses for development of SAGE-324. The amount for the nine months ended September 30, 2021 reflects a decrease in expenses of $0.3 million and a reduction in expenses of $6.2 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement;
- an increase of $13.3 million in expenses for development of SAGE-718. The increase in expenses was primarily attributable to the initiation of a Phase 2 clinical trial and clinical pharmacology studies that were initiated during 2021;
- an increase of $12.2 million in expenses for other research and development programs. The increase in expenses was primarily due to ongoing Phase 1 clinical trials of SAGE-689 and SAGE-904 and increased work on early-stage research programs;
- an increase of $2.4 million in unallocated expenses. The amount for the nine months ended September 30, 2021 reflects an increase in expenses of $9.6 million partially offset by a reduction in expenses of $7.2 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. The primary reason for the increase in expenses was an increase in the hiring of employees; and
- an increase of $8.3 million in non-cash stock-based compensation expense. The increase in non-cash stock-based compensation expense was primarily due to the determination that achievement of a milestone for certain outstanding performance restricted stock units was probable as of September 30, 2021, resulting in the recognition of $7.9 million of expense during the nine months ended September 30, 2021. There was no non-cash stock-based compensation expense recognized related to the achievement of performance-based vesting criteria during the nine months ended September 30, 2020.

Selling, General and Administrative Expenses

	Nine Months Ended September 30,		Increase (Decrease)
	2021	2020	
	(in thousands)		
Personnel-related	$ 34,592	$ 49,492	$ (14,900)
Stock-based compensation	43,383	41,192	2,191
Professional fees	26,648	26,371	277
Other	27,276	26,399	877
Total selling, general and administrative expenses	$ 131,899	$ 143,454	$ (11,555)

Selling, general and administrative expenses for the nine months ended September 30, 2021 were $131.9 million, compared to $143.5 million for the nine months ended September 30, 2020. The increase of $11.6 million was primarily due to the following:

- a decrease of $14.9 million in personnel-related costs. The amount for the nine months ended September 30, 2021 reflects a decrease in expenses of $12.8 million and a reduction in expenses of $2.1 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. The primary reason for the decrease in expenses was the termination of employees in the April 2020 restructuring;
- an increase of $2.2 million in non-cash stock-based compensation expense. The increase in expenses was primarily from the determination that achievement of a milestone for certain outstanding performance restricted stock units was probable as of September 30, 2021, resulting in the recognition of $4.7 million of expense during the nine months ended September 30, 2021, offset by the impact of the cancellation of stock option grants that had been made to terminated employees. There was no non-cash stock-based compensation expense recognized related to the achievement of performance-based vesting criteria during the nine months ended September 30, 2020;
- an increase of $0.3 million in professional fees. The amount for the nine months ended September 30, 2021 reflects an increase in expenses of $3.8 million partially offset by a reduction in expenses of $3.5 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. The primary reasons for the increase in expenses were an increase in activities focused on disease awareness and increased launch readiness activities for a potential product launch, if our zuranolone development efforts are successful; and
- an increase of $0.9 million in other costs. The amount for the nine months ended September 30, 2021 reflects an increase in expenses of $4.1 million partially offset by a reduction in expenses of $3.2 million due to net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement. The primary reason for the increase in expenses was corporate infrastructure costs, such as information technology costs.

Restructuring

In April 2020, we announced a restructuring plan to enable us to advance our corporate strategy and pipeline that included the elimination of approximately 53% of our workforce. The workforce reduction primarily affected the ZULRESSO commercial operation and related selling, general and administrative support functions. In the nine months ended September 30, 2020, we recorded $27.9 million of expense for restructuring, primarily for one-time termination benefits to the affected employees, primarily for cash payments of severance, healthcare benefits and outplacement assistance.

Interest Income, Net and Other Income, Net

Interest income, net, and other expense, net, for the nine months ended September 30, 2021 and 2020 were $2.2 million and $8.9 million, respectively. The primary reason for the decrease was the reduction in interest rates that started in early 2020.

Liquidity and Capital Resources

We began to generate revenue from product sales in the second quarter of 2019 in conjunction with the launch of our first product, ZULRESSO, in June 2019. To date, we have incurred recurring net losses, except for net income of $606.1 million for the year ended December 31, 2020, reflecting revenue recognized under the Biogen Collaboration Agreement. As of September 30, 2021, we had an accumulated deficit of $1.4 billion. On December 31, 2020, we completed the sale of 6,241,473 shares of our common stock in a private placement to BIMA at a price of approximately $104.14 per share, resulting in aggregate gross proceeds of $650.0 million. From our inception through September 30, 2021, we have received aggregate net proceeds of $2.8 billion from the sales of redeemable convertible preferred stock prior to our initial public offering, the issuance of convertible notes, and the sales of common stock in our initial public offering in July 2014, follow-on offerings and to BIMA. We also received $1.0 billion in upfront payments under our collaborations with Biogen and Shionogi.

As of September 30, 2021, our primary sources of liquidity were our cash, cash equivalents and marketable securities, which totaled $1.8 billion. We invest our cash in money market funds, U.S. government securities, corporate bonds, and commercial paper, and our primary objectives are to preserve principal, provide liquidity and maximize income without significantly increasing risk.

The following table summarizes the primary sources and uses of cash for the nine months ended September 30, 2021 and 2020:

	Nine Months Ended September 30,	
	2021	2020
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (280,681)	$ (346,691)
Investing activities	(972,187)	397,165
Financing activities	13,504	7,091
Total	$ (1,239,364)	$ 57,565

Operating Activities

During the nine months ended September 30, 2021, net cash used in operating activities primarily resulted from our net loss of $333.2 million, which was primarily attributable to our research and development activities and our selling, general and administrative expenses, along with changes in our operating assets and liabilities of $24.3 million, partially offset by $76.8 million of non-cash items.

During the nine months ended September 30, 2020, net cash used in operating activities primarily resulted from our net loss of $368.8 million, which was primarily attributable to our research and development activities and our selling, general and administrative expenses, along with changes in our operating assets and liabilities of $54.7 million, partially offset by $76.8 million of non-cash items.

Investing Activities

During the nine months ended September 30, 2021 and 2020, net cash used in investing activities was $972.2 million and net cash provided by investing activities was $397.2 million, respectively. During the nine months ended September 30, 2021 and 2020, we purchased marketable securities and had sales and maturities of our marketable securities as part of managing our cash and investments portfolio. Additionally, during the nine months ended September 30, 2021, we invested in marketable securities the majority of the cash that we received from Biogen under the Biogen Collaboration Agreement and related stock purchase agreement.

Financing Activities

During the nine months ended September 30, 2021 and 2020, net cash provided by financing activities was $13.5 million and $7.1 million, respectively. The increase is due to proceeds from the exercises of stock options.

Operating Capital Requirements

We began to generate revenue from product sales in the second quarter of 2019 in conjunction with the launch of our first product, ZULRESSO. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of our current and future product candidates, and seek regulatory approvals for those product candidates that are successfully developed; prepare for potential future commercialization of product candidates beyond ZULRESSO that are successfully developed and approved; begin to commercialize any such products, if successfully developed and approved; and continue our efforts to identify and develop new product candidates beyond our current portfolio. We also expect to incur significant costs associated with general operations. In addition, we expect to incur significant commercialization expenses for product sales, marketing and outsourced manufacturing with respect to ZULRESSO and any future products that are successfully developed and approved. Accordingly, we anticipate that we will need substantial additional funding in connection with our continuing operations.

Based on our current operating plans, we expect that our existing cash, cash equivalents and marketable securities as of September 30, 2021, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months from the filing date of this Quarterly Report. During that time, we expect to incur significant expenses as we continue to commercialize ZULRESSO; complete ongoing clinical trials of zuranolone and advance regulatory, pre-launch and launch-planning activities; advance development of our other product candidates; expand our research activities; and pursue our strategic plan.

Our current operating plan does not contemplate other activities that we may pursue or that all of our currently planned activities will proceed at the same pace, or that all of these activities will be fully initiated or completed during that time. We have based our estimates on assumptions that could change, and we may use our available capital resources sooner than we currently expect. We may also choose to change or increase our development, commercialization or other efforts. Because of the numerous risks and uncertainties associated with the development and commercialization of any product or product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete development of our current or future product candidates or to commercialize any approved product.

Our future capital requirements will depend on many factors, including:

- the amount and timing of revenues from sales of ZULRESSO, which we expect will continue to be impacted by a number of factors, including: the rate, degree and level of market acceptance for ZULRESSO for the treatment of PPD in the U.S.; our decision to focus our efforts primarily on geographies that have existing, active ZULRESSO treating sites; the continued availability of healthcare settings in those geographies to administer ZULRESSO and the ability and willingness of such healthcare settings to make sufficient capacity available; the level of reimbursement for both ZULRESSO and the infusion in the healthcare setting both by commercial and government payors, and the nature of limitations on coverage and reimbursement; the number of healthcare professionals willing to prescribe ZULRESSO and women with PPD who agree to be treated with ZULRESSO; and the scope, duration and timing of the impact of the COVID-19 pandemic;
- the timing and amount of costs associated with our commercialization of ZULRESSO;
- the costs of regulatory, pre-launch and launch-readiness activities associated with zuranolone and, if zuranolone is approved for one or more indications, the costs associated with its commercial launch;
- the initiation, progress, completion, timing, costs, and results of ongoing, planned and future non-clinical studies and clinical trials for our existing and future product candidates; the number and length of clinical trials required by regulatory authorities to support regulatory approval; and the costs of preparing, submitting and supporting regulatory filings for our product candidates;

- the length, severity and costs of disruptions, if any, associated with the COVID-19 pandemic on initiation and conduct of our clinical trials or on our supply chain;
- the ability of zuranolone, SAGE-324 and SAGE-718 and our other clinical-stage product candidates to progress through clinical development successfully; the outcome of discussions with regulatory authorities on regulatory pathways with respect to our product candidates; the timing, scope and outcome of regulatory filings and reviews and approvals of such product candidates, if we are successful in our development efforts; the scope and cost of any clinical trials or other commitments required post-approval for any approved products resulting from such development efforts, if successful; and the level, timing and amount of costs associated with permitted prelaunch activities and preparing for a potential future commercial launch of any such product candidate that is successfully developed and approved;
- the amounts we are entitled to receive, if any, from Biogen and Shionogi under our collaborations for cost-sharing, development, regulatory, and sales milestones, and royalty payments;
- the size of the PPD market and the portion of the population for which ZULRESSO may be prescribed; the size of the markets for which zuranolone and our other product candidates may be approved in the future, if successfully developed; the portion of the population in the approved indications for which our future products are actually prescribed; the rate and degree of market acceptance for our products, and the pricing, availability and level of reimbursement for our products;
- the number and characteristics of the product candidates we pursue in development and the nature and scope of our discovery and development programs;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other products and technologies; and
- our ability to establish any future collaboration arrangements on favorable terms, if at all.

Until such time, if ever, as we can generate substantial product revenue and achieve profitability, we expect to also finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other sources of funding. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of other strategic considerations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute the ownership interest of our stockholders. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or research programs or to grant licenses on terms that may not be favorable to us. Raising funds may present challenges. Markets may experience volatility or become disrupted in the future for any number of reasons, including if current efforts to control the COVID-19 pandemic are not successful. If we are unable to raise additional funds through equity or debt financings or other means when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

There have been no material changes to our contractual obligations and commitments as included in our Annual Report.

Off-Balance Sheet Arrangements

We do not currently have, nor did we have during the periods presented, any off-balance sheet arrangements as defined by SEC rules.

Application of Critical Accounting Policies

We have prepared our condensed consolidated financial statements in accordance with accounting principles generally accepted in the U.S. Our preparation of these condensed consolidated financial statements requires us to make estimates, assumptions, and judgments that affect the reported amounts of assets, liabilities, expenses, and related disclosures at the date of the condensed consolidated financial statements, as well as revenue and expenses recorded during the reporting periods. We evaluate our estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results could therefore differ materially from these estimates under different assumptions or conditions. While our significant accounting policies are described in more detail in the notes to our consolidated financial statements to our Annual Report, we believe that our most critical accounting policies are those relating to revenue recognition, collaborative arrangements, accrued research and development expenses, and stock-based compensation.

Except for the policy regarding collaborative arrangements described below, there have been no material changes to our critical accounting policies from those described in “Management’s Discussion and Analysis of Financial Condition and Results of Operations – Critical Accounting Policies and Significant Judgments and Estimates” included in our Annual Report.

Collaborative Arrangements

We analyze our collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of Topic 808. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of Topic 808 that contain multiple elements, we first determine which elements of the collaboration are deemed to be within the scope of Topic 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For those elements of the arrangement that are accounted for pursuant to Topic 606, we apply the five-step model and present the arrangement as collaboration revenue in the condensed consolidated statements of operations and comprehensive loss. For further discussion regarding the accounting for the Biogen Collaboration Agreement, please refer to Note 6, *Collaboration Agreements*, in the accompanying Notes to Condensed Consolidated Financial Statements appearing in Part I, Item 1 of this Quarterly Report.

For collaboration arrangements that are within the scope of Topic 808, we evaluate the income statement classification for presentation of amounts due from or owed to other participants associated with multiple activities in a collaboration arrangement based on the nature of each separate activity. Payments or reimbursements that are the result of a collaborative relationship, instead of a customer relationship, such as co-development and co-commercialization activities, are recorded as research and development expense or selling, general and administrative expense in the event of a payment to the collaborative partner in a period, or a reduction to these expense line items in the event of a reimbursement from the collaboration partner in a period, as appropriate.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is set forth in Note 2, *Summary of Significant Accounting Policies*, in the accompanying Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

We had cash, cash equivalents and marketable securities of approximately $1.8 billion as of September 30, 2021. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Our primary exposure to market risk relates to fluctuations in interest rates, which are affected by changes in the general level of U.S. interest rates. Given the short-term nature of our cash, cash equivalents and marketable securities, we do not expect that a sudden change in market interest rates would have a material impact on our financial condition and/or results of operations. We do not own any derivative financial instruments.

We contract with vendors in foreign countries and have subsidiaries in Europe. As such, we have exposure to adverse changes in exchange rates of foreign currencies associated with our foreign transactions. We believe this exposure to be immaterial. We do not hedge against this exposure to fluctuations in exchange rates.

We do not believe that our cash, cash equivalents and marketable securities have significant risk of default or illiquidity. While we believe our cash, cash equivalents and marketable securities do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash, cash equivalents and marketable securities at one or more financial institutions that are in excess of federally insured limits.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our results of operations during the nine months ended September 30, 2021 and 2020.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Securities Exchange Act of 1934) that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934 is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our President and Chief Executive Officer, who is our principal executive officer, and our Chief Financial Officer, who is also our principal financial and accounting officer, as appropriate, to allow timely decisions regarding required disclosure.

As of September 30, 2021, our management, with the participation of our principal executive officer and principal financial and accounting officer, evaluated the effectiveness of our disclosure controls and procedures. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial and accounting officer have concluded, based upon the evaluation described above, that, as of September 30, 2021, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

There were no changes to our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934) that occurred during the period covered by this Quarterly Report that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II — OTHER INFORMATION

Item 1. Legal Proceedings

In the ordinary course of our business, we may, from time to time, be involved in lawsuits, claims, and other legal proceedings related to contracts, employment arrangements, operating activities, intellectual property or other matters. While the outcome of any such proceedings cannot be predicted with certainty, as of September 30, 2021, we were not party to any legal proceedings that we would expect to have a material adverse impact on our financial position, results of operations or cash flow.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Quarterly Report on Form 10-Q, or Quarterly Report, and in our other public filings before making an investment decision. Our business, prospects, financial condition, or operating results could be harmed by any of these risks, as well as other risks not currently known to us or that we currently consider immaterial. If any such risks or uncertainties actually occur, our business, financial condition or operating results could differ materially from the plans, projections and other forward-looking statements included in this Quarterly Report, including in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this report and in our other public filings and public statements. The trading price of our common stock could decline due to any of these risks, and as a result, our stockholders may lose all or part of their investment.

Risks Related to Product Development, Regulatory Approval and Commercialization

We may never be able to generate meaningful revenues from sales of ZULRESSO® (brexanolone) CIV injection at levels or on timing necessary to support our investment and goals.

Our first product, ZULRESSO, was approved by the U.S. Food and Drug Administration, or FDA, in March 2019 as a treatment for postpartum depression, or PPD, in adults, and was made commercially available in June 2019. We may never be able to generate meaningful revenues from sales of ZULRESSO or revenues at levels or on timing necessary to support our investment and goals. Our revenues from sales of ZULRESSO has been negatively impacted by significant barriers arising from the complex requirements for treatment and, more recently, by the COVID-19 pandemic, and these factors are expected to continue to impact revenues negatively in the future.

