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 June 30, 2023

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 August 1, 2023, there were 59,883,943 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 expectations as to the timing of the completion of controlled substance scheduling of ZURZUVAE™ (zuranolone) by the U.S. Drug Enforcement Administration, or DEA, and commencement of the planned commercial launch, availability, and commercialization of ZURZUVAE in the U.S. as a treatment for adults with postpartum depression, or PPD; our plans for commercial launch of ZURZUVAE in PPD, and our views as to our readiness for such a launch; the potential benefit of ZURZUVAE in the treatment of women with PPD; the number of women with PPD and the potential market for ZURZUVAE for the treatment of women with PPD;
- our plans to evaluate next steps after receipt of a complete response letter issued by the U.S. Food & Drug Administration, or FDA, related to our new drug application for zuranolone for the treatment of major depressive disorder, or MDD, in adults; our views as to our potential to conduct one or more additional clinical trials, as required by the FDA, to try to obtain regulatory approval of zuranolone for MDD, and the potential expense, feasibility, outcome, and timing of such activities;
- our views as to the potential for zuranolone to be developed in additional indications;
- our expectations and estimates regarding: the level of expenses we may incur in connection with our activities; use of cash and projected cash balance at any given time; timing of future cash needs; capital requirements; sources of future financing; timing of receipt of potential milestone payments; our ability to obtain additional financing when needed to fund future operations; and our ongoing evaluation of resource allocation, including pipeline prioritization and a workforce reorganization, and other efforts to extend our cash runway;
- our plans for the development of our 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 enroll, complete and announce the results of ongoing or future clinical trials;
- our belief as to potential outcomes of our clinical development and commercialization activities;
- 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 PPD in adults;
- 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 with Biogen MA Inc., or BIMA, and Biogen International GmbH, or, together with BIMA, Biogen, and Shionogi & Co., Ltd., or Shionogi, 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 expectations with respect to the availability of supplies of ZULRESSO, ZURZUVAE and our product candidates, and the expected performance of our third-party manufacturers, including conformity with applicable regulatory requirements;
- 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 our products and product candidates in the indications we are pursuing or plan to study;
- the potential for our current products 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 the treatment of PPD, 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 changes to the macroeconomic environment and geopolitical events 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 in this Quarterly Report. 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 future business prospects depend heavily on our ability, with our collaborator Biogen, to successfully commercialize ZURZUVAE for the treatment of women with PPD and to gain approval for zuranolone for the treatment of adults with MDD. We may not be successful in our launch and commercialization efforts for ZURZUVAE for the treatment of women with PPD. ZURZUVAE may not achieve broad market acceptance, or reimbursement at sufficient levels, and we may not be able to generate revenues at the levels or on the timing we expect or at levels or timing necessary to support our goals. The number of women with PPD, the unmet need for additional treatment options, and the potential market for ZURZUVAE in this indication may be significantly smaller than we expect. Any setback or delay in our ability to market ZURZUVAE for the treatment of women with PPD may have a material adverse effect on our business and prospects. We may never achieve regulatory approval of zuranolone for the treatment of MDD; the FDA has taken the position that one or more additional clinical trials of zuranolone are required to support approval in MDD and even if we were to seek to appeal this in the future, the FDA may not change their position. If we conduct additional trials of zuranolone to support regulatory approval in the treatment of MDD, these trials may take a significant amount of time, significantly increase our expenses, or may not be successful.
- Our future business prospects also depend heavily on our ability to successfully develop and gain regulatory approval of our product candidates. We cannot be certain that we or our collaborators, where applicable, will be able to initiate new clinical trials, complete ongoing enrollment, dosing or data analysis of clinical trials, or announce results of ongoing or future clinical trials of our product candidates in each case on the timelines we expect or at all, or that the results of our development programs will be positive or sufficient to file for 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 such product candidates on the timelines we expect or at all. Any setback or delay in obtaining regulatory approval for any of 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 may never be able to generate meaningful revenues from sales of ZULRESSO® (brexanolone) CIV injection, or revenues at levels or on timing necessary to support our investment and goals.
- 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, are smaller than we anticipate, or our other assumptions with respect to the potential markets for our products and product candidates are incorrect, our ability to achieve profits from the commercialization of such products, if approved, 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. The results of non-clinical studies or clinical trials of our product candidates at any stage may not support further development or may not be sufficient to file for and obtain regulatory approval.
- 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, in clinical trials or under an expanded access program, if initiated for any of our products or product candidates, 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.

- Given recent developments, we are currently evaluating resource allocation, including pipeline prioritization and a workforce reorganization, with a goal of extending our cash runway. We may not achieve events tied to cash milestone payments from our collaboration partners on the timelines we expect or at all, or generate revenues from ZURZUVAE for the treatment of women with PPD, or any other of our products that may be successfully developed, at the levels we expect. Our expenses may also be higher than we expect, including as a result of unexpected events or changes in plans. As a result, our expectations as to our cash runway and the sufficiency of cash to fund our future operations may prove not to be correct. We may need to raise additional funding in the future, which may not be available on acceptable terms, or at all. Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish valuable rights.
- Any impairment of the ability of our third-party suppliers to supply product or to meet applicable regulatory standards may significantly negatively impact our ability to achieve our goals and plans and to meet the expectations for our business.
- Any of our current product candidates, if successfully developed and approved, and other future products, if any, may not have the profile we expect in clinical practice after launch or may not achieve broad market acceptance for the approved indications, or reimbursement at sufficient levels, and the results of our commercialization efforts may not meet our expectations, 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, ZURZUVAE, or any of our other current or future product candidates, if successfully developed and approved.
- 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 relating to development or commercialization strategy or appropriate program spending, that may hamper or delay our development and commercialization efforts or increase our costs. Our business may be adversely affected and we may be subject to delays, disputes, or litigation if we disagree significantly with any of our collaborators, or any of our collaborators fails to perform its obligations or terminates our collaboration in whole or in part.
- If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents 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.
- If we were to lose our rights to certain licensed intellectual property, or if we are not able to obtain licenses to intellectual property we may determine we need in the future, 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.
- Our stock price may fluctuate in response to a number of factors.
- The Inflation Reduction Act of 2022 and other existing, pending or future federal and state reforms aimed at reducing healthcare costs, including pricing and reimbursement of pharmaceutical products, may in the future result in reduced reimbursement and access for our approved products or cause us to curtail certain development plans because of concerns about commercial viability, any of which could adversely affect our ability to commercialize our products and generate revenue and negatively impact our business, results of operations and financial condition.

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)

	June 30, 2023	December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 121,416	$ 162,700
Marketable securities	881,200	1,109,794
Prepaid expenses and other current assets	46,321	50,826
Collaboration receivable - related party	15,090	13,660
Total current assets	1,064,027	1,336,980
Property and equipment, net	2,480	2,898
Restricted cash	1,332	1,269
Right-of-use operating asset	7,560	10,532
Other long-term assets	6,889	4,770
Total assets	$ 1,082,288	$ 1,356,449
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 9,283	$ 18,950
Accrued expenses	79,799	72,666
Operating lease liability, current portion	7,725	7,643
Total current liabilities	96,807	99,259
Operating lease liability, net of current portion	1,003	4,491
Other liabilities	102	100
Total liabilities	97,912	103,850
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Preferred stock, $0.0001 par value per share; 5,000,000 shares authorized at June 30, 2023 and December 31, 2022; no shares issued or outstanding at June 30, 2023 and December 31, 2022	—	—
Common stock, $0.0001 par value per share; 120,000,000 shares authorized at June 30, 2023 and December 31, 2022; 59,799,038 and 59,512,158 shares issued at June 30, 2023 and December 31, 2022; 59,796,005 and 59,509,125 shares outstanding at June 30, 2023 and December 31, 2022	6	6
Treasury stock, at cost, 3,033 shares at June 30, 2023 and December 31, 2022	(400)	(400)
Additional paid-in capital	3,325,737	3,291,369
Accumulated deficit	(2,335,323)	(2,028,170)
Accumulated other comprehensive loss	(5,644)	(10,206)
Total stockholders' equity	984,376	1,252,599
Total liabilities and stockholders' equity	$ 1,082,288	$ 1,356,449

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 June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
Product revenue, net	$ 2,460	$ 1,501	$ 5,754	$ 3,082
Collaboration revenue	14	—	14	—
Total revenue	2,474	1,501	5,768	3,082
Operating costs and expenses:				
Cost of goods sold	205	200	435	486
Research and development	97,161	77,297	189,987	155,315
Selling, general and administrative	75,565	52,411	141,273	98,888
Total operating costs and expenses	172,931	129,908	331,695	254,689
Loss from operations	(170,457)	(128,407)	(325,927)	(251,607)
Interest income, net	10,173	2,102	19,003	3,270
Other income (expense), net	(41)	45	(229)	22
Net loss	$ (160,325)	$ (126,260)	$ (307,153)	$ (248,315)
Net loss per share—basic and diluted	$ (2.68)	$ (2.13)	$ (5.14)	$ (4.20)
Weighted average number of common shares outstanding—basic and diluted	59,769,640	59,266,322	59,722,147	59,148,246
Comprehensive loss:				
Net loss	$ (160,325)	$ (126,260)	$ (307,153)	$ (248,315)
Other comprehensive items:				
Unrealized gain (loss) on marketable securities	(556)	(2,671)	4,562	(11,212)
Total other comprehensive gain (loss)	(556)	(2,671)	4,562	(11,212)
Total comprehensive loss	$ (160,881)	$ (128,931)	$ (302,591)	$ (259,527)

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)

	Six Months Ended June 30,	
	2023	2022
Cash flows from operating activities		
Net loss	$ (307,153)	$ (248,315)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	31,731	33,189
Premium on marketable securities	(71)	(1,454)
Amortization of premium (discount) on marketable securities	(7,570)	6,114
Depreciation expense	654	554
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	4,505	(1,614)
Collaboration receivable - related party	(1,430)	(5,216)
Other long-term assets	(2,119)	(656)
Right-of-use operating asset	2,972	2,730
Operating lease liabilities, current	82	95
Operating lease liabilities, non-current	(3,488)	(3,164)
Accounts payable	(9,566)	(5,225)
Accrued expenses and other liabilities	6,253	8,723
Net cash used in operating activities	(285,200)	(214,239)
Cash flows from investing activities		
Proceeds from sales and maturities of marketable securities	630,452	556,100
Purchases of marketable securities	(389,655)	(431,105)
Purchases of property and equipment	(337)	(291)
Net cash provided by investing activities	240,460	124,704
Cash flows from financing activities		
Proceeds from stock option exercises and employee stock purchase plan issuances	4,156	1,836
Payment of employee tax obligations related to vesting of restricted stock units	(637)	(24)
Net cash provided by financing activities	3,519	1,812
Net decrease in cash, cash equivalents and restricted cash	(41,221)	(87,723)
Cash, cash equivalents and restricted cash at beginning of period	163,969	295,502
Cash, cash equivalents and restricted cash at end of period	$ 122,748	$ 207,779
Supplemental disclosure of non-cash operating activities		
Purchases of property and equipment included in accounts payable	$ 36	$ 256

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, 2021	58,937,050	$ 6	3,033	$ (400)	$ 3,227,471	$ (2,660)	$ (1,495,386)	$ 1,729,031
Issuance of common stock from exercises of stock options	105,474	—	—	—	646	—	—	646
Issuance of common stock under the employee stock purchase plan	23,625	—	—	—	1,153	—	—	1,153
Stock-based compensation expense	—	—	—	—	18,268	—	—	18,268
Change in unrealized loss on available-for-sale securities	—	—	—	—	—	(8,541)	—	(8,541)
Net loss	—	—	—	—	—	—	(122,055)	(122,055)
Balances at March 31, 2022	59,066,149	6	3,033	(400)	3,247,538	(11,201)	(1,617,441)	1,618,502
Issuance of common stock from exercises of stock options	31,801	—	—	—	37	—	—	37
Stock-based compensation expense	—	—	—	—	14,652	—	—	14,652
Change in unrealized loss on available-for-sale securities	—	—	—	—	—	(2,671)	—	(2,671)
Vesting of restricted stock units, net of employee tax obligations	290,779	—	—	—	(24)	—	—	(24)
Net loss	—	—	—	—	—	—	(126,260)	(126,260)
Balances at June 30, 2022	59,388,729	$ 6	3,033	$ (400)	$ 3,262,203	$ (13,872)	$ (1,743,701)	$ 1,504,236
Balances at December 31, 2022	59,509,125	$ 6	3,033	$ (400)	$ 3,291,369	$ (10,206)	$ (2,028,170)	$ 1,252,599
Issuance of common stock from exercises of stock options	52,058	—	—	—	438	—	—	438
Issuance of common stock under the employee stock purchase plan	76,105	—	—	—	2,863	—	—	2,863
Stock-based compensation expense	—	—	—	—	19,568	—	—	19,568
Change in unrealized loss on available-for-sale securities	—	—	—	—	—	5,118	—	5,118
Vesting of restricted stock units, net of employee tax obligations	124,713	—	—	—	(629)	—	—	(629)
Net loss	—	—	—	—	—	—	(146,828)	(146,828)
Balances at March 31, 2023	59,762,001	6	3,033	(400)	3,313,609	(5,088)	(2,174,998)	1,133,129
Issuance of common stock from exercises of stock options	20,032	—	—	—	855	—	—	855
Stock-based compensation expense	—	—	—	—	11,281	—	—	11,281
Change in unrealized loss on available-for-sale securities	—	—	—	—	—	(556)	—	(556)
Vesting of restricted stock units, net of employee tax obligations	13,972	—	—	—	(8)	—	—	(8)
Net loss	—	—	—	—	—	—	(160,325)	(160,325)
Balances at June 30, 2023	59,796,005	$ 6	3,033	$ (400)	$ 3,325,737	$ (5,644)	$ (2,335,323)	$ 984,376

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 with a mission to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive.

The Company's second product ZURZUVAE™ (zuranolone) was approved by the U.S. Food and Drug Administration (the "FDA") on August 4, 2023 for the treatment of postpartum depression ("PPD") in adults. Additionally, the FDA issued a complete response letter related to the Company's new drug application ("NDA") for zuranolone for the treatment of major depressive disorder ("MDD"). The CRL stated that the NDA did not provide substantial evidence of effectiveness to support the approval of zuranolone for the treatment of MDD and that one or more additional clinical trials will be needed. The Company is reviewing the feedback from the FDA and evaluating next steps.

The Company's first product, ZULRESSO® (brexanolone) CIV injection, is approved in the U.S. for the treatment of 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.

Risks and Uncertainties

The Company is subject to risks and uncertainties common to companies in the biopharmaceutical industry, 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 direct or indirect impacts of the macroeconomic environment and geopolitical events on its development activities, operations and financial condition.

The product candidates developed by the Company require approvals from the 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, or that the Company's current products, ZULRESSO and ZURZUVAE, will maintain, 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 for any of its product candidates, including zuranolone for the treatment of MDD, such occurrences may have a material adverse impact on the Company's business and its financial condition.

The Company is also subject to additional risks and uncertainties arising from changes to the macroeconomic environment and geopolitical events. U.S. and global financial markets have experienced volatility and disruption due to macroeconomic and geopolitical events such as rising inflation, the risk of a recession and the ongoing conflict between Russia and Ukraine. In addition, if equity and credit markets deteriorate, including as a result of past and potential future

bank failures, it may make any future debt or equity financing more difficult to obtain on favorable terms, and potentially more dilutive to our existing stockholders. The Company cannot predict at this time to what extent it and its collaborators, employees, suppliers, contract manufacturers and/or vendors could potentially be negatively impacted by these events.

Going Concern

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 in each year 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 June 30, 2023, the Company had an accumulated deficit of $2.3 billion. From its inception through June 30, 2023, 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 ("IPO"), the issuance of convertible notes, and the sales of common stock in its 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/or collaboration revenue and achieve sustained 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.

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, 2022, included in the Company's Annual Report on Form 10-K for the year ended December 31, 2022.