ZULRESSO is administered as a continuous infusion given over two and a half days. Because of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness during the ZULRESSO infusion, ZULRESSO is approved for administration only in a medically-supervised healthcare setting that has been certified under a Risk Evaluation and Mitigation Strategy, or REMS, program and meets the other requirements of the REMS program, including requirements related to monitoring of the patient during the infusion. The actions required for a healthcare setting to be ready and willing to treat women with PPD are complex and time-consuming. These actions include becoming REMS-certified; achieving formulary approvals; establishing protocols for administering ZULRESSO; and securing satisfactory reimbursement. Sites must often negotiate reimbursement on a payor-by-payor basis under commercial coverage. These requirements have created significant barriers to treatment for women with PPD. We expect these barriers will continue to negatively impact ZULRESSO revenue growth, but we do not know the extent of the anticipated impact. The COVID-19 pandemic has compounded these barriers and further impacted sales of ZULRESSO in the U.S. The spread of COVID-19 in the U.S. resulted in a significant number of sites of care pausing treatment of new patients with ZULRESSO and potential new sites pausing site activation activities for a period of time. We believe concerns about the risk of exposure to the virus have also caused a significant reduction in the number of women with PPD seeking treatment with ZULRESSO and in physicians willing to prescribe it. We expect the significant adverse impact of the pandemic on ZULRESSO revenues to continue for the foreseeable future. Given the evolving nature of the pandemic, we cannot predict the length or scope of such continued adverse impact.

In April 2020, we implemented a workforce reduction that primarily affected the ZULRESSO commercial operation and related support functions, including eliminating the entirety of our salesforce at that time. While we remain committed to working with healthcare providers and women with PPD seeking access to ZULRESSO and plan to continue to evaluate opportunities to raise awareness and help reduce hurdles to appropriate treatment, our ongoing commercial efforts, including our small account management field-based team and a small number of sales representatives, are primarily focused on geographies that have existing, active ZULRESSO treating sites. We expect that this approach may continue to substantially limit the revenue opportunity for ZULRESSO, and may make it difficult for us to achieve revenue growth and meet our revenue goals. Given this approach, the number of new healthcare settings that become treating sites for ZULRESSO, if any, may also be limited. We may also find that certain healthcare settings that have in the past been active treating sites may not be willing to remain infusion-ready as a result of the complex requirements related to administration of ZULRESSO and compliance with the REMS, related limitations and restrictions, or because of actual or perceived difficulties obtaining satisfactory reimbursement or limitations on coverage and reimbursement or for other reasons. Healthcare settings that are active treating sites may also limit capacity used for ZULRESSO infusions.

We may encounter other issues and challenges in commercializing ZULRESSO and generating revenues, including:

- Women with PPD who need treatment may find it too onerous to undergo an infusion or to be treated at a certified healthcare setting overnight for the length of stay required for treatment, or to be enrolled in the registry that is part of the process or may be concerned about the risk of excessive sedation and sudden loss of consciousness.

- We may never be able to generate sufficient data for the FDA to permit administration of ZULRESSO in the home setting, even with monitoring and supervision requirements, and even if we were able to generate such data and obtain such approval, such approval may not result in an increase in market acceptance of ZULRESSO or an increase in revenues.

- More healthcare providers than we expected have been unwilling to accept ZULRESSO as a treatment paradigm for women with PPD and this may continue; we believe this unwillingness is due primarily to the product profile and reimbursement challenges associated with ZULRESSO.

- We may not be able to compete effectively with lower cost anti-depressants.

- Given the mode of administration, the nature of the REMS and the limitation on the administration of ZULRESSO to a medically-supervised healthcare setting certified under the REMS, use of ZULRESSO in the U.S. has been focused primarily on women with more severe symptoms of PPD, and we expect that to continue.

- We may be unable to fully comply with our obligations under the ZULRESSO REMS, which include auditing of healthcare settings, collection and analysis of required data, and other requirements, to the satisfaction of the FDA, or the FDA may require modifications to or additional restrictions under the ZULRESSO REMS.

We may also continue to encounter challenges related to coverage and reimbursement of ZULRESSO. These include restrictions related to the severity of PPD cases for which ZULRESSO will be reimbursed, requirements that other treatments be used prior to ZULRESSO, or other limitations in the scope, breadth, availability or amount of reimbursement covering ZULRESSO or the infusion. For example, the availability, terms and timing of coverage for ZULRESSO by state Medicaid systems is expected to continue to vary significantly by state, and we may encounter states that impose significant restrictions or lengthy delays. Similarly, certain healthcare settings or patients may determine that the financial burdens of treatment are not acceptable. For example, a number of healthcare settings that are willing to administer ZULRESSO to women with PPD who have commercial insurance do not currently treat Medicaid patients, which adversely affects our ability to generate revenue from ZULRESSO.

Any of these issues could impair our ability to generate revenues or to meet our expectations with respect to the amount or timing of revenues. Any issues or hurdles related to our commercialization efforts may materially adversely affect our business, results of operations, financial condition and prospects and could lead us to make significant further changes to the scope and nature of our efforts. There is no guarantee that we will be successful in our commercialization

efforts with respect to ZULRESSO, or that we will be able to generate meaningful revenues or revenues at the levels or on the timing necessary to support our investment and goals.

Our future business prospects depend heavily on our ability, alone or through our collaborations, to successfully develop and gain regulatory approval of our current product candidates, including zuranolone (SAGE-217), which is in Phase 3 clinical development for major depressive disorder, or MDD, and PPD and for which we intend to submit an NDA for the treatment of MDD in the second half of 2022 and an additional filing for the treatment of PPD in the first half of 2023. We may not be successful in our plans to file for and obtain regulatory approval of zuranolone in the treatment of MDD or PPD on the timelines we expect or at all. We cannot be certain that we will be able to initiate planned clinical trials, to complete ongoing clinical trials or to announce results of such trials, with respect to any of our other product candidates, on the timelines we expect or at all, that the results of our development programs will be positive. We cannot be certain that we or our collaborators will be able to advance our product candidates into additional trials or to successfully develop, obtain regulatory approval for, or successfully commercialize any of our current or future product candidates.

Our future business prospects depend heavily on our ability, alone or through our collaborations, to successfully develop and gain regulatory approval of product candidates beyond ZULRESSO, including zuranolone. Drug development and obtaining regulatory approval for a product involves a long, expensive and uncertain process, involving a high degree of risk.

Before obtaining regulatory approvals for the commercial sale of any product candidate, non-clinical studies and clinical trials must demonstrate that the product candidate is safe and effective for use in each target indication. We or our collaborators may not be able to demonstrate the efficacy and safety of any of our current product candidates or any future product candidate at each stage of clinical development or we may encounter other issues with any clinical trials or non-clinical studies required for regulatory submissions. Success in non-clinical studies or in earlier clinical trials or interim results of clinical trials may not be repeated or observed in ongoing, future or completed studies or trials involving the same compound or other product candidates. Some or all of our or our collaborators' clinical trials may fail to meet their primary or key secondary endpoints, raise safety issues or generate mixed results. For example, in December 2019, we announced that the MOUNTAIN Study, a Phase 3 clinical trial of zuranolone for the treatment of MDD, did not meet its primary endpoint. We may find that studying alternate formulations of our product candidates or doses that achieve higher or lower patient exposure may result in unexpected adverse events or raise other safety issues or may otherwise generate negative results. For example, we continue to evaluate a 50 mg dose in our ongoing pivotal Phase 3 clinical trials for zuranolone, as we did in the WATERFALL Study, which has achieved higher patient exposures than previously observed in patients enrolled in our prior multi-dose trials of zuranolone. In our planned dose-ranging study of SAGE-324, we plan to evaluate multiple doses, including the same maximum dose of SAGE-324 that we evaluated in prior studies, but we plan to increase the duration of dosing. In the case of zuranolone, we or our collaborators may encounter issues with the efficacy or durability of short-term treatment, or co-initiated treatment with zuranolone and traditional antidepressants, or safety and efficacy concerns with respect to retreatment that require additional studies be conducted. We might decide to evaluate different doses, formulations, and durations of dosing for any of our product candidates with other studies or programs in the future. The results of clinical trials or non-clinical studies of our product candidates at any stage may not support further development or may not be sufficient to file for and obtain regulatory approval on the timelines we expect or at all. Other decisions or actions of the FDA or other regulatory agencies may affect our plans, progress or results.

Changes in formulation or the need to refine or scale-up the manufacturing process as we do for any of our product candidates could also delay development or require us to conduct additional clinical trials or non-clinical studies or conduct post-approval analyses, or could lead to different results than achieved with the earlier formulation or processes. We or our collaborators may not be able to initiate or complete our clinical trials or announce results from our clinical trials on the timelines we expect. We or our collaborators may experience slower than expected recruitment of sites or enrollment and randomization of patients in our clinical trials, particularly in clinical trials where an in-patient stay or frequent site visits are required, the patient population is small, enrollment criteria are more selective than historically used or there are existing therapies. There is also the potential for slower than expected clinical site initiation, delays or problems in analyzing data, the potential need for additional analysis or data or the need to enroll additional patients, or other unexpected issues such as adverse events in any of our clinical trials. These types of delays or issues could lead to delays in the completion of a trial and announcement of results.

The continuing COVID-19 pandemic in the U.S. and outside the U.S. may negatively impact our ongoing and planned development activities. Continuing concerns about COVID-19 and related precautions and restrictions may make it difficult to enroll patients in our clinical trials or may increase the rates of patients withdrawing from our clinical trials following enrollment. Some clinical sites may decline or delay participation in our trials so as to prioritize medical resources to the treatment of COVID-19 patients or as a result of recommended or required restrictions on nonessential businesses. These concerns, precautions and restrictions arising from the COVID-19 pandemic may substantially slow clinical site recruitment and initiation and enrollment in our clinical trials, or cause us to pause trials, in each case which may significantly impact our ability to meet our expected timelines or may significantly impact our costs or other aspects of our business or cause us to have to change our plans. For example, we have seen slower recruitment in certain of our clinical trials, especially with respect to older patients and, in our SKYLARK Study, in patients with PPD. We believe the slower than expected enrollment in the SKYLARK Study is due to a lower number of women seeking care for PPD and a lower rate of childbirth during the COVID-19 pandemic. As a result of the slower than expected enrollment, we revised our expected timeline for reporting topline data from the SKYLARK Study.

In response to the COVID-19 pandemic or as a result of restrictions imposed or recommended by federal, state or local authorities, we or our clinical sites have, in some cases, taken steps to help minimize the number of visits a clinical trial participant is required to make to a site, including by limiting or modifying clinical trial procedures and visits for data collection. Similarly, some clinical sites have imposed other restrictions or limitations on key clinical trial activities such as restrictions related to monitoring of the sites by clinical research organizations. Some of these measures may continue or increase in the future depending on a number of factors, including the COVID-19 case rate in a particular community, the success of vaccination campaigns, and any adverse impact of the spread of variants of the virus that causes COVID-19, including “breakthrough” cases among fully-vaccinated people. Limitations or modifications to study procedures, study visits or data collection, restrictions on key clinical trial activities such as monitoring or auditing, or other restrictions that may affect data analysis activities may require additional assessment and evaluation from institutional review boards; negatively impact the integrity or completeness of our trial data, the powering of a trial, the integrity or relevance of clinical study endpoints; or impact the timing of availability of results.

The drug development process can take many years, and may include post-marketing studies and surveillance, which will require the expenditure of substantial resources. Of the large number of drugs in development in the U.S., only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized. Accordingly, even if we have the requisite financial resources, when needed, to continue to fund our development efforts, we cannot assure you that any of our current or future product candidates will be successfully developed or commercialized either in the U.S. or in any country outside the U.S. Even if we or our collaborators conduct the trials required by or discussed with the FDA, the FDA may ultimately decide that the design, number and type of trials, number of patients studied or results, even if positive, are not sufficient to file for or gain regulatory approval of any of our product candidates in the indications we study, or do not support the safety or efficacy or our intended profile for the product. For example, we may not be successful in our plans to file with the FDA for and obtain regulatory approval of zuranolone in the treatment of MDD or PPD on the timelines we expect or at all. The FDA may find inadequacies and deficiencies in our planned NDA for zuranolone and in the data we submit, despite our prior discussions with the FDA, and may decide not to accept the NDA for filing. Even if the FDA accepts an NDA seeking approval of zuranolone for filing, the FDA may find that the data included in the NDA are not sufficient for approval and may not approve the NDA. We may receive negative results from ongoing clinical trials of zuranolone that adversely affect our ability to obtain approval of zuranolone or that impair the potential product profile of zuranolone. The FDA may require additional trials or data to approve zuranolone as a treatment for MDD and/or PPD, any of which may significantly delay and put at risk our efforts to obtain approval and may not be successful. The FDA may not meet expected review timelines or there may be delays at any point in the regulatory submission and review cycle that negatively impact our plans and expectations, including anticipated launch timelines and plans in MDD or PPD, if zuranolone is approved. Other decisions or actions of the FDA or other regulatory agencies may also adversely affect the zuranolone program, our plans, progress or results and the potential product profile and success of zuranolone.

Even if we or a collaborator of ours gains approval of any of our current or future product candidates, we may never be able to successfully commercialize such new product or to meet our expectations with respect to timing and revenues or profits from sales of such product. For example, even if zuranolone is approved, we cannot be certain that we or our collaborators will be able to successfully commercialize zuranolone in the approved indications.

ZULRESSO, our current or future product candidates and any future products, if successfully developed and approved, may cause undesirable side effects that limit their commercial profile; delay or prevent further development or regulatory approval; cause regulatory authorities to require labeling statements, such as boxed warnings or a REMS; or result in other negative consequences.

We may observe undesirable side effects or other potential safety issues in nonclinical studies or in clinical trials at any stage of development of our product candidates. Clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, certain side effects of ZULRESSO, any current or future product candidates, or any future products, if successfully developed and approved, may only be uncovered with a larger number of patients exposed to the product. Those side effects could be serious or life-threatening. If we or others identify undesirable side effects caused by ZULRESSO, any existing or future product candidate or any future approved product:

- regulatory authorities may withdraw or limit their approval of such products;
- the FDA or regulatory authorities outside the U.S. may impose a clinical hold or partial clinical hold prior to the initiation of development or during development of our product candidates which could cause us or our collaborators to have to stop, delay or restrict further development; or we or our collaborators may, even without a clinical hold, decide to interrupt, delay or halt existing non-clinical studies and clinical trials or stop development;
- we may have difficulty enrolling patients in our clinical trials and completing such trials on the timelines we expect or at all, or we may have to conduct additional non-clinical studies or clinical trials as part of a development program;
- if a new drug application, or NDA, for any of our product candidates is reviewed by an advisory committee of the FDA, the advisory committee may recommend against approval of the application or may recommend that the FDA require, as a condition of approval, additional non-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions, and the FDA may ultimately agree with the recommendations of the advisory committee;
- we or our collaborators may not be able ultimately to demonstrate, to the satisfaction of the FDA or other regulatory authorities, that our product candidates are safe and that the benefits outweigh the safety risks, and the FDA or applicable foreign regulatory authorities may not approve the product candidate;
- regulatory authorities may require the addition of labeling statements, such as a boxed warning or additions to an existing boxed warning, or a contraindication, including as a result of inclusion in a class of drugs for a particular disease, or may require a REMS, or modifications to an existing REMS;
- we or our collaborators may be required to change the way such products are distributed or administered, conduct post-approval studies or change the labeling of the products;
- we or our collaborators may be subject to regulatory investigations and government enforcement actions;
- we or our collaborators may decide to remove such products from the marketplace;
- we or our collaborators could be sued and held liable for injury caused to individuals exposed to or taking our products or product candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected products, could substantially increase the risks and costs of developing our product candidates or commercializing our products, and could significantly adversely impact our ability and that of our collaborators to successfully develop, gain regulatory approval for, and commercialize our current product candidates or future products and generate revenues.

Obtaining regulatory approval to market any of our product candidates is a complex, lengthy, expensive and uncertain process, and the FDA and regulatory authorities outside of the U.S. may delay, limit or deny approval of any of our product candidates for many reasons. Any setback or delay in obtaining regulatory approval for our product

candidates or in our ability to commence marketing of our products, if approved, may have a material adverse effect on our business and prospects.