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 June 30, 2023, its results of operations and comprehensive loss for the three and six months ended June 30, 2023 and 2022, its cash flows for the six months ended June 30, 2023 and 2022, and its statements of changes in

stockholders' equity for the three and six months ended June 30, 2023 and 2022. The consolidated balance sheet at December 31, 2022 was derived from audited financial statements, but does not include all disclosures required by GAAP. The results for the three and six months ended June 30, 2023 are not necessarily indicative of the results for the year ending December 31, 2023, 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 year ended December 31, 2022. 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.

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 or as performance obligations are satisfied by transferring control of promised goods or services to a customer, 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 or milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties or milestone payments 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 or milestone payment 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 revenue, 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 June 30, 2023, as customer invoicing generally occurs before or at the time of revenue recognition. The Company did not have any contract liabilities at June 30, 2023, 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 June 30, 2023 and December 31, 2022, 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 revenue 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 revenue and accounts receivable at the time the Company recognizes the related revenue.

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 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 not been significant to date and are not expected to be significant in the future.

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 June 30, 2023 and December 31, 2022 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 June 30, 2023 and December 31, 2022, respectively.

Recently Issued Accounting Pronouncements

Accounting standards that have been issued or proposed by the Financial Accounting Standards Board 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 Company performs validation procedures to ensure the reasonableness of this data. The Company performs its own review of prices received from the independent pricing services by comparing these prices to other sources. After completing the validation procedures, the Company did not adjust or override any fair value measurements provided by the pricing services as of June 30, 2023 and December 31, 2022.

The following tables summarize the Company's cash equivalents and marketable securities as of June 30, 2023 and December 31, 2022:

	June 30, 2023			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
	(in thousands)			
Cash equivalents:				
Money market funds	$ 104,261	$ 104,261	$ —	$ —
U.S. commercial paper	15,919	—	15,919	—
Total cash equivalents	120,180	104,261	15,919	—
Marketable securities:				
U.S. government securities	227,933	—	227,933	—
U.S. corporate bonds	227,695	—	227,695	—
International corporate bonds	86,356	—	86,356	—
U.S. commercial paper	59,317	—	59,317	—
International commercial paper	100,870	—	100,870	—
U.S. certificates of deposit	13,893	—	13,893	—
U.S. municipal securities	165,136	—	165,136	—
Total marketable securities	881,200	—	881,200	—
	$ 1,001,380	$ 104,261	$ 897,119	$ —

	December 31, 2022			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
	(in thousands)			
Cash equivalents:				
Money market funds	$ 161,185	$ 161,185	$ —	$ —
Total cash equivalents	161,185	161,185	—	—
Marketable securities:				
U.S. government securities	302,911	—	302,911	—
U.S. corporate bonds	354,495	—	354,495	—
International corporate bonds	127,248	—	127,248	—
U.S. commercial paper	63,114	—	63,114	—
International commercial paper	133,163	—	133,163	—
U.S. certificates of deposit	15,613	—	15,613	—
U.S. municipal securities	113,250	—	113,250	—
Total marketable securities	1,109,794	—	1,109,794	—
	$ 1,270,979	$ 161,185	$ 1,109,794	$ —

During the six months ended June 30, 2023 and 2022, 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 June 30, 2023 and December 31, 2022:

	June 30, 2023				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Credit Losses	Fair Value
			(in thousands)		
Assets:					
U.S. government securities	$ 229,757	$ 2	$ (1,826)	$ —	$ 227,933
U.S. corporate bonds	229,502	3	(1,810)	—	227,695
International corporate bonds	86,906	1	(551)	—	86,356
U.S. commercial paper	59,392	—	(75)	—	59,317
International commercial paper	101,055	—	(185)	—	100,870
U.S. certificates of deposit	13,893	—	—	—	13,893
U.S. municipal securities	166,339	—	(1,203)	—	165,136
	$ 886,844	$ 6	$ (5,650)	$ —	$ 881,200

	December 31, 2022				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Credit Losses	Fair Value
			(in thousands)		
Assets:					
U.S. government securities	$ 307,173	$ —	$ (4,262)	$ —	$ 302,911
U.S. corporate bonds	358,019	6	(3,530)	—	354,495
International corporate bonds	128,374	7	(1,133)	—	127,248
U.S. commercial paper	63,234	—	(120)	—	63,114
International commercial paper	133,338	—	(175)	—	133,163
U.S. certificates of deposit	15,613	—	—	—	15,613
U.S. municipal securities	114,249	31	(1,030)	—	113,250
	$ 1,120,000	$ 44	$ (10,250)	$ —	$ 1,109,794

The following tables summarize the fair value and the unrealized losses of the Company's marketable securities that have been in a loss position for either less than twelve months or greater than twelve months as of June 30, 2023 and December 31, 2022:

	June 30, 2023					
	Less than 12 months		Greater than 12 months		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
			(in thousands)			
U.S. government securities	$ 140,520	$ (804)	$ 72,484	$ (1,022)	$ 213,004	$ (1,826)
U.S. corporate bonds	160,348	(1,130)	47,918	(680)	208,266	(1,810)
International corporate bonds	69,198	(392)	14,160	(159)	83,358	(551)
U.S. commercial paper	58,232	(75)	—	—	58,232	(75)
International commercial paper	83,020	(185)	—	—	83,020	(185)
U.S. municipal securities	145,520	(824)	19,615	(379)	165,135	(1,203)
	$ 656,838	$ (3,410)	$ 154,177	$ (2,240)	$ 811,015	$ (5,650)

	December 31, 2022					
	Less than 12 months		Greater than 12 months		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
	(in thousands)					
U.S. government securities	$ 112,243	$ (1,517)	$ 185,691	$ (2,745)	$ 297,934	$ (4,262)
U.S. corporate bonds	208,507	(1,989)	130,633	(1,541)	339,140	(3,530)
International corporate bonds	50,982	(497)	68,993	(636)	119,975	(1,133)
U.S. commercial paper	24,768	(120)	—	—	24,768	(120)
International commercial paper	30,987	(175)	—	—	30,987	(175)
U.S. municipal securities	86,251	(497)	14,466	(533)	100,717	(1,030)
	$ 513,738	$ (4,795)	$ 399,783	$ (5,455)	$ 913,521	$ (10,250)

As of June 30, 2023 and December 31, 2022, the unrealized losses on the Company's investments in U.S. government securities, U.S. corporate bonds, and international corporate bonds were caused by interest rate increases. The Company purchased those investments at a premium relative to their face amount. The current credit ratings are all within the guidelines of the investment policy of the Company and the Company does not expect the issuers to settle any security at a price less than the amortized cost basis of the investment. The Company does not intend to sell the investments and it is not probable that the Company will be required to sell the investments before recovery of their amortized cost basis.

As of June 30, 2023, 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 municipal securities with a fair value of $144.5 million and maturities of one to two years.

As of December 31, 2022, 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 municipal securities with a fair value of $211.2 million and 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.

There have been no impairments of the Company's assets measured and carried at fair value during the six months ended June 30, 2023 and the year ended December 31, 2022.

4. Accrued Expenses

The following table summarizes accrued expenses as of June 30, 2023 and December 31, 2022:

	June 30, 2023	December 31, 2022
	(in thousands)	
Accrued research and development costs	$ 45,322	$ 32,565
Employee-related	19,194	29,372
Professional services	14,413	10,172
Other	870	557
	$ 79,799	$ 72,666

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 1.5 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, 2022, the Company leased office space in two 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 and 40,419 square feet in the second building, under an operating lease that will expire on August 31, 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.

License Agreements

CyDex License Agreement

In September 2015, the Company amended and restated its existing commercial license agreement with CyDex Pharmaceuticals, Inc. ("CyDex"), a wholly owned subsidiary of Ligand Pharmaceuticals Incorporated. 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 for 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. From the effective date of the agreement to June 30, 2023, 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. From the effective date of the agreement to June 30, 2023, the Company has recorded research and development expense and made cash payments of $3.6 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 six months ended June 30, 2023 and 2022, 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, and the Company began to pay these royalties in 2019. 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 was required to make payments of $15,000 for annual maintenance fees until the calendar year following the first sale of ZULRESSO. 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. From the effective date of the agreement to June 30, 2023, 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 six months ended June 30, 2023 and 2022, the Company did not record any expense or make any milestone payments under the license agreements with the Regents.

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 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 the Company to supply zuranolone clinical material to Shionogi.

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 of zuranolone 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. As between the Company and Shionogi, 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 of 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.

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 is obligated to 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 six months ended June 30, 2023 and 2022, 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 the treatment of 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") under which BIMA purchased 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 from Biogen 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, including a milestone payment of $75.0 million for the first commercial sale of ZURZUVAE for the treatment of PPD in the U.S. and, if approved, a milestone payment of $150.0 million for the first commercial sale of ZURZUVAE for the treatment of MDD in the U.S., 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, and the challenges of launching and commercializing a product, if approved, 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. are 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 upon FDA approval and commencement of product sales, 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. Biogen will be the principal and record sales of SAGE-217 products globally. The Company will be the principal and record sales of SAGE-324 products in the U.S. and Biogen will be the principal and record sales of SAGE-324 products in the Biogen Territory.

The Company will supply API and bulk drug product for the Biogen Territory and API, bulk drug product 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. During the six months ended June 30, 2023 and 2022, no collaboration revenue – related party was 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 six months ended June 30, 2023, the Company recorded a net reimbursement of $14.9 million and $29.2 million, respectively, for the amounts due from Biogen as a reduction of or an addition to the related operating expense categories in the condensed consolidated statements of operations and comprehensive loss. During the three and six months ended June 30, 2022, the Company recorded a net reimbursement of $23.8 million and $43.8 million, respectively, for the amounts due from Biogen as a reduction of the related operating expense categories in the condensed consolidated statements of operations and comprehensive loss.

As of June 30, 2023, the Company recorded a Collaboration Receivable – Related Party of $15.1 million in the condensed consolidated balance sheet for the amounts due for the three months ended June 30, 2023. During the six months ended June 30, 2023, the Company made no payments to Biogen and the Company received $27.8 million from Biogen for the amounts due for the three months ended December 31, 2022 and the three months ended March 31, 2023.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
	(in thousands)			
Expenses related to the Biogen Collaboration Agreement incurred by Sage	$ 71,524	$ 59,218	$ 127,660	$ 107,972
Net reimbursement to (from) Biogen reflected in the condensed consolidated statements of operations and comprehensive loss:				
Research and development expenses	(22,418)	(20,983)	(39,700)	(39,497)
Selling, general and administrative expenses	7,476	(2,835)	10,510	(4,309)
	(14,942)	(23,818)	(29,190)	(43,806)
Total net expenses related to the Biogen Collaboration Agreement in the condensed consolidated statements of operations and comprehensive loss	$ 56,582	$ 35,400	$ 98,470	$ 64,166

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 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, which period expired on June 30, 2022, and to limit sales and transfers of the Biogen Shares for an additional eighteen-month period, which expires December 31, 2023, 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. 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 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, 2023, 2,380,365 shares of common stock, representing 4% of the Company's outstanding shares of common stock as of December 31, 2022, 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 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% vesting at the one-year anniversary. All stock option awards expire 10 years after the date of grant.

As of June 30, 2023, the total number of shares underlying outstanding awards under all equity plans was 10,907,261 and the total number of shares available for future issuance under all equity plans was 7,968,438 shares.

On June 16, 2022, the Company's stockholders approved an amendment to the amended 2014 Employee Stock Purchase Plan (the "ESPP"), which had been previously approved by the Board, to add 300,000 shares of common stock to the ESPP. On June 15, 2023, the Company's stockholders approved another amendment to the ESPP, which had been previously approved by the Board, to add an additional 500,000 shares of common stock to the ESPP. As amended, a total of 1,082,000 shares of common stock have been authorized for issuance under the ESPP.

Restricted Stock Units

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

	Shares	Weighted Average Grant Date Fair Value
Outstanding as of December 31, 2022	1,415,481	$ 48.73
Granted	1,192,938	$ 42.93
Vested	(153,067)	$ 65.04
Forfeited	(50,016)	$ 46.64
Outstanding as of June 30, 2023	2,405,336	$ 44.86

Time-based restricted stock units

During the year ended December 31, 2021, the Company granted 268,119 time-based restricted stock units to certain employees of the Company that vest over four years. In September 2022, 25% vested on the one-year anniversary of the vesting start date and the remaining 75% vest ratably in quarterly increments over the remaining three years. During the three and six months ended June 30, 2023, 14,083 and 28,577, respectively, of these time-based restricted stock units vested, with a fair value of $0.7 million and $1.3 million, respectively, on the dates of vesting.

During the year ended December 31, 2020, the Company granted 550,890 time-based restricted stock units to certain employees of the Company. These time-based restricted stock units vested 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 were in April 2021 and April 2022, respectively. During the year ended December 31, 2021, 113,941 of these time-based restricted stock units vested, with a fair value on the date of vesting equal to $8.8 million. During the three months ended June 30, 2022, 291,505 of these time-based restricted stock units vested, with a fair value on the date of vesting equal to $9.5 million. During the three months ended March 31, 2022, no time-based restricted stock units vested.

During the three months ended March 31, 2023, the Company granted 330,617 time-based restricted stock units to certain employees and consultants of the Company. These time-based restricted stock units vest over four years, with 25% vesting at the one-year anniversary of the vesting start date and the remaining 75% vesting in equal installments on each

anniversary of the vesting start date for the following three years. During the three months ended June 30, 2023, the Company granted no time-based restricted stock units.

During the six months ended June 30, 2022, the Company granted no time-based restricted stock units.

As of June 30, 2023, 445,421 time-based restricted stock units were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was $18.6 million.

Performance restricted stock units

During the three months ended June 30, 2023 and 2022, the Company granted 39,603 and 96,365 performance restricted stock units, respectively, to its employees and consultants. The majority of the performance restricted stock units granted during the three months ended June 30, 2023 and 2022 vest upon the achievement of certain clinical and regulatory development milestones related to product candidates and certain commercial milestones.

During the six months ended June 30, 2023 and 2022, the Company granted 862,321 and 511,930 performance restricted stock units, respectively, to its employees and consultants. The majority of the performance restricted stock units granted during the six months ended June 30, 2023 and 2022 vest upon the achievement of certain clinical and regulatory development milestones related to product candidates and certain commercial milestones. Certain performance restricted stock units granted during the three months ended March 31, 2023 vest upon the Company reaching specified measures of total stockholder return.

Recognition of stock-based compensation expense associated with performance restricted stock units, except for those with milestones that are measures of total stockholder return, 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. Recognition of stock-based compensation associated with performance restricted stock units with milestones that are measures of total stockholder return commences on the grant date and is recorded independently of the vesting outcomes of the grants.

As of June 30, 2023 and 2022, for performance restricted stock units that were outstanding, except for those with milestones that are measures of total stockholder return, the achievement of the milestones that had not been met was considered not probable, and therefore no expense has been recognized related to these awards during the six months ended June 30, 2023 and 2022, respectively.

During the three months ended March 31, 2023, one milestone for outstanding performance restricted stock units was achieved. The fair value of the performance restricted stock units that vested upon achievement was $5.5 million and the Company recognized stock-based compensation expense related to this milestone of $8.5 million. 27% of the performance restricted stock units that were granted during the year ended December 31, 2021 included this milestone as a vesting condition.

No performance restricted stock units vested during the six months ended June 30, 2022.

As of June 30, 2023, 1,959,915 performance restricted stock units were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was $88.6 million.

Stock Option Rollforward

The following table 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, 2022	7,788,350	$ 77.95	6.36	$ 7,275
Granted	881,254	$ 46.03		
Exercised	(65,940)	$ 16.58		
Forfeited	(101,739)	$ 86.24		
Outstanding as of June 30, 2023	8,501,925	$ 75.02	6.27	$ 25,890
Exercisable as of June 30, 2023	5,568,114	$ 83.45	5.09	$ 17,901

As of June 30, 2023, the Company had unrecognized stock-based compensation expense related to its outstanding and unvested time-based stock option awards of $65.9 million, which is expected to be recognized over the remaining weighted average vesting period of 2.96 years.

The intrinsic value of stock options exercised during the six months ended June 30, 2023 and 2022 was $1.9 million and $4.2 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.

As of June 30, 2023 and 2022, for performance-based stock option grants that were outstanding, the achievement of the milestones that had not been met was considered not probable, and therefore no expense has been recognized related to these awards during the six months ended June 30, 2023 and 2022, respectively.