We are not permitted to market any of our product candidates in the U.S. until we or our collaborators receive approval of an NDA from the FDA or in any foreign countries until we or our collaborators receive the requisite marketing approval from such countries. Obtaining approval of an NDA in the U.S. or marketing approval in any country outside the U.S. is a complex, lengthy, expensive and uncertain process. The FDA and regulatory authorities outside the U.S. may delay, limit or deny approval of any of our product candidates for many reasons, including, among others:

- we or our collaborators may not be able to demonstrate, to the satisfaction of the FDA or other regulatory authorities, that our product candidates are safe and effective in any indication and that the benefits outweigh the safety risks;
- the results of our non-clinical studies and clinical trials may be negative, or may not meet the level of statistical or clinical significance or other criteria required by the FDA or regulatory authorities outside the U.S. for marketing approval;
- the FDA or regulatory authorities outside the U.S. may impose a clinical hold or partial clinical hold prior to the initiation of development or during development of our product candidates which could cause us to have to stop, delay or restrict further development;
- the FDA or regulatory authorities outside the U.S. may disagree with our interpretation of data from our non-clinical studies and clinical trials, or may not accept data generated at one or more of our sites conducting non-clinical studies or clinical trials which may cause the study or trial to fail;
- the FDA or regulatory authorities outside the U.S. may determine that the number, design, size, conduct, implementation or result of our non-clinical studies or clinical trials is inadequate for regulatory approval or that changes in dosing or drug formulation used in our non-clinical studies or clinical trials require additional trials or studies, even if the regulatory authorities have previously reviewed and commented on the design and details of our plans;
- the FDA or regulatory or other government authorities outside the U.S. may require that we or our collaborators conduct additional non-clinical studies and clinical trials prior to approval or post-approval;
- the FDA or applicable foreign regulatory authorities may not approve the formulation, labeling or specifications of any of our product candidates;
- if an NDA for any of our product candidates is reviewed by an advisory committee of the FDA, the advisory committee may recommend against approval of the application or may recommend that the FDA require, as a condition of approval, additional non-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions, and the FDA may ultimately agree with the recommendations of the advisory committee;
- the FDA or applicable foreign regulatory authorities may approve a product candidate for which we or our collaborators are seeking regulatory approval for a more limited patient population than expected or with substantial use restrictions;
- as was the case with ZULRESSO, the FDA may require a REMS as a condition of approval or post-approval for our product candidates, or may modify an existing REMS;
- the FDA or applicable foreign regulatory authorities may determine that the manufacturing processes or facilities of third-party contract manufacturers with which we contract do not conform to applicable requirements, including current Good Manufacturing Practices, or cGMPs; or

- the FDA or applicable foreign regulatory agencies may change their approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize or delay our or our collaborators' ability to obtain regulatory approval for and successfully market our product candidates. Even if we or our collaborators receive marketing approval for any of our product candidates, regulatory or other governmental authorities may still impose significant restrictions, including restrictions on the indicated use or marketing, or may impose ongoing requirements for potentially costly post-approval studies. For example, the FDA has imposed post-approval obligations in connection with approval of ZULRESSO. We may not be able to fulfill these obligations in accordance with the FDA's timelines, or at all. The FDA may recommend scheduling with respect to any of our current or future product candidates. In such event, as was the case with ZULRESSO, prior to a product launch, the U.S. Drug Enforcement Administration, or DEA, will need to determine the controlled substance schedule of the product, taking into account the recommendation of the FDA. The timing of the scheduling process is uncertain and may delay our ability to market any product candidate that is successfully developed and approved.

Additionally, disruptions at the FDA and other agencies may 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, the U.S. government has shut down several times and certain regulatory agencies, including the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs in the future, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Fast Track and Breakthrough Therapy designations from the FDA or PRIority Medicines, or PRIME, designation from the European Medicines Agency, or EMA, do not necessarily lead to a faster development pathway or regulatory review process, and do not increase the likelihood of regulatory approval. The FDA may withdraw Fast Track designation or Breakthrough Therapy designation, and the EMA may withdraw PRIME designation, if the relevant agency believes that the designation is no longer supported by data from our clinical development programs.

The COVID-19 pandemic has adversely impacted and may continue to adversely impact our business, including our sales of ZULRESSO and our initiation, conduct and completion of non-clinical studies and clinical trials.

The COVID-19 pandemic in the U.S. resulted in a significant number of sites of care pausing treatment of new patients with ZULRESSO and potential new sites of care pausing site activation activities for a period of time. We believe concerns about exposure to the virus have also caused a significant reduction in the number of women with PPD seeking treatment with ZULRESSO and in physicians willing to prescribe it. Given continuing concerns about the COVID-19 pandemic across the country, including as a result of the spread of variants and "breakthrough" cases among fully-vaccinated people, we expect the significant adverse impact of the pandemic on ZULRESSO revenues to continue. The scope and timing of the expected negative impact will depend on, among other factors, the scope and duration of the pandemic; the effectiveness of vaccination campaigns, vaccine mandates, and other efforts to control the pandemic; the duration of the vaccines' efficacy against COVID-19 and its variants; the extent to which variants of the virus that causes COVID-19 negatively impact vaccination and other efforts to control the pandemic; the duration and severity of any restrictive measures taken to curb the spread of COVID-19; and the impact of the pandemic on the Company's customers and vendors. We cannot predict for how long and to what extent the COVID-19 pandemic will have an adverse impact on ZULRESSO sales.

As a result of the COVID-19 pandemic, we may also continue to experience delays or other disruptions that could negatively impact our ongoing and planned development activities, including the timing of initiation and completion of non-clinical studies and clinical trials or the integrity, completeness or usefulness of the data we collect in those studies or trials. These delays and disruptions may include:

- delays or difficulties in recruiting clinical sites and in clinical site initiation, or the diversion of other healthcare resources and personnel, due to prioritization of medical resources to the treatment of COVID-19 patients or as a result of recommended or required precautions or limitations intended to curb the spread of the virus;

- delays or difficulties in enrolling patients in our clinical trials, including, for example, with respect to recruiting older patients and PPD patients as we have seen in certain of our clinical trials, or an increase in the number of

patients who withdraw from our clinical trials prior to completion as a result of concerns about COVID-19 or as a result of recommended or required precautions or limitations intended to curb the spread of the virus, or the potential that patients in our trials may have or contract COVID-19 which may impact the trial results;

- delays or disruptions in non-clinical studies due to precautions taken by contract research organizations, or CROs, or other vendors in light of the spread of COVID-19 or related restrictions recommended or imposed by federal, state or local authorities;

- limitations or modifications to study procedures, the number and type of study visits or data collection or data analysis activities, or other restrictions on other key clinical trial activities such as monitoring and auditing, in response to the COVID-19 pandemic or as a result of restrictions imposed or recommended by federal, state or local governments;

- interruption or delays in the operations of the FDA and foreign regulatory agencies, which may impact timelines for initiation of clinical trials, amendments of protocols, or inspections of manufacturing facilities;

- interruption of, or delays in, availability of supplies of our product candidates if the COVID-19 pandemic continues in surges or recurs in waves for an extended period, including the potential for shortages of raw materials, other drugs or materials used in our clinical trials, including the standard antidepressant therapy being assessed in combination with zuranolone in the CORAL Study, or staff available to our contract manufacturing organizations or other vendors in the supply chain or as the result of restrictions or limitations in their businesses or activities; and

- limitations on employee resources that would otherwise be focused on the conduct of our non-clinical studies and clinical trials, including due to illness as a result of the COVID-19 pandemic.

The COVID-19 pandemic has also caused economic disruption, which could impair our business prospects. Additionally, future surges of COVID-19 or the failure of current efforts to control the pandemic may cause further economic disruptions and may in the future adversely impact the capital markets and make additional capital unavailable to us on acceptable terms, or at all if we were to seek it.

The number of people with the diseases and disorders for which our products and product candidates are targeted may be smaller than we expect or our other assumptions with respect to the potential markets for our products and product candidates may not be correct and the markets may be significantly smaller than we expect.

Our lead product, ZULRESSO, has been approved in the U.S. for the treatment of PPD in adults. We are developing our product candidate, zuranolone, for the treatment of MDD, PPD, and other potential indications. We are developing SAGE-324 as a potential oral therapy for neurological conditions, such as essential tremor, epilepsy and Parkinson's disease. We are exploring SAGE-718 as a potential treatment for certain cognition-related disorders associated with NMDA receptor dysfunction, including cognitive dysfunction associated with diseases such as Huntington's disease, Parkinson's disease and Alzheimer's disease. There is no precise method of establishing the actual number of patients with any of these disorders in any geography over any time period. With respect to PPD, MDD, essential tremor and the other indications in which we are developing, or plan to develop, our product candidates, we estimate the prevalence of the disease or disorder, and our estimates as to prevalence, including the assumptions we apply in determining our estimate, may not be accurate. In each case, there is a range of estimates in the published literature and in marketing studies, which include estimates within the range that are lower than our estimates. For example, our estimates of the prevalence of PPD are higher than estimates reported in some of the published literature and results obtained from certain studies analyzing claims databases. We believe these differences may be the result of variations in analytical methodologies and possibly under-diagnosis of PPD as a result of lack of screening and under-reporting and some patients being reluctant to seek treatment in clinical practice. The actual number of patients with PPD, MDD, essential tremor or any other indication in which we elect to pursue development of our product candidates may, however, be significantly lower than we believe. Even if our prevalence estimates are correct, any approved product that we develop may only be indicated for or used by a subset of patients with the relevant disease or disorder. Our assumptions and estimates about the market for ZULRESSO and the potential market for our current and future product candidates may not be accurate. In the event the number of patients with the diseases and disorders we are studying is significantly lower than

we expect, we or our collaborators may have difficulties in enrolling patients in our clinical trials which may delay or prevent development of our product candidates. If our prevalence estimates with respect to any indication or our other market assumptions are not accurate, the markets for any approved product for these indications may be smaller than we anticipate, which could limit our revenues and our ability to achieve profitability or to meet our expectations with respect to the level and timing of revenues or profits.

Positive results from non-clinical studies and clinical trials of our product candidates are not necessarily predictive of the results of later non-clinical studies and clinical trials of our product candidates in the same indications or other indications. Interim results from non-clinical studies and clinical trials may not be predictive of results of such non-clinical studies or clinical trials once completed. If we cannot replicate the positive results from our earlier non-clinical studies and clinical trials of our product candidates in our later non-clinical studies and clinical trials in the same indications or other indications, or we cannot replicate our interim results in our completed non-clinical studies and clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

Positive results from non-clinical studies and clinical trials of our product candidates may not necessarily be predictive of the results we or our collaborators may obtain from subsequent non-clinical studies or clinical trials using the same product candidate or other product candidates. For example, unlike earlier trials of zuranolone in MDD and PPD, the Phase 3 MOUNTAIN Study evaluating zuranolone in patients with MDD did not meet its primary endpoint. We or our collaborators may find that ongoing or future clinical trials of zuranolone or any of our other product candidates may also fail to meet their primary endpoints. Similarly, interim results from non-clinical studies and clinical trials may not be predictive of results of a non-clinical study or clinical trial once completed.

We or our collaborators may also observe safety issues in clinical trials or non-clinical studies of our product candidates that we or they did not observe or appreciate in earlier stage clinical studies or non-clinical studies, or a different rate or severity of events, including as a result of an increase in dosing or in frequency or duration of dosing, studying a different patient population or different indication than previously studied, or administering a product candidate with a concomitant medication. For example, we evaluated a 50 mg dose of zuranolone in our WATERFALL Study in patients with MDD, and as part of our ongoing clinical development efforts, we continue to evaluate a 50 mg dose in our ongoing pivotal Phase 3 clinical trials for zuranolone, which has achieved higher patient exposures than those observed in patients in earlier clinical trials of zuranolone. In our planned dose-ranging study of SAGE-324, we plan to evaluate multiple doses, including the same maximum dose of SAGE-324 that we evaluated in prior studies, but we plan to increase the duration of dosing. Any of these studies may result in unexpected adverse events or raise other safety issues or may otherwise generate negative results.

The results from non-clinical animal models may not be replicated in clinical trials. Many product candidates, including many targeting central nervous system disorders, with promising non-clinical profiles have failed to demonstrate similar safety, non-toxicity and efficacy in humans.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later-stage clinical trials after achieving positive results in earlier-stage development, and we cannot be certain that we will not face similar setbacks. Many drugs have failed to replicate efficacy and safety results in larger or more complex later stage trials. Moreover, non-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in non-clinical studies and clinical trials nonetheless failed to obtain FDA approval. If we or our collaborators fail to produce positive results in our ongoing and planned non-clinical studies or clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected.

Failures or delays in the commencement or completion of our ongoing and planned clinical trials of our current and future product candidates could cause us not to meet our expected timelines or result in increased costs to us, and

could delay, prevent or limit our ability to gain regulatory approval of any such product candidate and to generate revenue from resulting products, if any.

Successful completion of clinical trials at each applicable stage of development is a prerequisite to submitting an NDA to the FDA or equivalent filings outside the U.S. and, consequently, the ultimate approval and commercial marketing of any of our product candidates for the indications in which we develop them. We do not know whether any of our ongoing clinical trials will be completed, and results announced, or whether future trials will begin, as planned or expected, if at all, as the commencement and completion of clinical trials and announcement of results can be delayed or prevented for a number of reasons, including, among others:

- denial by the FDA or other regulatory authority of permission to proceed with our planned clinical trials or any other clinical trials we may initiate, or placement of one or more clinical trials on full or partial clinical hold;
- delay or inability to satisfy the requirements of the FDA to commence clinical trials, including chemistry, manufacturing and control, or CMC, requirements, or to file or receive approvals of additional investigational new drug applications, or INDs, that may be required;
- negative or inconclusive results from our ongoing non-clinical studies or clinical trials;
- challenges in identifying, recruiting, enrolling and retaining patients to participate in clinical trials;
- the impact of the COVID-19 pandemic;
- delays in reaching or failing to reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- inadequate quantity or quality of supplies of a product candidate or other materials necessary to conduct clinical trials;
- difficulties obtaining Institutional Review Board, or IRB, approval, and equivalent approval for sites outside the U.S., to conduct a clinical trial at a prospective site or sites;
- delays or problems in analyzing data, or the need for additional analysis or data or the need to enroll additional patients;
- the occurrence of serious adverse events or unexpected drug-related side effects experienced by patients in a clinical trial or unexpected results in ongoing non-clinical studies;
- delays in validating endpoints utilized in a clinical trial;
- the FDA or applicable regulatory authorities outside the U.S. disagreeing with our clinical trial design and our interpretation of data from clinical trials, or changing the requirements for approval even after the regulatory authority has reviewed and commented on the design for our clinical trials; and
- reports from non-clinical or clinical testing of other therapies that raise safety or efficacy concerns.

In addition, a clinical trial may be suspended or terminated by us, the FDA or other regulatory authorities, the IRB or Ethics Committee, or EC, at the sites where the IRBs or ECs are overseeing a clinical trial, or recommended for termination or suspension by a data and safety monitoring board overseeing the clinical trial at issue or other regulatory authorities due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;

- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a partial or full clinical hold;

- unforeseen safety issues, including any that could be identified in our ongoing non-clinical studies, or adverse side effects or lack of effectiveness identified in ongoing clinical trials;

- changes in government regulations or administrative actions; and

- problems with clinical supply materials.

Additionally, changes in regulatory requirements or guidance or unanticipated events during our non-clinical studies and clinical trials may force us or our collaborators to amend non-clinical studies and clinical trial protocols or the applicable regulatory authorities may impose additional non-clinical studies and clinical trial requirements. Amendments or changes to clinical trial protocols would require resubmission to the FDA and IRBs for review and approval, which may adversely impact the cost, timing or successful completion of clinical trials. If we or our collaborators experience delays completing, or if we or our collaborators terminate, any of our non-clinical studies or clinical trials, or if we or our collaborators are required to conduct additional non-clinical studies or clinical trials, the development pathway, and ultimately the commercial prospects, for our product candidates may be harmed and our ability to generate product revenue from resulting products, if any, will be delayed.

We or our collaborators may never seek or receive regulatory approval to market any of our products or product candidates outside of the U.S., or receive pricing and reimbursement outside the U.S. at acceptable levels.

We or our collaborators may not seek, or may seek but never receive, regulatory approval to market our products or product candidates outside of the U.S. or in any particular country or region. In order to market any product outside of the U.S., we or our collaborators must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional non-clinical studies or clinical trials, additional work related to manufacturing and analytical testing on controls, and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in other countries. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the U.S. as well as other risks. In particular, in many countries outside of the U.S., products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval may require additional studies and data, and can result in substantial delays in bringing products to market in such countries and such investment may not be justified from a business standpoint given the market opportunity or level of required investment. Even if we or our collaborators generate the data and information which we believe may be sufficient to file an application for regulatory approval of any of our products or product candidates in a region or country outside the U.S., the relevant regulatory agency may find that we did not meet the requirements for approval, or even if our application is approved, we may have significant post-approval obligations.

Even if we or our collaborators are able to successfully develop our product candidates and obtain marketing approval in a country outside the U.S., we or they may not be able to obtain pricing and reimbursement approvals in such country at acceptable levels or at all, and any pricing and reimbursement approval we or they may obtain may be subject to onerous restrictions such as caps, rebates or other hurdles or restrictions on reimbursement. Failure to obtain marketing and pricing approval in countries outside the U.S. without onerous restrictions or limitations related to pricing, or any delay or other setback in obtaining such approval, would impair our ability or that of our collaborators to market our product candidates successfully or at all in such foreign markets. Any such impairment would reduce the size of our potential market or revenue potential, which could have a material adverse impact on our business, results of operations and prospects.