During the six months ended June 30, 2023 and 2022, the Company granted no stock options to purchase shares of common stock that contain performance-based vesting criteria.

During the six months ended June 30, 2023 and 2022, no milestones were achieved under performance-based stock options.

As of June 30, 2023, 650,000 performance-based stock options were both outstanding and unvested, the total unrecognized stock-based compensation expense related to these awards was $9.0 million and the timing of recognition of this stock-based compensation expense is subject to judgment of the Company as to when the performance conditions are considered probable of being achieved.

Stock-Based Compensation Expense

The following table summarizes stock-based compensation expense recognized during the three and six months ended June 30, 2023 and 2022:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
	(in thousands)			
Research and development	$ 4,496	$ 6,458	$ 13,269	$ 15,073
Selling, general and administrative	7,197	8,178	18,462	18,116
	$ 11,693	$ 14,636	$ 31,731	$ 33,189

The following table summarizes stock-based compensation expense by award type recognized during the three and six months ended June 30, 2023 and 2022:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
	(in thousands)			
Stock options	$ 9,663	$ 13,202	$ 19,678	$ 28,667
Restricted stock units	1,618	1,450	11,171	4,253
Employee stock purchase plan	412	(16)	882	269
	$ 11,693	$ 14,636	$ 31,731	$ 33,189

For stock option awards, the fair value is estimated at the grant date using the Black-Scholes option-pricing model, taking into account the terms and conditions upon which stock options are granted. The fair value of the stock options is amortized on a straight-line basis for stock option awards to employees, non-employee directors and non-employee consultants over the requisite service period of the awards.

The weighted average grant date fair value per share of stock options granted under the Company's stock option plans during the six months ended June 30, 2023 and 2022 was $30.41 and $26.32, respectively.

8. Net Loss Per Share

The following table shows the calculation of basic and diluted net loss per share for the three and six months ended June 30, 2023 and 2022:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
Basic net loss per share:				
Numerator:				
Net loss (in thousands)	$ (160,325)	$ (126,260)	$ (307,153)	$ (248,315)
Denominator:				
Weighted average common stock outstanding —basic	59,769,640	59,266,322	59,722,147	59,148,246
Dilutive effect of shares of common stock equivalents resulting from common stock options and restricted stock units	—	—	—	—
Weighted average common stock outstanding —diluted	59,769,640	59,266,322	59,722,147	59,148,246
Net loss per share—basic and diluted	$ (2.68)	$ (2.13)	$ (5.14)	$ (4.20)

The following table summarizes common stock equivalents outstanding that were excluded from the calculation of diluted net loss per share because including them would have been anti-dilutive as of June 30, 2023 and 2022:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
Stock options	7,851,925	6,999,816	7,851,925	6,999,816
Restricted stock units	445,421	243,159	445,421	243,159
Employee stock purchase plan	87,938	33,614	87,938	33,614
	8,385,284	7,276,589	8,385,284	7,276,589

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.

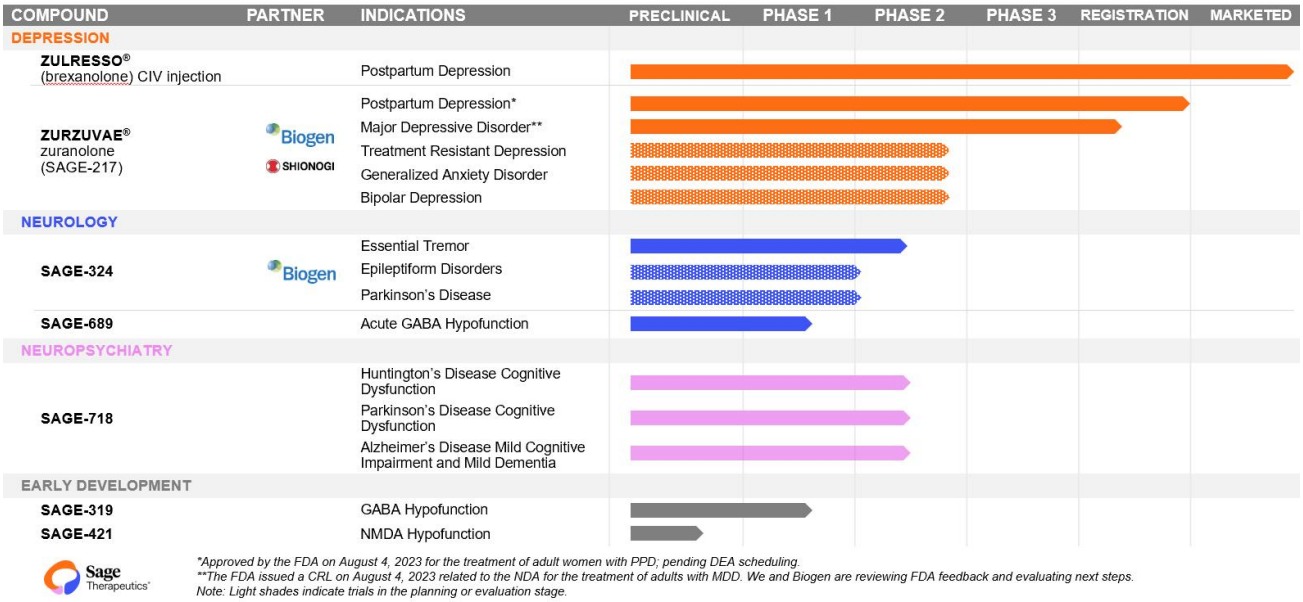
Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

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, 2022, 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 Quarterly 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 with a mission to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive. We are currently targeting diseases and disorders of the brain with three key focus areas: depression, neurology and neuropsychiatry. Our focus as a company is on brain health, and we are currently targeting 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.

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



ZURZUVAE™ (zuranolone), our second product, was approved by the U.S. Food and Drug Administration, or FDA, on August 4, 2023 for the treatment of postpartum depression, or PPD, in adults. ZURZUVAE is a neuroactive steroid that is a positive allosteric modulator of $GABA_A$ receptors, targeting both synaptic and extrasynaptic $GABA_A$ receptors. ZURZUVAE is expected to commercially launch in the U.S. for the treatment of women with PPD in the fourth quarter of 2023, following controlled substance scheduling by the U.S. Drug Enforcement Administration, or DEA, which is anticipated to be completed within 90 days after FDA approval. ZURZUVAE is the first oral, once-daily, 14-day treatment specifically indicated for adults with PPD. ZURZUVAE includes a boxed warning that instructs healthcare providers to advise patients that ZURZUVAE causes driving impairment due to central nervous system depressant effects, and that people who take ZURZUVAE should not drive a motor vehicle or engage in other potentially hazardous activities requiring complete mental alertness until at least 12 hours after ZURZUVAE administration for the duration of the 14-day treatment course. ZURZUVAE can cause CNS depressant effects such as somnolence and confusion. Healthcare professionals should consider changing the therapeutic regimen, including discontinuing ZURZUVAE, in patients whose depression becomes worse or who experience emergent suicidal thoughts and behaviors and advise females of reproductive potential to use effective contraception during treatment with ZURZUVAE and for one week after the final dose. ZURZUVAE was generally well-tolerated with a consistent safety profile across both pivotal clinical trials in adult women with PPD. The most common side effects include sleepiness or drowsiness, dizziness, common cold, diarrhea, feeling tired, weak, or having no energy, and urinary tract infection.

Additionally, on August 4, 2023 the FDA issued a complete response letter, or CRL, related to the new drug application, or NDA, for zuranolone for the treatment of major depressive disorder, or MDD. The CRL stated that the NDA did not provide substantial evidence of effectiveness to support the approval of zuranolone for the treatment of MDD and that one or more additional clinical trials will be needed. We and Biogen MA Inc., or BIMA, and Biogen International GmbH, or, together with BIMA, Biogen, under our collaboration and license agreement, or the Biogen Collaboration Agreement, are reviewing the feedback from the FDA and evaluating next steps.

The approval of ZURZUVAE to treat PPD in adults was based on two pivotal clinical trials in adult women with PPD. We have also completed four pivotal clinical trials of zuranolone for the treatment of adults with MDD. The completed pivotal trials evaluating zuranolone for the treatment of PPD and three of the four completed pivotal trials evaluating zuranolone for the treatment of MDD met their primary endpoints. We are currently conducting an open-label Phase 3 clinical trial of zuranolone for the treatment of MDD, known as the SHORELINE Study, which is designed to

evaluate the safety, tolerability, and need for repeat dosing of zuranolone in adults for up to one year. Enrollment in a 50 mg cohort of the SHORELINE Study has been completed and the study is ongoing. In August 2023, we announced additional data from the SHORELINE Study, specifically from the cohort of patients (n=277) that rolled over into the SHORELINE Study from the CORAL Study. In this cohort, the adverse event profile and the data generated on repeat treatments were similar to previously reported data from other cohorts of the SHORELINE Study, with no new safety signals identified. Sage plans to present further analyses from the SHORELINE Study at future medical congresses. We and Biogen may in the future develop zuranolone for other affective disorders.

Under the Biogen Collaboration Agreement, we are jointly developing zuranolone and another of our late-stage compounds, SAGE-324, in the U.S. with Biogen, and we will jointly commercialize any products containing zuranolone, which, including ZURZUVAE, 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. 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. For so long as a Licensed Product is being sold in the U.S., we and Biogen will equally share in all operating profits and losses arising from such Licensed Product. The Biogen Collaboration Agreement provides that Biogen will record sales of Licensed 217 Products globally. We will record sales of Licensed 324 Products in the U.S., and Biogen will record sales of Licensed 324 Products outside of the U.S., in each case if approved.

We also have a collaboration agreement with Shionogi for the development of zuranolone in the Shionogi Territory. In September 2021, Shionogi reported completion of a Phase 2 clinical trial of zuranolone for the treatment of patients with moderate to severe MDD in Japan, which Shionogi reported achieved its primary endpoints. Shionogi has also reported that it is conducting two Phase 3 trials of zuranolone for the treatment of patients with moderate to severe MDD as a monotherapy and as an add-on to other antidepressants, and announced that, pending results from these trials, it is aiming to submit an NDA to the Pharmaceuticals and Medical Devices Agency in Japan in the first quarter of 2024 seeking approval of zuranolone for the treatment of MDD.

Our first approved product, ZULRESSO® (brexanolone) CIV injection, is approved in the U.S. for the treatment of PPD in adults. We launched ZULRESSO commercially in the U.S. for the treatment of PPD in June 2019. ZULRESSO may only be administered in qualified, medically-supervised healthcare settings. Brexanolone is chemically identical to allopregnanolone, a naturally occurring neuroactive steroid that, like zuranolone, acts as a positive allosteric modulator of $GABA_A$ receptors.

We also are developing a portfolio of other novel compounds that target $GABA_A$ receptors including SAGE-324, which is a novel $GABA_A$ receptor positive allosteric modulator intended for chronic oral dosing. We are currently enrolling patients with essential tremor in a Phase 2b dose-ranging clinical trial of SAGE-324, known as the KINETIC 2 Study. In May 2022, we also initiated an open-label Phase 2 clinical trial designed to evaluate the long-term safety and tolerability of SAGE-324 in patients with essential tremor, with incidence of treatment-emergent adverse events as the primary endpoint. This is intended to be a multi-year clinical trial, and will initially be open to rollover patients from other SAGE-324 clinical trials in patients with essential tremor, including the KINETIC 2 Study. We believe SAGE-324 also has potential for the treatment of a number of other neurological conditions, including epilepsy and Parkinson’s disease. Additional development plans for SAGE-324 will be determined as part of our strategic collaboration with Biogen.

Our second area of focus for development is novel compounds that target the NMDA receptor. Our 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.

The FDA has granted SAGE-718 Fast Track designation as a potential treatment for patients with Huntington’s disease. In addition, in February 2023, the European Medicines Agency granted Orphan Drug Designation to SAGE-718

for the potential treatment of Huntington's disease. SAGE-718 is currently being studied in three ongoing clinical trials in patients with Huntington's disease cognitive impairment:

- **DIMENSION Study**

  In February 2022, dosing commenced in the DIMENSION Study, a double-blind placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with Huntington's disease cognitive impairment. The DIMENSION Study is designed to evaluate the efficacy of once-daily dosed SAGE-718 over three months.

- **SURVEYOR Study**

  In March 2022, we initiated the SURVEYOR Study, a placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with Huntington's disease cognitive impairment, with a healthy volunteer component, with the goal of generating evidence linking efficacy signals on cognitive performance to domains of real-world functioning.

- **PURVIEW Study**

  In December 2022, we initiated the PURVIEW Study, a Phase 3 open-label study to evaluate the long-term safety and tolerability of SAGE-718 in patients with Huntington's disease cognitive impairment.

We are also evaluating SAGE-718 for the treatment of cognitive issues associated with Parkinson's disease and Alzheimer's disease. In March 2022, we initiated a double-blind, placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with mild cognitive impairment due to Parkinson's disease, known as the PRECEDENT Study. The PRECEDENT Study is designed to evaluate the safety and efficacy of SAGE-718 in patients with mild cognitive impairment due to Parkinson's disease over 42 days, followed by a controlled follow-up period.

In December 2022, we initiated the LIGHTWAVE Study, a randomized placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with mild cognitive impairment and mild dementia due to Alzheimer's disease. The LIGHTWAVE Study is designed to evaluate the safety and efficacy of SAGE-718 dosed over an 84-day period, followed by a controlled follow-up period.

We have other programs at earlier stages of development with a focus on both acute and chronic brain health disorders. Our earlier stage product candidates include SAGE-689, a balanced $GABA_A$ receptor positive allosteric modulator in Phase 1 clinical development intended for intramuscular administration, and SAGE-319, an extrasynaptic $GABA_A$ receptor-preferring positive allosteric modulator in Phase 1 clinical development for its potential use as an oral therapy in treating disorders of social interaction. We also have earlier stage compounds focused on NMDA receptor modulation, including SAGE-421, an NMDA receptor positive allosteric modulator that we plan to study for potential use in neurodevelopmental disorders and cognitive recovery and rehabilitation. We expect to continue our work on allosteric modulation of the $GABA_A$ and NMDA receptor systems in the brain. The $GABA_A$ 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. Depending on the outcome of our expense and pipeline prioritization efforts, 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, and also believe that we may have the opportunity to use our scientific approach to explore targets beyond the $GABA_A$ 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. In the fourth quarter of 2020, we recorded revenue from the strategic collaboration with and stock purchase by Biogen.

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 $2.3 billion as of June 30, 2023. Our net loss was $307.2 million for the six months ended June 30, 2023. 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 operating losses for the foreseeable future.

Based on our current estimates, we expect that our existing cash, cash equivalents and marketable securities as of June 30, 2023, in addition to anticipated funding from our ongoing collaborations and potential revenue, will enable us to support our operations into 2025. See "—Liquidity and Capital Resources".

Additionally, given recent developments, we are currently evaluating resource allocation, including pipeline prioritization and a workforce reorganization, with a goal of extending our cash runway. As a result, we expect that our operating expenses will decrease in 2024 as compared to 2023. We expect to continue to incur costs in connection with our ongoing activities, including if and as we:

- prepare for a planned commercial launch of ZURZUVAE for the treatment of women with PPD in the U.S. after DEA scheduling has been completed; evaluate feedback from the FDA and potentially advance work to support the regulatory approval of zuranolone for the treatment of MDD, including potentially conducting one or more additional clinical trials in patients with MDD; and potentially advance the development of zuranolone in additional indications as part of our strategic collaboration with Biogen;
- continue our commercialization efforts with respect to ZULRESSO for the treatment of women with PPD in the U.S., with a primary focus on geographies that have existing, active ZULRESSO treating sites;
- complete the ongoing and planned clinical trials of SAGE-324 as part of our strategic collaboration with Biogen;
- complete ongoing and planned clinical trials of SAGE-718;
- 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;
- depending on the outcome of our ongoing evaluation of resource allocation and pipeline prioritization efforts, advance our earlier-stage compounds; continue our research and development efforts to evaluate the potential for our existing product candidates for 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 NDAs with the FDA and conduct permitted pre-launch activities with respect to any of our product candidates that we believe have been successfully developed;
- commercialize any product candidates for which we obtain regulatory approval, including the manufacture of commercial supplies;
- evaluate the market potential and regulatory pathways for our product candidates beyond zuranolone and SAGE-324 in the European Union and other jurisdictions 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 licenses, collaborations or other agreements or alliances with other biotechnology and 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 on a sustained basis from product sales and/or from collaborations, 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, ZURZUVAE, 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, successfully 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.