Any setback or delay in obtaining regulatory approval or commencing marketing, if approved, for our product candidates in a country or region outside the U.S. where we or our collaborators have decided it makes business sense to proceed may have a material adverse effect on our business and prospects.

We rely, and expect that we will continue to rely, on third parties to conduct any clinical trials for our product candidates. If these third parties do not successfully carry out their contractual duties, comply with applicable standards and meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our products, if approved, and our business could be substantially harmed.

We do not have the ability to independently conduct clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct clinical trials of our product candidates. We enter into agreements with third-party CROs to provide monitors for and to manage data for our ongoing clinical trials. We rely heavily on these parties for execution of clinical trials for our product candidates and control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these clinical trials and the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- fail to comply with current Good Clinical Practices, or GCPs, or experience other regulatory compliance issues;
- undergo changes in priorities or become financially distressed;
- form relationships with other entities, some of which may be our competitors; or
- be impacted by the COVID-19 pandemic in ways that adversely affect our business.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials, and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements, and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We, clinical investigators, and our CROs are required to comply with regulations and guidelines, including GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities for any product candidates in clinical development or where clinical trials are being conducted. If we or our CROs or contract manufacturers fail to comply with these regulations or if the quality or accuracy of the clinical data obtained is compromised due to the failure to adhere to our clinical protocols or other regulatory requirements or for other reasons, and we are unable to rely on clinical data collected, we may be required to repeat clinical trials or extend the duration of, or increase the size of our clinical trials. This would delay the regulatory approval process, and could also subject us to enforcement action up to and including civil and criminal penalties. If any of our relationships with third-party CROs terminate or if a CRO needs to be replaced, we may not be able to enter into arrangements with alternative CROs in a timely manner or at all. Any of these issues could significantly delay or prevent regulatory approval of our product candidates and require significantly greater expenditures. In such an event, we believe that our financial results might be harmed, our costs could increase and our ability to generate revenue from products beyond ZULRESSO could be delayed.

We rely completely on third-party suppliers to manufacture commercial supplies of ZULRESSO and clinical drug supplies for our product candidates, and we intend to rely on third parties to produce non-clinical, clinical and commercial supplies of our approved products and product candidates in the future.

We do not currently have, nor do we plan to acquire or develop, the infrastructure or capability internally to manufacture supplies of ZULRESSO for commercial use, or of any of our other existing or future product candidates, for use in the conduct of our clinical trials and non-clinical studies or for future commercial use, and we rely completely on third-party suppliers for both active drug substances and finished drug products.

We rely on our contract manufacturers for commercial supplies of active drug substance, finished drug product and packaged and labeled product with respect to ZULRESSO. We also rely on our contract manufacturers to manufacture sufficient quantities of zuranolone, SAGE-324, SAGE-718, SAGE-689, SAGE-904 and our other product candidates for ongoing and planned clinical trials and non-clinical studies and expect to rely on them to scale our manufacturing processes for future clinical trials, if our development efforts are successful. We expect our contract manufacturers to comply with cGMPs in the manufacture of our products. The facilities used by our contract manufacturers to manufacture the active pharmaceutical ingredient and final drug product must typically complete a pre-approval inspection by the FDA and other comparable foreign regulatory agencies to assess compliance with applicable requirements, including cGMPs, after we submit the relevant NDA or equivalent foreign regulatory submission to the applicable regulatory agency. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, and pass regulatory inspections, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities with respect to our products. In addition, we have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel. Furthermore, all of our third-party contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our third-party contract manufacturers to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our contract manufacturers' facilities generally. If the FDA or an applicable foreign regulatory agency determines now or in the future that these facilities for the manufacture of our products and product candidates are noncompliant, we may need to find alternative manufacturing facilities, which would significantly adversely delay or impact our commercialization efforts for any approved product and our ability to develop and obtain regulatory approval for our product candidates. Our reliance on contract manufacturers also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information. Also, if a natural disaster were to interrupt or halt production of our drug substance or drug product at one of our third-party contract manufacturers, or cause the loss of batches, we could encounter a supply shortage or face significant costs to rebuild our supply.

We have long-term supply agreements with our contract manufacturers with respect to ZULRESSO drug substance and drug product. We have an inventory of ZULRESSO drug product and drug substance in place to help mitigate any potential supply risks, but there is no guarantee that this inventory will be adequate. We do not yet have long-term supply agreements in place with our contract manufacturers with respect to drug substance or drug product for any of our product candidates. Each batch of drug substance and drug product for our product candidates is individually contracted through a purchase order governed by our master service and quality agreements. If our existing contract manufacturers for our other product candidates are not willing to enter into long-term supply agreements, or are not willing or are unable to supply drug substance or drug product to us, we could be required to engage new contract manufacturers who would need to scale up the manufacturing process before we would be able to use the drug product or drug substance they manufacture for clinical trials or for future commercialization, if we are successful. In addition, any contract manufacturer will need to complete validation batches, pass an inspection by the FDA and other applicable foreign regulatory agencies, and be approved by regulatory authorities as our manufacturer before we would be able to use drug product or drug substance they manufacture for commercial purposes, which could result in significant delays or gaps in product availability. We plan to continue to rely upon contract manufacturers to manufacture commercial quantities of our products, if approved. If we are unable to maintain arrangements for third-party manufacturing, or are unable to do so on commercially reasonable terms, or are unable to obtain timely regulatory approvals in connection with our contract manufacturers, we may not be able to successfully commercialize any approved product or successfully complete development of our current or future product candidates.

ZULRESSO or any future product, if our ongoing development efforts are successful, may not achieve broad market acceptance or reimbursement at sufficient levels, which would limit the revenue that we generate from its sales.

The commercial success of ZULRESSO or of any of our current or future product candidates, if successfully developed and approved by the FDA or other applicable regulatory authorities, will depend upon the awareness and acceptance among the medical community, including physicians, patients and healthcare payors, and reimbursement at sufficient levels.

The availability of coverage and adequacy of reimbursement is essential for most patients to be able to access and afford treatments. Patients who are prescribed medications for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Government authorities, including the Centers for Medicare and Medicaid Services, or CMS, an agency within the Department of Health and Human Services, or HHS, in the U.S., and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels for those medications. Cost containment is a primary concern in the U.S. healthcare industry and elsewhere. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Payors may adopt restrictions on coverage such as requiring patients to try other lower cost therapies prior to being prescribed our product, requiring patients to meet severity or other criteria more restrictive than the approved label for our product, or requiring onerous and time-consuming prior authorization procedures, or they may limit the amount of reimbursement. These restrictions or limitations might impede appropriate use of our product for the approved indication. Restrictions and limitations on reimbursement or delays in obtaining coverage may vary significantly among payors and payor types. As a result, there is significant uncertainty related to third-party payor coverage and reimbursement of approved drugs. Regulatory approvals, pricing and reimbursement for drug products vary widely from country to country. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is a covered benefit under its health plan; safe, effective and medically necessary; appropriate for the specific patient; cost-effective; and neither experimental nor investigational.

The inability of us or our collaborators to promptly obtain and maintain coverage and adequate reimbursement rates from both government-funded and private payors for ZULRESSO and any other approved products that we develop could have a material adverse effect on our operating results, our ability to successfully commercialize our products, our ability to raise capital and our overall financial condition. Even if coverage is provided, we may not be able to establish or maintain pricing sufficient to realize a sufficient return on our investment.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor can be an expensive and time-consuming process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to the payor. For example, the availability, terms and timing of coverage for ZULRESSO varies from payor to payor, both for commercially insured patients and from state Medicaid systems, and we have encountered some states that impose significant coverage restrictions or lengthy delays on reimbursement of ZULRESSO. As a result, certain healthcare settings will not treat Medicaid patients with ZULRESSO even if they are active treating sites of care for ZULRESSO. The industry competition to be included in third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement, often leads to downward pricing pressures on pharmaceutical products. In addition, 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 generic equivalent or other alternative is available. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors, and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply when such metrics are not submitted accurately and on a timely basis. Before granting reimbursement approval, payors may require us to demonstrate that our product candidates, in addition to treating the target indications, also provide incremental health benefits to patients or healthcare costs savings. We cannot be sure that adequate coverage or reimbursement will be available for any product candidate that we or our collaborators commercialize.

Market acceptance will depend on a number of factors, including, among others:

- the efficacy and safety of our products as demonstrated in clinical trials;
- the potential and perceived advantages and limitations of our products over current or future alternative treatment options, including in the case of ZULRESSO, the impact of limitations arising from the intravenous infusion mode of administration, the length of stay required for treatment, restrictions on site of care to REMS certified healthcare settings and other requirements of the REMS, the risk of excessive sedation and loss of consciousness

during administration, and, in the case of ZULRESSO and zuranolone, if successfully developed and approved, the availability of lower cost antidepressants;

- the incidence and severity of any side effects of the products;
- limitations or warnings contained in the labeling approved for our products by the FDA or other applicable regulatory authorities;
- the clinical indications and size of patient populations for which our products are approved;
- the convenience, benefit, ease and availability of alternative treatments already approved or expected to be commercially launched in the near future;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, and our ability to increase awareness of our approved products through marketing efforts;
- the strength and effectiveness of our sales, marketing and distribution strategies and support or that of our collaborators;
- publicity concerning our products or competing products and treatments;
- pricing and cost effectiveness; or
- the availability of sufficient third-party coverage or reimbursement, and the willingness of patients to pay out-of-pocket in the absence of such coverage or reimbursement, including in the case of ZULRESSO for both the product and the cost of the infusion.

Our efforts to change the treatment paradigm for a given disorder or to educate the medical community and third-party payors about the benefits of any current or future products, to the extent permitted, may require significant resources and may never be successful. If ZULRESSO, or any of our product candidates that may be approved in the future, do not achieve an adequate level of acceptance by patients, physicians, healthcare settings and payors, or reimbursement at reasonable levels, or if the patient population for which any such product is approved is smaller than we expect, we may not generate sufficient revenue from our products to become or remain profitable or to adequately fund operations or may not do so on the timelines we expect.

Even if marketing approval is granted for a product, we may face significant post-marketing obligations and future development and regulatory difficulties.

Regulatory authorities may impose significant and potentially costly post-marketing obligations with respect to approval of any product, including post-marketing studies, additional CMC work and additional pediatric studies. For example, the FDA has imposed post-marketing commitments with respect to approval of ZULRESSO, and we may encounter issues or delays in the conduct of these post-marketing commitments or we may generate unexpected results.

In the event we or our collaborators elect, or are required, to proceed with pediatric studies of any of our product candidates in any indication, regulatory authorities may also require additional non-clinical studies or clinical trials be completed prior to commencement of such pediatric studies.

As was the case with brexanolone, the FDA may recommend controlled substance scheduling for our current or future product candidates, if approved. In such event, the DEA will need to determine the controlled substance schedule taking into account the recommendation of the FDA. If products are determined to be controlled substances, the manufacturing, shipping, storing, selling and using of the products will be subject to an additional regulation. Distribution, prescribing and dispensing of these drugs are also regulated. Because of their restrictive nature, these laws and regulations could limit commercialization of our product candidates containing controlled substances. Failure to comply with these laws and regulations could also result in withdrawal of our DEA registrations, disruption in manufacturing and

distribution activities, consent decrees, criminal and civil penalties and state actions, among other consequences. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use, and may not be marketed or sold in the U.S. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. Brexanolone is currently regulated as a Schedule IV controlled substance. Other Schedule IV controlled substances include sedative hypnotics such as benzodiazepines.

ZULRESSO is, and any future approved products will also be, subject to ongoing FDA requirements governing the labeling, packaging, storage and promotion of the product and record-keeping and submission of safety and other post-market information. The FDA has significant post-marketing authority, including, for example, the authority to require labeling changes based on new safety information and to require post-marketing studies or clinical trials to evaluate serious safety risks, safety and efficacy in pediatric populations or alternate doses or dose regimens.

The FDA also has the authority to require, as part of an NDA or post-approval, the submission of a REMS. For example, the FDA has required a REMS for ZULRESSO. Any REMS required by the FDA may lead to increased costs to assure compliance with the REMS and with additional post-approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue. In addition, if we are unable to comply with the ZULRESSO REMS or any REMS imposed for a future product, we may face additional restrictions, limitations or substantial penalties, any of which may materially adversely affect our business and results of operations.

We, our collaborators and the third-party manufacturers of our drug substance and drug products and our respective facilities are subject to extensive regulations in the manufacture of our products and product candidates, including GMP, and are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with GMPs and other regulations. If we, our collaborators or a regulatory agency discover problems with our approved products or product candidates such as poor control of production processes or other problems with the facility where our products are manufactured or in the manufacturing process, introduction of contaminants, or adverse events of unanticipated severity or frequency, a regulatory agency may impose restrictions on our products, the manufacturer or us or our collaborators, including requiring withdrawal of such products from the market or suspension of manufacturing. If we, our collaborators, our approved products, our product candidates, or the manufacturers for our products or product candidates fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw marketing approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require that we initiate a product recall.

Competing therapies may exist or could emerge that adversely affect the amount of revenue we are able to generate from the sale of ZULRESSO or any of our current or future product candidates, if successfully developed and approved.

The biopharmaceuticals industry is highly competitive. There are many public and private companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our products or product candidates or address similar markets. It is probable that the number of companies seeking to develop products and therapies similar to our products or targeting similar indications will increase. Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do, and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. We expect competition in the indications we are pursuing will focus on efficacy, safety, convenience, availability, and price. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are perceived to be safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Currently, there are no pharmacological therapies specifically approved for the treatment of PPD other than ZULRESSO. Current standard of care for PPD commonly consists of psychotherapy; however, patients with moderate or severe PPD are often prescribed antidepressant medications such as selective serotonin reuptake inhibitors, or SSRIs, and serotonin and norepinephrine reuptake inhibitors, or SNRIs.

Our most advanced product candidate, zuranolone, is in Phase 3 development for MDD and PPD. Patients with MDD are typically treated with a variety of antidepressant medications, including SSRIs and SNRIs. If successfully developed and approved, zuranolone may also face competition from esketamine, which is approved in the treatment of treatment resistant depression. A number of companies are developing product candidates intended for the treatment of MDD, including NMDA receptor antagonists or partial antagonists such as dextromethorphan/ bupropion. In April 2021, Axsome Therapeutics, Inc. announced that the FDA had accepted and granted priority review to the NDA package for its NMDA receptor antagonist, AXS-05, which received Breakthrough Therapy designation for MDD in March 2019. In addition, if zuranolone is successfully developed and approved for PPD, it could reduce our commercial opportunity for ZULRESSO.

In the field of neuroactive steroids focused specifically on modulation of GABAA receptors, we also face competition from a number of companies, including Marinus Pharmaceuticals, Inc., or Marinus, and Praxis Precision Medicines, or Praxis. In August 2021, Marinus announced the submission of its NDA to the FDA for its product candidate ganaxolone, a known GABAA positive allosteric modulator neuroactive steroid, to treat seizures associated with CDKL5 deficiency disorder, a rare, genetic epilepsy. Ganaxolone is also in Phase 3 development for status epilepticus and tuberous sclerosis complex. Praxis is developing PRAX-114, a GABAA receptor modulating neuroactive steroid, for MDD that is currently in Phase 2/3 development.

SAGE-324, a novel GABAA receptor positive allosteric modulator, is in Phase 2 development in essential tremor. If successfully developed and approved, SAGE-324 may face competition from a Phase 2b-ready T-type calcium channel modulator in development for essential tremor by Jazz Pharmaceuticals, Inc., or a Phase 2 T-type calcium channel modulator in development for essential tremor by Praxis.

A number of companies are working to develop products targeted at the NMDA receptor, both antagonists and agonists. Aptinyx Inc. has multiple Phase 2 NMDA receptor modulators in development for multiple indications, including NYX-458 for the treatment of cognitive impairment in Parkinson’s disease.

Our existing collaborations with Biogen and Shionogi, and any future collaborations, may not lead to the successful development or regulatory approval of product candidates or commercialization of products. Our collaborators may have competing priorities, conflicting incentives, or different views than us on key decisions, including appropriate program spending, that may hamper or delay our development and commercialization efforts or increase our costs. Our business may be adversely affected if any of our collaborators fails to perform its obligations or terminates our collaboration, or if we are not able to establish future collaborations that we believe to be important to our business on commercially reasonable terms.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates in some or all markets.