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 as a treatment for PPD, in June 2019.

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 are expected to continue to limit future ZULRESSO revenue growth.

Our ZULRESSO commercial operations, including our account management field-based team and sales representatives, are primarily focused on geographies that have existing, active ZULRESSO treating sites. We expect that this approach to our commercial efforts will 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 ZURZUVAE unless and until we and Biogen successfully launch and commercialize ZURZUVAE for the treatment of women with PPD in the U.S., and 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. If ZURZUVAE is successfully launched and commercialized for the treatment of women with PPD, it could further limit our commercial opportunity for ZULRESSO.

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 the treatment of MDD, and potentially other indications, in the Shionogi Territory. In October 2018, we also entered into a supply agreement with Shionogi under which we supply Shionogi with 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 for aggregate consideration of $650.0 million. The Biogen Collaboration Agreement became effective in December 2020, and the sale of the common stock under the stock purchase agreement closed on December 31, 2020. As a result of the 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, jointly 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, as well as the profits and losses, upon FDA approval of the Licensed Products, 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. Biogen will be the principal and record sales of SAGE-217 products globally. We will be the principal and record sales of SAGE-324 products in the U.S. and Biogen will be the principal and record sales of SAGE-324 Products in the Biogen Territory. In the year ended December 31, 2020, we recorded collaboration revenue – related party 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, 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 revenue recognition model and present 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, 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. For further discussion regarding the accounting for collaborative arrangements, 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.

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. We have the potential to receive from Biogen a milestone payment of $75.0 million for the first commercial sale of ZURZUVAE for the treatment of PPD in the U.S. and, if approved, a

milestone payment of $150.0 million for the first commercial sale of zuranolone for the treatment of MDD in the U.S. For further discussion regarding our collaboration agreements with Shionogi and Biogen and the accounting for revenue from collaboration agreements, refer to Note 2, *Summary of Significant Accounting Policies* and 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

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 revenue and amortization of intangible assets associated with ZULRESSO. Cost of goods sold may also include period costs related to certain inventory manufacturing services, inventory adjustment charges, as well as manufacturing variances. We estimate that our cost of goods sold as a percentage of net product revenue will remain in the high-single digit to low-double digits 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 consist 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;
- 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 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-development and co-manufacturing activities are accounted for as an increase to or reduction of research and development expense. During the three and six months ended June 30, 2023, we recorded net reimbursement of $22.4 million and $39.7 million, respectively; and during the three and six months ended June 30, 2022, we recorded net reimbursement of $21.0 million and $39.5 million, respectively, from Biogen, in each case, which was deducted from our research and development expenses because we incurred a greater amount of these expenses than Biogen.

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, healthcare and vendor staffing shortages and disruption to the U.S. healthcare system, which began as a result of the COVID-19 pandemic, and/or the impact of other macroeconomic and geopolitical conditions, may also negatively impact our ongoing and planned development activities and increase our research and development costs. Concerns, precautions and restrictions, staffing shortages, or other changes to the macroeconomic environment may substantially slow clinical site identification and activation and enrollment in our clinical trials, may impair or delay 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 experienced slower than anticipated recruitment in certain clinical trials, including our ongoing KINETIC 2 Study of SAGE-324 in patients with essential tremor, for which we now expect to complete enrollment in late 2023, rather than in late 2022 as we had initially projected.

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 ZURZUVAE and ZULRESSO; permitted pre-launch and launch-readiness activities related to ZURZUVAE; 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.

Our ongoing commercial efforts with respect to ZULRESSO, including our account management field-based team and sales representatives, 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. Given recent developments, we are currently evaluating resource allocation, including pipeline prioritization and a workforce reorganization, with a goal of extending our cash runway. As a result, we expect that our selling, general and administrative expenses will decrease in 2024 as compared to 2023. We expect to continue to incur selling, general and administrative expenses as we prepare for the planned launch and commercialization of ZURZUVAE in the U.S. for the treatment of women with PPD in the fourth quarter of 2023 following DEA scheduling, which is anticipated to be completed within 90 days after FDA approval. These expenses will include the costs associated with engagement in permitted pre-launch and launch-readiness activities, the hiring and training of a direct sales force for ZURZUVAE, and progression of our development efforts for our current or future product candidates and commercialization of those products, 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 six months ended June 30, 2023, we recorded net reimbursement from us to Biogen of $7.5 million and $10.5 million, respectively, that was added to our selling, general and administrative expenses. During the three and six months ended June 30, 2022, we recorded net reimbursement of $2.8 million and $4.3 million, respectively, from Biogen that was deducted from our selling, general and administrative expenses.

Results of Operations

Comparison of the Three Months Ended June 30, 2023 and 2022

The following table summarizes our results of operations for the three months ended June 30, 2023 and 2022:

	Three Months Ended June 30,		Increase (Decrease)
	2023	2022	
		(in thousands)	
Product revenue, net	$ 2,460	$ 1,501	$ 959
Collaboration revenue	14	—	14
Total revenue	2,474	1,501	973
Operating costs and expenses:			
Cost of goods sold	205	200	5
Research and development	97,161	77,297	19,864
Selling, general and administrative	75,565	52,411	23,154
Total operating costs and expenses	172,931	129,908	43,023
Loss from operations	(170,457)	(128,407)	(42,050)
Interest income, net	10,173	2,102	8,071
Other income (expense), net	(41)	45	(86)
Net loss	$ (160,325)	$ (126,260)	$ (34,065)

Product Revenue, Net

During the three months ended June 30, 2023 and 2022, we recognized $2.5 million and $1.5 million, respectively, of net product revenue related to sales of ZULRESSO. Sales allowances and accruals consisted of chargebacks, discounts, distribution fees, rebates and patient financial assistance, and were not significant during either period.

Cost of Goods Sold

During the three months ended June 30, 2023 and 2022, cost of goods sold was $0.2 million and $0.2 million, respectively, and is made up of 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 revenue and amortization of intangible assets associated with ZULRESSO. Cost of goods sold may also include period costs related to certain inventory manufacturing services, inventory adjustment charges, as well as manufacturing variances. Prior to receiving initial FDA approval for ZULRESSO in March 2019, we manufactured ZULRESSO inventory to be sold upon commercialization and recorded $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 June 30, 2023 and 2022. We estimate that our cost of goods sold as a percentage of net product revenue will remain in the high-single digit to low-double digits 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

The following table summarizes our research and development expenses for the three months ended June 30, 2023 and 2022:

	Three Months Ended June 30,		Increase (Decrease)
	2023	2022	
		(in thousands)	
ZURZUVAE (zuranolone)	$ 30,502	$ 27,827	$ 2,675
SAGE-324	10,356	8,469	1,887
SAGE-718	13,132	9,015	4,117
Other research and development programs	21,691	16,201	5,490
Unallocated expenses	39,402	30,310	9,092
Stock-based compensation	4,496	6,458	(1,962)
Net reimbursement from Biogen	(22,418)	(20,983)	(1,435)
	$ 97,161	$ 77,297	$ 19,864

Research and development expenses for the three months ended June 30, 2023 were $97.2 million, compared to $77.3 million for the three months ended June 30, 2022. The increase of $19.9 million was primarily due to the following:

- an increase of $2.7 million in expenses for development of ZURZUVAE, primarily due to an increase in spending for the SHORELINE study and partially offset by decreases due to the completion of studies after the three months ended June 30, 2022;
- an increase of $1.9 million in expenses for development of SAGE-324, primarily due to activities directed toward the conduct of a clinical pharmacology study and a Phase 2 clinical trial during the three months ended June 30, 2023;
- an increase of $4.1 million in expenses for development of SAGE-718, primarily due to activities directed towards the conduct of a Phase 2 clinical trial which was initiated during 2023;
- an increase of $5.5 million in expenses for other research and development programs, primarily due to increased work on early-stage research programs;
- an increase of $9.1 million in unallocated expenses, primarily due to an increase in the hiring of employees and corporate infrastructure costs, such as information technology costs, to support the growth in our research and development operations; and
- the net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement increased by $1.4 million. For the three months ended June 30, 2023, the amount of net reimbursement was $15.4 million for zuranolone, $4.9 million for SAGE-324 and $2.1 million for costs that are reimbursable and included in unallocated expenses. For the three months ended June 30, 2022, the amount of net reimbursement was $13.8 million for zuranolone, $4.2 million for SAGE-324 and $2.9 million for costs that are reimbursable and included in unallocated expenses. The primary reason for the increase in net reimbursement was the increase in spending for zuranolone, primarily due to an increase in spending for the SHORELINE study.