Our existing and future collaborations, if any, may not lead to the successful development and commercialization of any products. Our collaborators face both the same challenges and hurdles that we would face in the development and commercialization of product candidates if we were engaged in the activities ourselves, as well as additional challenges related to operating under a collaboration. For example, we have entered into a collaboration and license agreement with Biogen MA Inc., or BIMA, and Biogen International GmbH, or, collectively with BIMA, Biogen, to jointly develop and commercialize zuranolone and SAGE-324 in the U.S. and granting Biogen rights to develop and commercialize those product candidates in the rest of the world other than Japan, Taiwan and South Korea, or the Shionogi Territory, in the case of zuranolone. We have a separate collaboration with Shionogi & Co., Ltd., or Shionogi, under which we granted rights to Shionogi for the development and commercialization of zuranolone in the Shionogi Territory. The efforts under these collaborations may not be successful and we may never receive any additional milestone payments, profit-share revenue or royalty payments from Biogen or Shionogi. In addition, under most collaborations, including our existing collaborations, a certain degree of control in decision-making is transferred to or shared with our collaborators. Our collaborators may use their decision-making authority to make decisions that could delay, decrease the potential of, or otherwise adversely impact, development and commercialization of our product candidates. Similarly, where we share decision-making authority, the need to gain alignment on decisions may slow or impede advancement of our programs and cause us not to be able to meet our timelines or achieve our goals. Our collaborators may have competing priorities or different incentives that cause them to divert resources away from our collaboration, or we may not agree on appropriate spending levels, which could hamper our overall development and commercialization efforts or increase our overall spending. Our collaborators may independently develop, or develop with a competitor, competitive products or may believe that product candidates being evaluated in the collaboration could be competitive with the collaborator's own products. In the case of the collaboration with Biogen, both companies have agreed to certain exclusivity provisions in specified indications which may limit certain development opportunities outside the collaboration. In addition, if we depend on collaborators for capabilities and funding for major product development efforts globally or in key territories then our business may be adversely affected if our collaborator fails to perform its obligations under the agreement or the collaboration terminates. Disputes may also arise with respect to the ownership of rights to technology or products developed with collaborators, which could have an adverse effect on our ability to develop and commercialize any affected product candidate.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all.

We may not be successful in our efforts to identify or discover additional product candidates beyond our existing product candidates or to file investigational new drug, or IND, applications for clinical development of new compounds at the rate we expect, or we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

The success of our business depends upon our and our collaborators' ability to successfully develop, gain approval of and commercialize products based on our current product candidates and on our ability to generate new compounds for development in the future and to successfully complete the non-clinical work necessary to file INDs to pursue clinical development of such new compounds. Our research programs may fail to generate new compounds that meet the standards for non-clinical development, and, if even we are successful in generating such compounds, we may not be able to produce the non-clinical and other data necessary to support IND applications for clinical development, in each case in the number or at the rate we expect or at all for a number of reasons. For example, we may not be able to identify a sufficient number of new targets in areas of interest to us. Our research methodology may be unsuccessful in generating a sufficient number of new compounds appropriate for non-clinical testing in the target areas we identify. Even if we generate new compounds in areas of interest to us, we may determine that those compounds are not appropriate for non-clinical development, or we may generate data in non-clinical development that do not support IND filings for clinical development. We may not have, or devote, sufficient technical, financial, and human resources to our research efforts at the various stages needed to identify targets, generate compounds, conduct non-clinical studies and prepare INDs. Additional potential product candidates may be shown to have harmful side effects or may not have a positive risk/benefit profile or may have other characteristics that may make the product candidates not appropriate for further development or unlikely to receive marketing approval.

Because we have limited financial and management resources, we focus on a limited number of clinical and research programs and product candidates and are currently focused on certain brain health disorders. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful and may not yield any commercially viable drugs. Our resource allocation decisions may cause us to fail to capitalize on other viable opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights through future collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain such sole development and commercialization rights. If any of these events occur, it may have a material adverse effect on our business.

If our development efforts related to our current and future product candidates are successful, we expect to need to significantly develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

Given the complexity and level of activities and resources that may be necessary to commercialize future products, if our development efforts are successful, we expect in the future to need to significantly increase our number of employees and the scope of our operations. For example, if we are ultimately successful in our development efforts with respect to our product candidates, we will need to recruit and train additional qualified personnel, and continue to implement and improve our managerial, operational and financial systems. We may not be able to effectively manage any expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure and give rise to operational mistakes or delays, loss of business opportunities, loss of employees and reduced productivity among remaining employees. If our management is unable to effectively manage any potential significant expansion, our expenses may increase more than expected, and our ability to successfully develop and gain regulatory approval of our product candidates and generate or increase our revenue, if such product candidates are approved, could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize any future products that we successfully develop, and to compete effectively will depend, in part, on our ability to effectively manage the potential future expansion of our company.

Our future success depends on our ability to attract, retain and motivate qualified personnel.

To accomplish our objectives, we require a strong management team with expertise in research and development, clinical development and commercialization. Although we have entered into employment agreements with each of our executive officers, each of them is employed "at will" and may terminate his or her employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. Recruiting and retaining qualified personnel is critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. Failure to succeed in clinical trials or in obtaining regulatory approval may make it more challenging to recruit and retain qualified personnel. If we are unable to continue to attract and retain high quality personnel, our development efforts, business, financial condition, results of operations and growth prospects could be adversely affected.

We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability.

The sale of ZULRESSO and any future approved products and use of our product candidates in clinical trials will expose us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others using, prescribing, selling or otherwise coming into contact with our products and product candidates. For example, we may be sued if any product or product candidate allegedly causes injury or is found to be otherwise unsuitable during clinical trials, manufacturing, marketing, sale or commercial use. 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, including as a result of interactions with alcohol or other drugs, knowledge of risks, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection laws. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of patients from our clinical trials, or difficulty in enrolling clinical trials;
- substantial monetary awards to patients or other claimants;
- decreased demand for our approved products;
- damage to our reputation and exposure to adverse publicity;
- increased FDA warnings on product labels;
- litigation costs;
- distraction of management's attention from our primary business;
- loss of revenue; and
- withdrawal of products from the market or our inability to successfully gain approval of product candidates.

We maintain product liability insurance coverage with a $20.0 million annual aggregate coverage limit. Nevertheless, our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our financial condition, business and prospects could be materially adversely affected.

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

The Medicaid Drug Rebate Program, which we participate in, and other governmental programs impose obligations to report pricing figures to the federal government, require us to pay rebates and participate in discount programs. Other programs impose limits on the price we are permitted to charge certain entities for ZULRESSO or for any future products for which we receive regulatory approval. Statutory and regulatory changes or binding guidance regarding these programs and their requirements could negatively affect the coverage and reimbursement by these programs of ZULRESSO or any future products for which we receive regulatory approval and could negatively impact our results of operations. Our failure to comply with these price reporting and rebate payment obligations could negatively impact our financial results. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to herein as the ACA, and regulations promulgated thereunder could affect our obligations in ways we cannot anticipate.

Pricing and rebate calculations vary among products and programs. The calculations are complex and are often subject to interpretation by us, governmental or regulatory agencies and the courts. If we become obligated to restate or recalculate the amounts we report under these programs, our costs for complying with the laws and regulations governing the Medicaid Drug Rebate Program and our price discounts and rebates could be increased. Additionally, we could be held liable for errors associated with our submission of pricing data under the Medicaid Drug Rebate Program and other federal or state drug pricing programs, including retroactive rebates and program refunds, and if we are found to have knowingly submitted false average manufacturer price or best price information to the government, civil monetary penalties per item of false information. Certain failures to submit required data could result in a civil monetary penalty for each day the information is late beyond the due date and be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program. In the event that CMS terminates our rebate agreement, no federal payments would be available under Medicaid or Medicare Part B for our covered outpatient drugs.

We are subject to other laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

We are subject to a number of healthcare and other statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business.

Our current or future interactions and arrangements with third-party payors, healthcare providers, patients, healthcare settings, and others who play a role in the recommendation, prescription, reimbursement and administration of ZULRESSO and will play similar role with respect to any of our future products, if successfully developed and approved, are governed in part by broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute ZULRESSO or expect to market, sell and distribute any future approved products. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- The federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly (including any kickback, bribe or certain rebates), in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on the one hand, and prescribers, purchasers and formulary managers, among others, on the other.

- The federal False Claims Act imposes criminal and civil penalties, including those from civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties. Pharmaceutical companies have been prosecuted under the False Claims Act in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal health

care programs for the product, among other activities. In addition, the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes privacy, security and breach reporting obligations, including mandatory contractual terms, with respect to safeguarding the privacy and security of individually identifiable health information upon covered entities subject to the rule.

- The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.

- The federal transparency requirements, sometimes referred to as the “Sunshine Act”, under the ACA, require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program to report to HHS information related to physician payments and other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners.

- Analogous state laws and regulations, such as state anti-kickback and false claims laws and transparency laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and drug pricing.

- Various federal and state health information and data protection laws and regulations, and similar types of laws outside the U.S., govern the collection, use, disclosure and protection of health-related and other personal information by us and our collaborators.

Ensuring that our future practices and business arrangements comply with applicable healthcare laws and regulations is costly. It is possible that governmental authorities will conclude that our business practices and arrangements do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our practices or operations, including activities conducted by our commercial team or other of our employees, consultants or vendors, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines and exclusion from government funded healthcare programs, such as Medicare and Medicaid, any of which could substantially disrupt our operations and materially adversely affect our business and financial condition. If any of the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

We and our employees are also subject to other statutes and regulations related to our business, including: regulations imposed by the FDA and applicable non-U.S. regulators, as previously discussed; anti-bribery and anti-corruption laws and regulations applicable to activities outside the U.S.; rules on reporting financial and other information or data timely and accurately; and rules related to insider trading.

Although we have adopted a code of conduct, it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure by our employees to comply with these laws or regulations.

Data collection is governed by restrictive regulations governing the use, processing, and cross-border transfer of personal information.

We must comply with numerous federal, state and non-U.S. laws which govern the privacy and security of health and other personal information. As described above, HIPAA, as amended by HITECH and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH increased the civil and criminal penalties that may be imposed and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA rules and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, when we conduct clinical trials in the U.S., any personal information that is collected in connection with these trials also is regulated by the Federal Policy for the Protection of Human Subjects (the Common Rule) which creates obligations for our company when conducting these trials.

In the event we enroll subjects in our ongoing or future clinical trials in the European Union, or EU, or other countries, we may be subject to additional privacy restrictions, including restrictions relating to the collection, use, storage, transfer, and other processing of personal data, including personal health data, regarding these individuals. Clinical trial activities in the EEA, for example, are governed by the General Data Protection Regulation, or GDPR, in relation to the processing of personal data. The GDPR imposes several requirements on companies that process personal data, strict rules on the transfer of personal data out of the EEA, including to the U.S. and fines and penalties for failure to comply with the requirements of the GDPR and the related national data protection laws of the EU Member States. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR in some situations. The obligations under the GDPR may be onerous and adversely affect our business, financial condition, results of operations and prospects. Compliance with the GDPR 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, litigation, and reputational harm in connection with any European activities. The issues related to the transfer of personal data are subject to substantial uncertainty at this time, and there can be no reasonable level of confidence that any such data transfers will be found to be consistent with EU law if they are challenged. Further, the United Kingdom's exiting of the EU, often referred to as Brexit, has created additional uncertainty with regard to data protection regulation in the United Kingdom and the ability to transfer data from the EU to the UK and then from the UK to the U.S. At this time, it is unclear how data transfers to and from the United Kingdom will be regulated. Similar laws exist in many other countries around the world, and these laws (which are evolving and expanding) create complicated and potentially inconsistent obligations that may impact our business.

We are also subject to the California Consumer Privacy Act, or CCPA, which creates individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. The CCPA also has been amended through a recent referendum in California that creates additional obligations beginning in 2023. At least two states have passed general privacy legislation that may impact our business activities in the future, and additional states are evaluating similar kinds of general privacy legislation. The uncertainty, ambiguity, complexity and potential inconsistency surrounding the implementation and interpretation of CCPA and other enacted or potential laws in other states exemplify the vulnerability of our business to the evolving regulatory environment related to the privacy, security and confidentiality of personal data and protected health information.

The FDA and other regulatory and enforcement agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted off-label uses, we may become subject to significant liability.

The FDA and other regulatory and enforcement agencies strictly regulate the promotional claims that may be made about prescription products, and enforce laws and regulations prohibiting the promotion of off-label uses. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the approved labeling of the product. If we are found to have promoted off-label uses for any product, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. Any promotion of the off-label use of ZULRESSO or any of our future approved products by us or any of our employees could subject us to significant liability, which would materially adversely affect our business and financial condition.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens, price controls, reimbursement issues and other risks and uncertainties, and could negatively impact our U.S. business.

Our future profitability may depend, in part, on our ability, ourselves or through our collaborators, to commercialize our products and product candidates in foreign markets.

The pricing of prescription pharmaceuticals is subject to governmental control outside the U.S. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of regulatory approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

In some countries, including Member States of the EU, the pricing of prescription drugs is subject to governmental control. Additional countries may adopt similar approaches to the pricing of prescription drugs. There can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution, or arbitrage between low-priced and high-priced countries, can further reduce prices. In the U.S., recent legislative proposals and various Trump administration proposals have advanced some form of international reference pricing, with the intent of lowering drug prices in the U.S. by benchmarking U.S. drug prices to prices of similar drugs in other countries which, if passed by Congress and adopted by the Biden administration, might mean that pricing decisions by us or our collaborators outside the U.S. in the future may limit the prices we are able to charge for our products in the U.S. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales by us or our collaborators and the potential profitability of our products in those countries would be negatively affected.

Commercializing our products and product candidates in foreign markets would subject us to additional risks and uncertainties, including:

- our inability to directly control commercial activities to the extent we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, including the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;

- longer accounts receivable collection times;
- reduced protection of intellectual property rights, and the existence of additional potentially relevant third-party intellectual property rights, in some foreign countries; and
- foreign currency exchange rate fluctuations.

Foreign sales of our product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs. For example, Brexit has already and may continue to adversely affect European and/or worldwide regulatory conditions. Brexit could continue to lead to legal uncertainty and potentially divergent national laws and regulations in the EU and the United Kingdom, including those related to the pricing of prescription pharmaceuticals, as the United Kingdom determines which EU laws to replicate or replace, which could impair our ability to transact business in the EU and the United Kingdom in the future, if we elect to seek to commercialize any of our products there.

Risks Related to Our Intellectual Property Rights

If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our products and compositions, their methods of use and any other inventions that are important to the development of our business. We may also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents, should they issue; preserve the confidentiality of our trade secrets; and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain the proprietary position of our product candidates.

We cannot provide any assurances that any of our pending patent applications will mature into issued patents. For example, the U.S. Patent and Trademark Office, or U.S. PTO, has issued a final rejection against one of our patent applications claiming one of our proprietary GABAA positive allosteric modulator compounds, asserting a lack of novelty and non-obviousness. We are in the process of preparing an appeal to the Patent Trial and Appeal Board, and may not be successful in overturning the rejection.

We may be unable to obtain issued patents covering our proprietary compounds. We cannot provide any assurances that any of our issued patents will be enforceable, or include claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. For example, the issued patent and patent applications that provide coverage for ZULRESSO only cover particular formulations and particular methods of using such formulations to treat depressive disorders such as PPD and MDD. As a result, such issued patent and any patent that may issue from such patent applications, would not prevent third-party competitors from creating, making and marketing alternative formulations of brexanolone that fall outside the scope of the patent claims or from practicing alternative methods. Moreover, other parties have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. Such third-party patent positions may limit or even eliminate our ability to obtain patent protection for certain inventions.

The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Patents, if issued, may be challenged, deemed unenforceable,

invalidated, or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, derivation proceedings, *ex parte* reexamination, or *inter partes* review proceedings, post-grant review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition, post-grant review, or comparable proceedings lodged in various foreign, both national and regional, patent offices. These 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. In addition, such proceedings may be costly. For example, our granted European patent covering brexanolone i.v. has been opposed by a third party, and the opposition proceedings are ongoing. Thus, any patents, should they issue, that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding or a derivation proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates. Furthermore, though a patent, if it were to issue, is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability, and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Even if a patent issues, and is held to be valid and enforceable, competitors may be able to design around our patents, such as using pre-existing or newly developed technology. Other parties may develop and obtain patent protection for more effective technologies, designs or methods.

We also may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, vendors, former employees and current employees. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the U.S., and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales if any of our product candidates are approved in those countries. Our ability to enforce our patent rights depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product. Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time-consuming, and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents, if and when issued, could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents, if and when issued, covering our product or product candidates is invalidated or found unenforceable, our financial position and results of operations may be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered our product candidates, our financial position and results of operations may also be materially and adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our pending patent applications, if issued as a patent, will include claims having a scope sufficient to protect our current product candidates or any other products or product candidates;
- any of our pending patent applications will issue as patents at all;
- we will be able to generate significant revenue from sales of ZULRESSO or any of our product candidates, if successfully developed and approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our pending patent applications and any patents that may issue in the future;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe any patents that may be issued to us;

- others will not use pre-existing technology to effectively compete against us;
- any of our patents, if issued or as issued, will provide us with a competitive advantage and be found ultimately to be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- that our commercial activities or products will not infringe upon the patents or proprietary rights of others.

We may rely upon unpatented trade secrets and depend on unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our CROs, collaborators and consultants. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing ZULRESSO and our other product candidates, if approved.

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties. The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our products or product candidates or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. As we continue to develop our current product candidates and commercialize ZULRESSO and any future products, competitors may claim that our technology infringes their intellectual property rights as part of business strategies designed to impede our successful commercialization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, third parties may have currently pending patent applications which may later result in issued patents that our product or product candidates may infringe, or which such third parties claim are infringed by our technologies. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Patent litigation is costly and time-consuming. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney’s fees if we are found to be willfully infringing another party’s patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license. In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing our product or product candidates. In the case of trademark claims, if we are found to be infringing, we may be required to redesign, or rename, some or all of our product candidates to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if

possible, could be costly and time-consuming. Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, CROs, outside scientific collaborators, and other advisors. These agreements 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. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign to us any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign all such intellectual property to his or her employing institution or another party.

Most of our employees have also been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We also engage advisors and consultants who are concurrently employed at universities or who perform services for other entities. We may be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees which could have a materially adverse effect on our business.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other formalities and provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming, and unsuccessful.

Even if the patent applications we own or license are issued, competitors may infringe these patents. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents should be interpreted narrowly and do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings or derivation proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the U.S.

Furthermore, because of the substantial amount of 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. There could also 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 material adverse effect on the price of our common stock.

Issued patents covering our product or any of our product candidates could be found invalid or unenforceable if challenged in court.

If we or one of our collaborators or licensors initiated legal proceedings against a third party to enforce a patent, if and when issued, covering our product or any of our product candidates, the defendant could counterclaim that the patent covering our product or any of our product candidates is invalid and/or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness, lack of written description, or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the U.S. PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *ex parte* reexamination, *inter partes* review, derivation proceedings or interferences and equivalent proceedings in foreign jurisdictions, e.g., opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. For example, our granted European patent covering brexanolone i.v. has been opposed by a third party, and the opposition proceedings are ongoing. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on the applicable product or product candidates. Such a loss of patent protection would have a material adverse impact on our business.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing patent applications and prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. could be less extensive than those in the U.S., assuming that rights are obtained in the U.S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications.

Competitors may use our technologies in jurisdictions where we do not pursue patent protection. They may pursue and obtain their own patent protection to develop their own products. Further, they may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U.S. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our

patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology and pharmaceuticals. For example, a 2020 report from the Office of the U.S. Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights in such jurisdictions. Many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Furthermore, proceedings to enforce our patent rights in foreign jurisdictions could, among other things, result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

For ZULRESSO and certain of our product candidates, we are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing certain of our products or product candidates, if approved. If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates or technology from third parties or, in certain cases, we fail to meet certain development deadlines, we could lose license rights that are important to our business.

We are a party to a number of license agreements under which we are granted rights to intellectual property that are important to our business and we expect that we may need to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose on us, 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 a bankruptcy, 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. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms.

As we have done previously, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents do not exist that might be enforced against our current product candidates or future products in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. If we fail to obtain a license, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. 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 patent and other rights to third parties under licenses or collaborative development relationships;
- 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; 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 be unable to successfully commercialize our product or to successfully develop and commercialize the affected product candidates.

We have entered into several licenses to support our various programs. We may enter into additional licenses to third-party intellectual property that are necessary or useful to our business. Our current licenses and any future licenses that we may enter into impose various royalty payment, milestone, and other obligations on us. For example, the licensor may retain control over patent prosecution and maintenance under a license agreement, in which case, we may not be able to adequately influence patent prosecution or prevent inadvertent lapses of coverage due to failure to pay maintenance fees. If we fail to comply with any of our obligations under a current or future license agreement, the licensor may allege that we have breached our license agreement, and may accordingly seek to terminate our license. In addition, future licensors may decide to terminate their licenses with us at will. Termination of any of our current or future licenses could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop a product candidate or commercialize a product, as well as harm our competitive business position and our business prospects.

In addition, if our licensors fail to abide by the terms of the license, if the licensors fail to prevent infringement by third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms, our business could materially suffer.

Some intellectual property which we have licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-U.S. manufacturers.

Some of the intellectual property rights we have licensed may have been generated through the use of U.S. government funding and may therefore be subject to certain federal regulations. For example, some of the intellectual property rights licensed to us under the license agreement with The Regents of the University of California may have been generated using U.S. government funds. As a result, the U.S. government may have certain rights to intellectual property embodied in our current product or current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if the government determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government

action is necessary to meet requirements for public use under federal regulations (also referred to as “march-in rights”). The U.S. government also has the right to take title to these inventions if we fail, or the applicable licensor fails, to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. In addition, the U.S. government may acquire title to these inventions in any country in which a patent application is not filed within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us, or the applicable licensor, to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the U.S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the U.S. or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

If we enter into future arrangements involving government funding, and we discover compounds or product candidates as a result of such funding, intellectual property rights to such discoveries may be subject to the applicable provisions of the Bayh-Dole Act.

If we do not obtain new chemical entity or other types of marketing and data exclusivity for our product candidates and if we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent terms of our product candidates, our business may be materially harmed.

Marketing exclusivity provisions under the Federal Food, Drug, and Cosmetic Act, or FDCA, can delay the submission or the approval of certain marketing applications by other companies for a product with the same active moiety as a product we sell or may in the future sell. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity, or NCE. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for a full NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. We have obtained NCE exclusivity for brexanolone and plan to seek NCE exclusivity for our current and future product candidates. There is no guarantee that our product candidates will qualify for marketing or data exclusivity under these provisions or that such exclusivity for any of our products will alone be sufficient for our business. The applicable five-year and three-year exclusivity periods of NCE or data exclusivity under the FDCA will not delay the submission or approval of a full NDA.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of the U.S. patents we own or license may be eligible for limited patent term restoration in the future under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. Even if, at the relevant time, we have a valid issued patent covering our product, we may not be granted an extension if we were to fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, and we do not have any other exclusivity, our competitors may obtain approval of competing products following our patent expiration and our business, financial condition or results of operations could be adversely affected.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

Our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the U.S. has recently enacted wide-ranging patent reform legislation: the Leahy-Smith America Invents Act, referred to as the America Invents Act. The America Invents Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. It is not yet clear what, if any, impact the America Invents Act will have on the operation of our business. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents that may issue from our patent applications, all of which could have a material adverse effect on our business and financial condition.

In addition, U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. For example, in March 2012, in *Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al. v. Prometheus Laboratories, Inc.*, the U.S. Supreme Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patentable subject matter. The decision appears to impact diagnostics patents that merely apply a law of nature via a series of routine steps and it has created uncertainty around the ability to obtain patent protection for certain inventions. Additionally, in June 2013, in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that claims to isolated genomic DNA are not patentable, but claims to complementary DNA molecules are patent eligible because they are not a natural product. In June 2014, in *Alice Corporation Pty. Ltd. v. CLS Bank International, et al.*, a case involving patent claims directed to a method for mitigating settlement risk, the U.S. Supreme Court held that the patent eligibility of claims directed to abstract ideas, products of nature, and laws of nature should be determined using the same framework set forth in *Prometheus*. The U.S. PTO has issued a set of guidelines setting forth procedures for determining subject matter eligibility of claims directed to abstract ideas, products of nature, and laws of nature in line with the *Prometheus*, *Myriad*, and *Alice* decisions. The guidance does not limit the application of *Myriad* to DNA but, rather, applies the decision to other natural products. The full impact of these decisions on our business is not yet known.

In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions by the U.S. Congress, the federal courts and the U.S. PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that may issue in the future.

Proposed legislation in Congress, if passed into law, could limit the patent exclusivity on our products or facilitate earlier entry of generic competition.

Members of Congress have proposed numerous legislative initiatives aimed at limiting the patent exclusivity on drug products or facilitating earlier entry of generic versions of approved drugs. Examples of bills that have been proposed include a bill that, if passed, would create a presumption of invalidity for patents beyond the first patent covering a drug product thus shifting the burden to the innovator to prove that these subsequent patents are separately patentable inventions, distinct from the first patent; a bill that, if passed, would empower the Federal Trade Commission to investigate whether large patent portfolios covering a drug product constitute an anti-competitive practice and to file antitrust lawsuits in such instances; and a bill that, if passed, would limit the availability of a 30-month stay on approval by the FDA of a generic version of a drug to only those instances where the ANDA litigation involves a composition of matter patent claiming the drug substance. Such legislation, if passed into law, could adversely affect ZULRESSO or any future products or result in earlier entry into the market of generic versions of our drugs.

Risks Related to our Industry

Healthcare regulations aimed at reducing healthcare costs may have a material adverse effect on our business or results of operation.

There have been, and likely will continue to be, legislation and legislative, administrative and regulatory proposals in the U.S., both at the federal and state level, and in many foreign jurisdictions aimed at reducing healthcare costs. The implementation of unreasonable cost containment measures, drug pricing controls or other reforms that do not recognize the clinical value of innovative medicines could have an adverse effect on our revenue from ZULRESSO or from the sales of any other products that are successfully developed and approved, and may limit our ability to achieve profitability.

For example, in March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, provided a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

There have been a number of significant changes to the ACA and its implementation, including as a result of lawsuits, provisions of other legislation such as The Tax Cuts and Jobs Act of 2017, and executive orders, including many issued by former President Trump. The ACA remains in effect, but it remains unclear how such litigation and other efforts to repeal and replace the ACA will impact the ACA and our business. Former President Trump took various executive actions to undermine or delay implementation of the ACA. However, President Biden has issued a new executive order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care and consider actions that will protect and strengthen that access. The ACA remains in effect, but it remains unclear how such litigation and other efforts to repeal and replace the ACA, and executive orders will impact the ACA and our business.

There has been increasing legislative and enforcement interest in the U.S. with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's proposed budget for fiscal year 2020 contained further drug price control measures and released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out-of-pocket costs of drug products paid by consumers. There have been multiple Congressional efforts to address specialty drug pricing. It is unclear whether any such legislation will be signed into law, and if enacted, what effect it could have on our business. It is also unclear how the Biden administration will approach the issue of drug prices. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and price transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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

- the demand for ZULRESSO and for any of our product candidates, if approved;

- our ability to receive or set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the amount of taxes that we are required to pay; and
- the availability of capital.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for any approved product. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue from sales of ZULRESSO, successfully commercialize any products approved in the future, and achieve profitability.

Our internal computer systems, or those of our collaborators, our third-party CROs or our other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our development programs.

Despite the implementation of security measures, our internal computer systems and those of our collaborators, our third-party CROs and our other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs or cause us to have liability for disclosure of personal information of our customers. For example, the loss of clinical trial data for our product candidates could result in delays in our regulatory submission and approval efforts and significantly increase our costs to recover or reproduce the data, if possible. To the extent that any disruption, disaster or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed or prevented.

We could be required to expend significant amounts of money and other resources to respond to these threats or breaches and to repair or replace information systems or networks. We also could suffer financial loss or the loss of valuable confidential information. In addition, we could be subject to regulatory actions and/or claims made by individuals and groups in private litigation involving privacy issues related to data collection and use practices and other data privacy laws and regulations, including claims for misuse or inappropriate disclosure of data, as well as unfair or deceptive practices. Although we develop and maintain systems and controls designed to prevent these events from occurring and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes are costly and require ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely and there can be no assurance that any measures we take will prevent cyber-attacks or security breaches that could adversely affect our business.

Risks Related to Our Financial Position and Need for Capital

We are a biopharmaceutical company with a limited operating history, and have not generated significant revenue to date. We have incurred significant operating losses since our inception, and anticipate that we will incur losses for the foreseeable future.

We are a biopharmaceutical company with a limited operating history on which investors can base an investment decision. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We were incorporated in April 2010. We have only one approved product, and only began generating revenue from product sales in the second quarter of 2019.

We have funded our operations to date primarily through proceeds from sales of common stock, including the sale of stock to BIMA; redeemable convertible preferred stock prior to our initial public offering and, to a lesser extent, the issuance of convertible notes. From our inception through September 30, 2021, we had received aggregate net proceeds of $2.8 billion from such transactions. We also received $1.0 billion in upfront payments under our collaborations with Biogen and Shionogi. As of September 30, 2021, our cash, cash equivalents and marketable securities were $1.8 billion. We have incurred net losses in each year since our inception, except for net income of $606.1 million for the year ended December 31, 2020, reflecting revenue recognized under a collaboration and license agreement with Biogen. Our net loss was $333.2 million for the nine months ended September 30, 2021, and our accumulated deficit was $1.4 billion as of September 30, 2021.

Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations. We expect to incur increasing levels of operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. We expect our research and development expenses to significantly increase, particularly as we advance our product candidates in non-clinical studies and clinical trials, seek regulatory approval for any product candidates that successfully complete clinical development, and continue our discovery efforts. We also incur significant selling, general and administrative costs in support of ongoing commercialization efforts with respect to ZULRESSO and in connection with other activities, including pre-launch and launch-readiness activities associated with zuranolone. In addition, if we obtain marketing approval for zuranolone or any of our other current or future product candidates beyond ZULRESSO, we will incur significant sales, marketing and outsourced-manufacturing expenses. We incur significant legal and accounting costs associated with operating as a public company. We expect to continue to incur additional significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate product revenue. We began to generate revenue from product sales in the second quarter of 2019 in conjunction with launch of our first product, ZULRESSO, which commenced in June 2019. We expect that our revenue opportunity for ZULRESSO will continue to be limited. Our ability to generate significant product revenue from any future approved product depends on a number of factors, including, but not limited to:

- our ability to initiate and successfully complete all efficacy and safety clinical trials and non-clinical studies required to file for, and obtain, U.S. and foreign marketing approval for our product candidates; and our ability to file for and receive marketing approval to commercialize our product candidates, if successfully developed; and

- with respect to an approved product, our ability, alone or with collaborators, to commercialize the product by developing and effectively deploying a sales force, and to achieve market acceptance and satisfactory reimbursement of such product in the medical community, with patients and with third-party payors.

If we are unable to generate significant product revenue, we will not become profitable, and may be unable to continue operations without continued funding.

We expect we will need to raise additional funding at some point in the future, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of other strategic considerations. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders in our company will be diluted.

We are currently commercializing ZULRESSO and advancing our product candidates through non-clinical and clinical development. Commercializing a product and developing additional small molecule products are expensive. We

expect our research and development expenses to increase significantly, particularly as we advance our product candidates in non-clinical studies and clinical trials and continue our discovery efforts. We also incur significant expenses in connection with the commercialization of ZULRESSO and in connection with other activities, including pre-launch and launch-readiness activities associated with zuranolone and would expect commercialization expenses to increase significantly to commercialize other products, including zuranolone, if approved. We expect we will require additional capital in the future to fund operating needs. We may need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for our product candidates, conduct additional clinical trials for indications we are already pursuing beyond the anticipated trials, identify new potential opportunities or otherwise expand our activities more rapidly than we presently anticipate.

As of September 30, 2021, our cash, cash equivalents and marketable securities were $1.8 billion. Based on our current operating plans, we expect that our existing cash, cash equivalents and marketable securities will be sufficient to fund our anticipated level of operations for at least the next 12 months from the filing date of this Quarterly Report. Our current operating plan does not contemplate other development activities we may pursue or that all of the currently planned activities will proceed at the same pace, or that all of the activities will be fully initiated or completed during that time. We may use available capital resources sooner than we expect under our current operating plan. In addition, our operating plan may change. We may need or choose to seek additional funds sooner than planned, through equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. In any event, we anticipate we will require additional capital to expand future development efforts for, obtain regulatory approval for, and to commercialize our product candidates. If the pandemic and related economic conditions continue for an extended period, or if our business prospects are impaired or the capital markets disrupted for any other reason, additional capital may not be available to us on acceptable terms, or at all. Failure to obtain capital if and when needed may force us to delay, limit or terminate our product development efforts or other operations. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of other strategic considerations.

We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. In the event we receive negative data from our key clinical programs or encounter other major setbacks in our development or regulatory activities or in our commercialization efforts, our stock price is likely to decline which would make a future financing more difficult and potentially more dilutive to our existing stockholders. For example, after the announcement of the topline results of the Phase 3 MOUNTAIN Study of zuranolone on December 5, 2019, our stock price declined significantly. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders. The issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The incurrence of indebtedness would result in increased fixed payment obligations, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders in our company will be diluted. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, our intellectual property, future revenue streams or grant licenses on terms that are not favorable to us.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any approved product, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

Risks Related to Our Common Stock

Market volatility may affect our stock price and the value of an investment in our stock.

The market price for our common stock, similar to that of other biopharmaceutical companies, is volatile. The market price of our common stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- the results of our commercialization efforts with respect to ZULRESSO, and our ability to attain commercial success;
- plans for, progress of, timing of, changes to, delays in or results from clinical trials or non-clinical studies of any of our product candidates, including positive or negative key data from such studies or clinical trials, serious adverse events arising in the course of development, or any delays or major announcements related to such studies or trials;
- the success or failure of any regulatory activities with respect to our product candidates, including our planned submission of an NDA to the FDA seeking approval of zuranolone in the treatment of MDD in the second half of 2022 and the planned submission of an additional filing for the treatment of PPD in the first half of 2023, and whether or not we receive FDA approval of zuranolone in such indications;
- the impact of the COVID-19 pandemic;
- announcements of new products, technologies, commercial relationships, acquisitions, collaborations or other events by us or our competitors;
- the success or failure of our therapies;
- regulatory or legal developments in the U.S. and other countries;
- adverse developments with respect to our intellectual property portfolio or failure to obtain or loss of exclusivity;
- failure of our future product candidates, if successfully developed and approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- the state of the U.S. and world economies, general market conditions and overall fluctuations in U.S. equity markets, including as a result of U.S. or world events;
- changes in healthcare laws affecting pricing, reimbursement or access;
- variations in our quarterly operating results;
- changes in our financial guidance or securities analysts' estimates of our financial performance;
- changes in accounting principles;
- our ability to raise additional capital and the terms on which we can raise it;
- sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;
- additions or departures of key personnel;
- discussion of us or our stock price by the press and by online investor communities; and
- other risks and uncertainties described in these risk factors.

We have broad discretion in how we use our existing cash and the proceeds from potential future follow-on public offerings, and may not use such cash and proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We have considerable discretion in the use of our cash and the application of the net proceeds from potential future follow-on public offerings. We may use cash and net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from any potential future follow-on offerings in a manner that does not produce income or that loses value.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, even one that may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Future sales of our common stock may cause our stock price to decline.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could significantly reduce the market price of our common stock, and impair our ability to raise adequate capital through the sale of additional equity securities. For example, the 6,241,473 shares of our common stock held by BIMA are subject to an 18-month lockup period, after which BIMA will be able to sell shares subject to certain sales volume limitations. Following a second 18-month period, BIMA will be able to sell shares without limitation.

Item 6. Exhibits

The exhibits filed as part of this Quarterly Report on Form 10-Q are set forth on the Exhibit Index, which is incorporated herein by reference.

Exhibit Index

Exhibit No.	Description
10.1*	Offer Letter by and between the Registrant and Christopher Benecchi, dated September 13, 2021
10.2*	Severance and Change in Control Agreement between the Registrant and Christopher Benecchi, dated September 13, 2021
10.3†*	Amendment No. 1 to Exclusive License Agreement, by and between the Registrant and Washington University, dated as of July 13, 2021
10.4*	Side Letter to Biogen Collaboration and License Agreement, by and among the Registrant, Biogen MA Inc. and Biogen International GmbH, dated October 21, 2021
31.1*	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350)
31.2*	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350)
32.1+	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350)
101.INS*	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document)
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.*)

* Filed herewith.

\+ The certifications furnished in Exhibit 32.1 hereto are deemed to be furnished with this Quarterly Report on Form 10-Q and will not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

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.

SAGE THERAPEUTICS, INC.

November 2, 2021

By: /s/ Barry E. Greene
Barry E. Greene
Chief Executive Officer, President and Director
(Principal Executive Officer)

November 2, 2021

By: /s/ Kimi Iguchi
Kimi Iguchi
Chief Financial Officer
(Principal Financial and Accounting Officer)

215 First Street, Cambridge, MA 02142
www.sagerx.com

EXHIBIT 10.1

August 4, 2021
Christopher Benecchi

Dear Christopher:

At Sage, our mission is to make life better for patients with central nervous systems diseases by discovering, developing, and delivering important new medicines to the market. Our success results from our people creating products with benefits for patients coupled with our drive to excel in all areas of our business.

On behalf of Sage Therapeutics, (the “Company” or “Sage”), I am pleased to extend an offer of employment to you. You have made an outstanding impression, and we welcome you to join our team and our quest to make a difference for patients. The purpose of this letter is to summarize the terms of your employment with the Company.

Position

Chief Commercial Officer, Reporting to Barry Greene.

This position is a key factor in Sage’s continued success, and we are confident that it will be an exciting opportunity for you as well. In considering this role, we ask that you agree to devote your full business time, best efforts, skill, knowledge, attention, and energies to the advancement of the Company's business and interests and to the performance of your duties and responsibilities as an employee of the Company.

Compensation

Your base rate of compensation will be $18,333.33 bi-monthly (annualized rate of $440,000.00), less all applicable federal, state, and local taxes and withholdings, to be paid in installments in accordance with the Company's standard payroll practices. Such base salary may be adjusted from time to time in accordance with normal business practices and at the sole discretion of the Company.

In addition, you will be eligible to participate in the Sage Bonus Plan at an annual target of 40.00% of your base salary, which will be prorated based upon your date of hire. Eligible employees starting on or before November 1 in the current plan year are eligible to participate in the plan. This discretionary bonus will be based on the Company's assessment and attainment of corporate and individual goals.

Subject to the approval of the Company's Board of Directors (the "Board") or designee and in connection with the commencement of your employment, you will be granted an equity award that includes a stock option grant (the "Option") and a performance share unit ("PSU") grant. The Option grant will be to purchase 45,000 shares of the Company's common stock, and the PSU grant will be for 22,500 units. The Option and PSUs will be granted on the first business day of the month following the commencement of your employment.

The exercise price of the Option will be equal to the fair market value of the Company's common stock on the date of grant. The Option will vest as follows: the Option will become exercisable as to 25% of the shares on the first anniversary of the Vesting Commencement Date, as defined below; and thereafter, shall become exercisable as to the remaining 75% of the shares in 36 equal monthly installments following the first anniversary of the Vesting Commencement Date until fully vested. The Vesting Commencement Date is your date of hire with the Company.

The PSUs will vest upon the achievement of certain performance goals of the Company. The goals and associated vesting are determined annually by the Board and are reflected in the grant agreement that will be provided to you. On any PSU vesting date, the tax liability will automatically be settled through net settlement of shares, and you will be issued the remaining vested shares. Vesting of both the Option and PSUs assumes continued employment with Sage on the relevant vesting date(s). The Option and PSU grants will be subject to the terms and conditions of the Company's then-current shareholder-approved equity plan and its standard form of equity agreements.

Sign On Bonus

The Company will provide you with a sign-on bonus of $200,000.00, to be paid on your first pay cycle, which will be subject to customary deductions and withholdings as required by law. If you should voluntarily terminate your employment with Sage within the first 12 months of receiving the sign-on bonus, you agree to return the net amount of the payment within 30 days of your departure date. If you should voluntarily terminate your employment with Sage within 13-24 months of receiving the sign-on bonus, you agree to return to the Company 50% of the net amount of the sign-on bonus within 30 days of your departure date.

Benefits

215 First Street, Cambridge, MA 02142
www.sagerx.com

Because we care about the well-being of our employees, we are pleased to provide you with a comprehensive benefits and wellness package. This is meant to assist you in staying healthy, planning for the future, and developing your career. Our benefits currently include medical, dental, vision, vacation, wellness benefit, flexible-spending accounts, 401k, and much more. Additional information about these benefits is outlined in the enclosed summary.

Eligibility for Employment

For purposes of federal immigration law, you will be required to provide the Company documentary evidence that you are eligible for employment in the United States and evidence of your identity. This requirement applies to U.S. citizens, as well as foreign nationals. Such documentation must be provided to the Company within three (3) business days of your date of hire. Please bring the appropriate documents with you on your first day of employment.

Employee Agreement

As a condition of your employment, you will be required to execute the "Agreement Concerning Loyalty, Confidential Business Information, Inventions and Post-Employment Activity" (the "Employee Agreement").

Employment Relationship

You acknowledge that this letter does not constitute a contract of employment for any particular period of time and does not affect the at-will nature of the employment relationship with the Company. Either you or Sage has the right to terminate your employment at any time, with or without cause, and with or without notice.

Prior Obligations

By signing this letter, you represent that you are not bound by any employment contract, restrictive covenant, or other restriction preventing you from entering into employment with or carrying out your responsibilities for the Company, or which is in any way inconsistent with the terms of this letter. Please note that this offer letter is your formal offer of employment and supersedes any and all prior or contemporaneous agreements, discussions, and understandings, whether written or oral, relating to the subject matter of this letter or your employment with the Company.

To accept this offer of employment, please sign this letter in the space provided below and return it to me along with the signed Employee Agreement. This offer will remain open for two business days from the date of this letter. This offer is contingent on a satisfactory background check and reference checks.

We are very enthusiastic about having you join our team! We believe you will make a critical contribution to our success and believe that the opportunities presented will allow you significant personal and professional growth. We hope that you will find Sage a rewarding experience. If you have any questions, please do not hesitate to call anytime.

215 First Street, Cambridge, MA 02142
www.sagerx.com

/s/ Christopher E. Benecchi
SIGNATURE

8/4/21
DATE

Very truly yours,
Sage Therapeutics

/s/ Michael McFarlane

By: Michael McFarlane
Director, Talent Acquisition, People Operations & Analytics

EXHIBIT 10.2

SEVERANCE AND CHANGE IN CONTROL AGREEMENT

This Severance and Change in Control Agreement (this "Agreement") is made as of September 13, 2021 by and between Sage Therapeutics, Inc., a Delaware corporation (the "Company"), and Christopher Benecchi (the "Executive") and shall become effective on the date of hire with the Company.

1. **Purpose**. The Company considers it essential to the best interests of its stockholders to promote and preserve the continuous employment of key management personnel. The Board of Directors of the Company (the "Board") recognizes that, as is the case with many corporations, the possibility of a Change in Control (as defined in Section 2 hereof) exists and that such possibility, and the uncertainty and questions that it may raise among management, may result in the departure or distraction of key management personnel to the detriment of the Company and its stockholders. Therefore, the Board has determined that appropriate steps should be taken to reinforce and encourage the continued attention and dedication of members of the Company's key management, including the Executive, to their assigned duties without distraction, including in the face of potentially disturbing circumstances arising from the possibility of a Change in Control. Nothing in this Agreement shall be construed to affect the at-will nature of the employment relationship, the Executive shall not have any right to be retained in the employ of the Company.

2. **Change in Control**. A "Change in Control" shall be deemed to have occurred upon the occurrence of any one of the following events: (a) the sale of all or substantially all of the assets of the Company on a consolidated basis to an unrelated person or entity, (b) a merger, reorganization or consolidation pursuant to which the holders of the Company's outstanding voting power and outstanding stock immediately prior to such transaction do not own a majority of the outstanding voting power and outstanding stock or other equity interests of the resulting or successor entity (or its ultimate parent, if applicable) immediately upon completion of such transaction, (c) the sale of all of the stock of the Company to an unrelated person, entity or group thereof acting in concert, or (d) any other transaction in which the owners of the Company's outstanding voting power immediately prior to such transaction do not own at least a majority of the outstanding voting power of the Company or any successor entity immediately upon completion of the transaction other than as a result of the acquisition of securities directly from the Company.

3. **Terminating Event**.

A "Terminating Event" shall mean any of the events provided in this Section 3:

(a) Termination by the Company. Termination by the Company of the employment of the Executive with the Company for any reason other than for Cause, death or Disability. For purposes of this Agreement, "Cause" shall mean, as determined by the Company in good faith:

(i) the indictment the Executive of any felony, any crime involving the Company, or any crime involving fraud, moral turpitude or dishonesty;

(ii) any unauthorized use or disclosure of the Company's proprietary information which has an adverse effect on the Company's business or reputation. As used in this paragraph, "Proprietary Information" means any information in whatever form, tangible or intangible, related to the business of the Company unless the information is publicly available in hard copy or electronic format, through lawful means;

(iii) any intentional misconduct or gross negligence on the Executive's part which has a materially adverse effect on the Company's business or reputation; or

(iv) the Executive's repeated and willful failure to perform the duties, functions and responsibilities of the Executive's position after a written warning from the Company.

A Terminating Event shall not be deemed to have occurred pursuant to this Section 3(a) solely as a result of the Executive becoming an employee of any direct or indirect successor to the business or assets of the Company, rather than continuing as an employee of the Company following a Change in Control. For purposes hereof, the Executive will be considered "Disabled" if, as a result of the Executive's incapacity due to physical or mental illness, the Executive shall have been absent from his duties to the Company on a full-time basis for 180 calendar days in the aggregate in any 12-month period.

(b) Termination by the Executive for Good Reason. Termination by the Executive of the Executive's employment with the Company for Good Reason. For purposes of this Agreement, "Good Reason" shall mean that the Executive has complied with the "Good Reason Process" (hereinafter defined) following, the occurrence of any of the following events:

(i) a material diminution in the Executive's responsibilities, authority or duties;

(ii) a material diminution in the Executive's base salary except for across-the-board salary reductions based on the Company's financial performance similarly affecting all or substantially all senior management employees of the Company;

(iii) a material change, defined as miles or more, in the geographic location at which the Executive is required to provides services to the Company, not including business travel and short-term assignments; or

(iv) a material breach of this Agreement by the Company.

"Good Reason Process" shall mean that (i) the Executive reasonably determines in good faith that a "Good Reason" condition has occurred; (ii) the Executive notifies the Company in writing of the first occurrence of the Good Reason condition within 60 days of the first occurrence of such condition; (iii) the Executive cooperates in good faith with the Company's efforts, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) the Executive provides a Notice of Termination to the Company within 60 days after the end of the Cure Period. If the Company cures the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred.

4. **Change in Control Payment**. In the event a Terminating Event occurs on or within the 12 months immediately after a Change in Control (such 12-month period, the "Change in Control

Period"), subject to the Executive signing a separation agreement containing, among other provisions, a general release of claims in favor of the Company and related persons and entities, confidentiality, return of property and non-disparagement, in the form attached hereto as Attachment A (the "Separation Agreement and Release") and the Separation Agreement and Release becoming irrevocable, all within 60 days after the Date of Termination or end of the Cure Period , the following shall occur

(a) the Company shall pay to the Executive an amount equal to the sum of (i) 9 months of the Executive's annual base salary in effect immediately prior to the Terminating Event (or the Executive's annual base salary in effect immediately prior to the Change in Control, if higher), and (ii) a pro rata portion of the Executive's target bonus for the fiscal year in which the termination of employment occurs, determined by multiplying the target bonus by a fraction, the numerator of which shall be the number of days during the fiscal year in which the Executive was employed by the Company and the denominator of which shall be 365;

(b) if the Executive was participating in the Company's group health plan immediately prior to the Date of Termination and elects COBRA health continuation , then the Company shall pay to the Executive a lump sum payment, in an amount equal to 12 times the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company;

(c) notwithstanding anything to the contrary in any applicable option agreement or stock-based award agreement, all stock options and other stock-based awards with time-based vesting held by the Executive shall immediately accelerate and become fully exercisable and nonforfeitable as of the Executive's Date of Termination conditioned upon the Separation Agreement and Release becoming irrevocable; and

(d) the amounts payable under this Section 4 shall be paid out in a lump sum commencing within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the amounts shall be paid in the second calendar year by the last day of such 60-day period. All other wages earned, including, but not limited to, accrued vacation, to the Date of Termination shall be paid on the Date of Termination.

5. **Severance Outside the Change in Control Period**. In the event a Terminating Event occurs at any time other than during the Change in Control Period, subject to the Executive signing the Separation Agreement and Release and the Separation Agreement and Release becoming irrevocable, all within 60 days after the Date of Termination, the following shall occur:

(a) the Company shall pay to the Executive an amount equal to 12 months times the Executive's annual base salary in effect immediately prior to the Terminating Event;

(b) if the Executive was participating in the Company's group health plan immediately prior to the Date of Termination and elects COBRA health continuation, then the Company shall pay to the Executive a monthly cash payment for 12 months in an amount equal to the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company; and

(c) the amounts payable under this Section 5 shall be paid out in substantially equal installments in accordance with the Company's payroll practice over 12 months commencing within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the Severance Amount shall begin to be paid in the second calendar year by the last day of such 60-day period; provided, further, that the initial payment shall include a catch-up payment to cover amounts retroactive to the day immediately following the Date of Termination. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2).

6. **Additional Limitation**.

(a) Anything in this Agreement to the contrary notwithstanding, in the event that the amount of any compensation, payment or distribution by the Company to or for the benefit of the Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a manner consistent with Section 280G of the Code and the applicable regulations thereunder (the "Compensatory Payments"), would be subject to the excise tax imposed by Section 4999 of the Internal Revenue Code of 1986, as amended (the "Code"), (or any successor provision), then the Compensatory Payments shall be reduced so that the sum of all of the Compensatory Payments shall be $1.00 less than the amount at which the Executive becomes subject to the excise tax imposed by Section 4999 of the Code (or any successor provision); provided that such reduction shall only occur if it would result in the Executive receiving a higher After Tax Amount (as defined below) than the Executive would receive if the Compensatory Payments were not subject to such reduction. In such event, the Compensatory Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Compensatory Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 280G of the Code: (i) cash payments not subject to Section 409A of the Code; (ii) cash payments subject to Section 409A of the Code; (iii) equity-based payments and acceleration; and (iv) non-cash forms of benefits; provided that in the case of all the foregoing Compensatory Payments all amounts or payments that are not subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c).

(b) For purposes of this Section 6, the "After Tax Amount" means the amount of the Compensatory Payments less all federal, state, and local income, excise and employment taxes imposed on the Executive as a result of the Executive's receipt of the Compensatory Payments. For purposes of determining the After Tax Amount, the Executive shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes.

(c) The determination as to whether a reduction in the Compensatory Payments shall be made pursuant to Section 6(a) shall be made by an accounting firm selected by the Company (the "Accounting Firm"), which shall provide detailed supporting calculations both to the Company and the Executive within 15 business days of the Date of Termination, if applicable, or at such earlier time as is reasonably requested by the Company or the Executive. Any determination by the Accounting Firm shall be binding upon the Company and the Executive.

7. **Section 409A**.

(a) Anything in this Agreement to the contrary notwithstanding, if at the time of the Executive's "separation from service" within the meaning of Section 409A of the Code, the Company determines that the Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that the Executive becomes entitled to under this Agreement on account of the Executive's separation from service would be considered deferred compensation subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after the Executive's separation from service, or (B) the Executive's death.

(b) The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

(c) All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by the Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(d) To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon the Executive's termination of employment, then such payments or benefits shall be payable only upon the Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

(e) The Company makes no representation or warranty and shall have no liability to the Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

8. **Term**. This Agreement shall take effect on the date first set forth above and shall terminate upon the earlier of (a) the termination of the Executive's employment with the Company for any reason other than the occurrence of a Terminating Event, or (b) the date all amounts have been paid to the Executive upon a Terminating Event pursuant to Section 4 or Section 5 hereof.

9. **Withholding**. All payments made by the Company to the Executive under this Agreement shall be net of any tax or other amounts required to be withheld by the Company under applicable law.

10. **Notice and Date of Termination**.

(a) Notice of Termination. After a Change in Control and during the term of this Agreement, any purported termination of the Executive's employment (other than by reason of death) shall be communicated by written Notice of Termination from one party hereto to the other party hereto in accordance with this Section 10. For purposes of this Agreement, a "Notice of Termination" shall mean a notice which shall indicate the specific termination provision in this Agreement relied upon.

(b) Date of Termination. "Date of Termination" shall mean: (i) if the Executive's employment is terminated by his death, the date of his death; (ii) if the Executive's employment is terminated on account of Executive's Disability or by the Company for Cause, the date on which Notice of Termination is given; (iii) if the Executive's employment is terminated by the Company without Cause the date on which a Notice of Termination is given; (iv) if the Executive's employment is terminated by the Executive without Good Reason, 30 days after the date on which a Notice of Termination is given, and (v) if the Executive's employment is terminated by the Executive with Good Reason, the date on which a Notice of Termination is given after the end of the Cure Period. Notwithstanding the foregoing, in the event that the Executive gives a Notice of Termination to the Company, the Company may unilaterally accelerate the Date of Termination and such acceleration shall not result in a termination by the Company for purposes of this Agreement.

11. **No Mitigation**. The Company agrees that, if the Executive's employment by the Company is terminated during the term of this Agreement, the Executive is not required to seek other employment or to attempt in any way to reduce any amounts payable to the Executive by the Company pursuant to Section 4 or Section 5 hereof. Further, the amount of any payment provided for in this Agreement shall not be reduced by any compensation earned by the Executive as the result of employment by another employer.

12. **Consent to Jurisdiction**. The parties hereby consent to the jurisdiction of the Superior Court or the Commonwealth of Massachusetts and the United States District Court for the District of Massachusetts. Accordingly, with respect to any such court action, the Executive (a) submits to the personal jurisdiction of such courts; (b) consents to service of process; and (c) waives any other requirement (whether imposed by statute, rule of court, or otherwise) with respect to personal jurisdiction or service of process.

13. **Integration**. This Agreement constitutes the entire agreement between the parties with respect to severance pay, benefits and accelerated vesting in connection with any termination of employment, to the extent inconsistent with any prior agreements supersedes the inconsistent provisions of such prior agreements between the parties concerning such subject matter, including without limitation any provisions of any offer letter or employment agreement relating to severance pay or benefits in connection with the ending of Executive's employment relationship with the Company. In the interest of clarity, any agreement relating to confidentiality, noncompetition, nonsolicitation or assignment of inventions shall not be affected by the Agreement.

14. **Successor to the Executive**. This Agreement shall inure to the benefit of and be enforceable by the Executive's personal representatives, executors, administrators, heirs, distributees, devisees and legatees. In the event of the Executive's death after a Terminating Event but prior to the completion by the Company of all payments due him under this Agreement, the Company shall continue such payments to the Executive's beneficiary designated in writing to the Company prior to his death (or to his estate, if the Executive fails to make such designation).

15. **Enforceability**. If any portion or provision of this Agreement (including, without limitation, any portion or provision of any Section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

16. **Waiver**. No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement, or the waiver by any party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

17. **Notices**. Any notices, requests, demands and other communications provided for by this Agreement shall be sufficient if in writing and delivered in person or sent by a nationally recognized overnight courier service of by registered or certified mail, postage prepaid, return receipt requested, to the Executive at the last address the Executive has filed in writing with the Company, or to the Company at its main office, attention of the Board of Directors.

18. **Amendment**. This Agreement may be amended or modified only by a written instrument signed by the Executive and by a duly authorized representative of the Company.

19. **Effect on Other Plans and Agreements**. An election by the Executive to resign for Good Reason under the provisions of this Agreement shall not be deemed a voluntary termination of employment by the Executive for the purpose of interpreting the provisions of any of the Company's benefit plans, programs or policies. Nothing in this Agreement shall be construed to limit the rights of the Executive under the Company's benefit plans, programs or policies except as otherwise provided in Section 6 hereof, and except that the Executive shall have no rights to any severance benefits under any Company severance pay plan, offer letter or otherwise. In the event that the Executive is party to an agreement with the Company providing for payments or benefits under such agreement and this Agreement, the terms of this Agreement shall govern and Executive may receive payment under this Agreement only and not both. Further, Section 4 and Section 5 of this Agreement are mutually exclusive and in no event shall Executive be entitled to payments or benefits pursuant to Section 4 and Section 5 of this Agreement.

20. **Governing Law**. This is a Massachusetts contract and shall be construed under and be governed in all respects by the laws of the Commonwealth of Massachusetts, without giving effect to the conflict of laws principles of such Commonwealth. With respect to any disputes concerning federal law, such disputes shall be determined in accordance with the law as it would be interpreted and applied by the United States Court of Appeals for the First Circuit.

21. **Successor to Company**. The Company shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business or assets of the Company expressly to assume and agree to perform this Agreement to the same extent that the Company would be required to perform it if no succession had taken place. Failure of the Company to obtain an assumption of this Agreement at or prior to the effectiveness of any succession shall be a material breach of this Agreement.

22. **Gender Neutral**. Wherever used herein, a pronoun in the masculine gender shall be considered as including the feminine gender unless the context clearly indicates otherwise.

23. **Counterparts**. This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original; but such counterparts shall together constitute one and the same document.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Agreement effective on the date and year first above written.

SAGE THERAPEUTICS, INC.

By: /s/ Barry Greene

Name: Barry Greene

Title: Chief Executive Officer

/s/ Christopher Benecchi

Employee Name: Christopher Benecchi

[Signature Page to Severance and Change in Control Agreement]

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

EXHIBIT 10.3

AMENDMENT NO. 1 TO EXCLUSIVE LICENSE AGREEMENT

THIS AMENDMENT NO. 1 ("Amendment No. 1") is made as of July 13, 2021 ("Amendment No. 1 Effective Date") by and between **Sage Therapeutics, Inc.** ("Licensee") and **Washington University** ("WU").

WHEREAS, Licensee and WU entered into an Exclusive License Agreement effective November 11, 2013 (the "Agreement"); and,

WHEREAS, Licensee and WU wish to mutually amend the Agreement; and

NOW THEREFORE, for good and valuable mutual consideration, the receipt and sufficiency of which is hereby acknowledged, the parties hereto agree to amend the Agreement as follows:

1. Capitalized terms not otherwise defined herein will have the meaning given to them in the Agreement.

2. Exhibit B of the Agreement is hereby deleted in its entirety and replaced with Exhibit B-1 attached hereto, due to the reversion, on June 3, 2015, to WU of the rights to the following applications:

WU ref **US Patent/Publication or PCT No. (Appl. No.)**
[**] [**]

Exhibit B-1 is hereby incorporated into the Agreement.

3. WU hereby agrees to grant Licensee a second extension to the certain Non-Financial Diligence Milestone identified in the Agreement as "b. [**] by [**] months, to [**], and Licensee shall pay WU the Milestone Extension Fee of $[**] for such extension.

4. The table in the section of the Agreement entitled "Non-Financial Diligence Milestones" is hereby deleted in its entirety and replaced with the following:

Non-Financial Diligence Milestones:

Milestone Event	**Timeline**
a.[**]	within [**] after the Effective Date
b.[**]	within [**] after the Effective Date
c.[**]	within [**] after the Effective Date
d.[**]	within [**] after the Effective Date

5. The section of the Agreement entitled "License Maintenance Fee" is hereby deleted in its entirety.

As of the Amendment No. 1 Effective Date, Licensee agrees to pay License Maintenance Fee of twenty-five thousand dollars ($25,000) at each anniversary of the Effective Date following the Amendment No. 1 Effective Date until First Commercial Sale.

6. The Parties agree that notwithstanding anything to the contrary in the Agreement, Licensee shall have one remaining extension under the section of the Agreement entitled “Milestone Extensions”.

7. The section of the Agreement entitled “Term” is hereby deleted in its entirety and replaced with the following:

“The term of this Agreement shall commence on the Effective Date and continue on a Licensed Product-by-Licensed Product and country-by-country basis until the later of: (a) the last day that at least one Valid Claim exists that covers such Licensed Product in such country; or (b) the twelfth anniversary of the day of the First Commercial Sale of such Licensed Product in such country.”

8. Section 3.3 of the Agreement, entitled **“Changes to Development Plan,”** is hereby deleted in its entirety and replaced with the following:

“Licensee may not make material changes to the Development Plan without providing a written update thereof to WU. WU will be provided a reasonable opportunity to review and comment on any such material change of the Development Plan, and Licensee shall give due consideration to all comments by WU.”

WU acknowledges that the current Development Plan is attached to this Agreement as Exhibit A-1.

9. All other terms and conditions of the Agreement, as amended and modified, are hereby ratified, confirmed and approved. Except as set forth in this Amendment No. 1, the Agreement is unaffected and shall continue in full force and effect in accordance with its terms.

IN WITNESS WHEREOF, duly authorized representatives of the parties have signed this Amendment No.1 as of the Amendment No. 1 Effective Date.

Washington University

By: /s/ Nichole Mercier
duly authorized

Print Name: Nichole Mercier

Title: Assistant Vice Chancellor and Managing Director

Sage Therapeutics, Inc.

By: /s/ Albert J. Robichaud
duly authorized

Print Name: Albert J. Robichaud

Title: Chief Scientific Officer

EXHIBIT 10.4

October 21, 2021

Heinrich Schlieker, Ph.D.
Senior Vice President – Technical Operations Sage Therapeutics, Inc.
215 First Street
Cambridge, MA 02142

RE: Collaboration and License Agreement between Sage Therapeutics, Inc., ("Sage") Biogen MA Inc. and Biogen International GmbH (collectively, "Biogen") (the "Collaboration Agreement")

Dear Dr. Schlieker:

This Letter Agreement serves to memorialize recent discussions between Biogen and Sage (together, the "Parties") concerning the above-referenced Collaboration Agreement. Capitalized terms used but not otherwise defined in this Letter Agreement will have the meanings given to them in the Collaboration Agreement.

Together Biogen and Sage are collaborating on the Development, Manufacture and Commercialization of Licensed 217 Products and Licensed 324 Products. In connection with these efforts, Biogen desires to develop and evaluate potential modifications to the manufacturing process and formulation for Licensed 217 Products, and may decide to do so in the future with respect to the same for Licensed 324 Products. The Parties agree as follows with respect to the Know-How developed or conceived in the course of such efforts and related intellectual property rights:

1. Definitions

a. **"Biogen CMC Know-How"** shall mean any Biogen Collaboration Know-How that relates to a modification to the manufacturing process and/or formulation of any of the Licensed Products.

b. **"Biogen CMC Patents"** shall mean any Biogen Collaboration Patents that claim any Biogen CMC Know-How.

c. **"Biogen CMC Technology"** shall mean Biogen CMC Know-How and Biogen CMC Patents.

2. **Sharing Biogen CMC Know-How**: Notwithstanding anything to the contrary in the Collaboration Agreement, Biogen will promptly share copies of all **Biogen CMC Know-How** with Sage.

3. **License Grant:** In addition to the license grants to Sage set forth in the Collaboration Agreement with respect to Licensed Products, Biogen, on behalf of

itself and its Affiliates, hereby grants Sage a non-transferable (except as provided in Section 15.1 (Assignment) of the Collaboration Agreement), sublicensable (through multiple tiers), perpetual, irrevocable, non-exclusive, royalty-free, fully paid-up license under the Biogen CMC Technology to Exploit any products (excluding any Licensed Product unless it becomes a Terminated Product) in the Field in all countries of the world, provided, however, that Sage may only grant a sublicense of the rights granted by Biogen to Sage under this section (i) to subcontractors engaged by Sage or by any sublicensee permitted under clause (ii) in connection with Exploitation of products containing molecules proprietary to Sage or (ii) in connection with a license or collaboration to develop a molecule proprietary to Sage. The foregoing license will survive the termination of the Collaboration Agreement, in whole or in part, for any reason. For purposes of this section, the term "Sage" means Sage or any of its Affiliates.

4. **Use of Third Parties:** Notwithstanding anything to the contrary in the Collaboration Agreement, in the event Biogen uses a Third Party to perform any Development work with respect to potential modifications to the manufacturing process or formulation for any of the Licensed Products, Biogen will use commercially reasonable efforts to require such Third Party to assign or exclusively license (with the right to sublicense) to Biogen all intellectual property with respect to any such modification developed in the course of performing any such work.

Unless expressly stated, nothing herein otherwise amends, modifies or terminates the rights and obligations of Sage or Biogen under the terms of the Collaboration Agreement.

Warm regards,

Biogen MA, Inc. **Biogen International GmBH**

By: /s/ Alphonse Galdes By: /s/ Fred Lawson
Name: Alphonse Galdes Name: Fred Lawson
Title: EVP Pharmaceutical Operations & Technology Title: International Controller

Read, understood and agree:

Sage Therapeutics, Inc.

By: Heinrich Schlieker
Name: Heinrich Schlieker
Title: SVP Technical Operations

Exhibit 31.1

CERTIFICATIONS UNDER SECTION 302

I, Barry E. Greene, certify that:

1. I have reviewed this quarterly report on Form 10-Q for the period ended September 30, 2021 of Sage Therapeutics, Inc.;

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

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

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

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

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 2, 2021

/s/ Barry E. Greene

Name: Barry E. Greene
Title: Chief Executive Officer, President and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS UNDER SECTION 302

I, Kimi Iguchi, certify that:

1. I have reviewed this quarterly report on Form 10-Q for the period ended September 30, 2021 of Sage Therapeutics, Inc.;

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

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

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

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

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 2, 2021

/s/ Kimi Iguchi

Name: Kimi Iguchi
Title: Chief Financial Officer (Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATIONS PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Quarterly Report on Form 10-Q of Sage Therapeutics, Inc. (the "Company") for the period ended September 30, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers hereby certifies, pursuant to 18 U.S.C. (section) 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his or her knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Barry E. Greene
Name: Barry E. Greene
Title: Chief Executive Officer, President and Director (Principal Executive Officer)
Date: November 2, 2021

/s/ Kimi Iguchi
Name: Kimi Iguchi
Title: Chief Financial Officer (Principal Financial and Accounting Officer)
Date: November 2, 2021