Selling, General and Administrative Expenses

The following table summarizes our selling, general and administrative expenses for the three months ended June 30, 2023 and 2022:

	Three Months Ended June 30,		Increase (Decrease)
	2023	2022	
		(in thousands)	
Personnel-related	$ 33,393	$ 20,338	$ 13,055
Stock-based compensation	7,197	8,178	(981)
Professional fees	12,929	15,120	(2,191)
Other	14,570	11,610	2,960
Net reimbursement to (from) Biogen	7,476	(2,835)	10,311
	$ 75,565	$ 52,411	$ 23,154

Selling, general and administrative expenses for the three months ended June 30, 2023 were $75.6 million, compared to $52.4 million for the three months ended June 30, 2022. The increase of $23.2 million was primarily due to the following:

- an increase of $13.1 million in personnel-related costs, primarily due to hiring employees to support ongoing permitted pre-launch and launch-readiness activities with respect to ZURZUVAE and in anticipation of potential commercialization of ZURZUVAE;
- an increase of $3.0 million in other expenses, primarily due to an increase in corporate infrastructure costs such as information technology costs, to support the growth in our operations; and
- the net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement decreased by $10.3 million. For the three months ended June 30, 2023, the amount of net reimbursement from us to Biogen was $0.4 million for personnel-related costs and $7.0 million for external costs. For the three months ended June 30, 2022, the amount of net reimbursement from us to Biogen was $0.3 million for personnel-related costs and the amount of net reimbursement from Biogen to us was $3.1 million for external costs. The primary reason for the decrease in net reimbursement was an increase in the collaboration costs incurred by Biogen in anticipation of a potential commercialization of ZURZUVAE.

Interest Income, Net and Other Income, Net

Interest income, net, and other income, net, for the three months ended June 30, 2023 and 2022 were $10.1 million and $2.1 million, respectively. The primary reason for the increase was the increase in interest rates from the three months ended June 30, 2022 to the three months ended June 30, 2023.

Comparison of the Six Months Ended June 30, 2023 and 2022

The following table summarizes our results of operations for the six months ended June 30, 2023 and 2022:

	Six Months Ended June 30,		Increase (Decrease)
	2023	2022	
	(in thousands)		
Product revenue, net	$ 5,754	$ 3,082	$ 2,672
Collaboration revenue	14	—	14
Total revenue	5,768	3,082	2,686
Operating costs and expenses:			
Cost of goods sold	435	486	(51)
Research and development	189,987	155,315	34,672
Selling, general and administrative	141,273	98,888	42,385
Total operating costs and expenses	331,695	254,689	77,006
Loss from operations	(325,927)	(251,607)	(74,320)
Interest income, net	19,003	3,270	15,733
Other income (expense), net	(229)	22	(251)
Net loss	$ (307,153)	$ (248,315)	$ (58,838)

Product Revenue, Net

During the six months ended June 30, 2023 and 2022, we recognized $5.8 million and $3.1 million, respectively, of net product revenue related to sales of ZULRESSO. Sales allowances and accruals consisted of chargebacks, discounts, distribution fees, rebates and patient financial assistance, and were not significant during either period.

Cost of Goods Sold

During the six months ended June 30, 2023 and 2022, cost of goods sold was $0.4 million and $0.5 million, respectively, and is made up of 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 revenue and amortization of intangible assets associated with ZULRESSO. Cost of goods sold may also include period costs related to certain inventory manufacturing services, inventory adjustment charges, as well as manufacturing variances. Prior to receiving initial FDA approval for ZULRESSO in March 2019, we manufactured ZULRESSO inventory to be sold upon commercialization and recorded $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 six months ended June 30, 2023 and 2022. We estimate that our cost of goods sold as a percentage of net product revenue will remain in the high-single digit to low-double digits 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

The following table summarizes our research and development expenses for the six months ended June 30, 2023 and 2022:

	Six Months Ended June 30,		Increase (Decrease)
	2023	2022	
	(in thousands)		
ZURZUVAE (zuranolone)	$ 53,641	$ 50,109	$ 3,532
SAGE-324	16,612	18,504	(1,892)
SAGE-718	26,196	18,436	7,760
Other research and development programs	39,597	34,856	4,741
Unallocated expenses	80,372	57,834	22,538
Stock-based compensation	13,269	15,073	(1,804)
Net reimbursement from Biogen	(39,700)	(39,497)	(203)
	$ 189,987	$ 155,315	$ 34,672

Research and development expenses for the six months ended June 30, 2023 were $190.0 million, compared to $155.3 million for the six months ended June 30, 2022. The increase of $34.7 million was primarily due to the following:

- an increase of $3.5 million in expenses for development of ZURZUVAE, primarily due to an increase in manufacturing-related costs in anticipation of potential commercialization of ZURZUVAE; and an increase in spending for the SHORELINE study, partially offset by decreases due to the completion of studies after the six months ended June 30, 2022;
- a decrease of $1.9 million in expenses for development of SAGE-324, primarily due to the completion of clinical pharmacology studies after the six months ended June 30, 2022;
- an increase of $7.8 million in expenses for development of SAGE-718, primarily due to activities directed towards the conduct of a Phase 2 clinical trial which was initiated during 2023;
- an increase of $4.7 million in expenses for other research and development programs, primarily due to increased work on early-stage research programs;
- an increase of $22.5 million in unallocated expenses, primarily due to an increase in the hiring of employees and corporate infrastructure costs, such as information technology costs, to support the growth in our research and development operations; and
- the net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement increased by $0.2 million. For the six months ended June 30, 2023, the amount of net reimbursement was $26.8 million for zuranolone, $8.0 million for SAGE-324 and $4.8 million for costs that are reimbursable and included in unallocated expenses. For the six months ended June 30, 2022, the amount of net reimbursement was $24.8 million for zuranolone, $9.2 million for SAGE-324 and $5.5 million for costs that are reimbursable and included in unallocated expenses. The primary reason for the increase in net reimbursement was the increase in spending for ZURZUVAE, primarily due to an increase in manufacturing-related costs in anticipation of potential commercialization of ZURZUVAE; and an increase in spending for the SHORELINE study.

Selling, General and Administrative Expenses

The following table summarizes our selling, general and administrative expenses for the six months ended June 30, 2023 and 2022:

	Six Months Ended June 30,		Increase (Decrease)
	2023	2022	
		(in thousands)	
Personnel-related	$ 62,280	$ 38,605	$ 23,675
Stock-based compensation	18,462	18,116	346
Professional fees	24,490	25,629	(1,139)
Other	25,531	20,847	4,684
Net reimbursement to (from) Biogen	10,510	(4,309)	14,819
	$ 141,273	$ 98,888	$ 42,385

Selling, general and administrative expenses for the six months ended June 30, 2023 were $141.3 million, compared to $98.9 million for the six months ended June 30, 2022. The increase of $42.4 million was primarily due to the following:

- an increase of $23.7 million in personnel-related costs, primarily due to hiring employees to support ongoing permitted pre-launch and launch-readiness activities with respect to ZURZUVAE and in anticipation of a potential commercialization of ZURZUVAE;
- an increase of $4.7 million in other expenses, primarily due to an increase in corporate infrastructure costs such as information technology costs, to support the growth in our operations; and
- the net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement decreased by $14.8 million. For the six months ended June 30, 2023, the amount of net reimbursement from us to Biogen was $0.6 million for personnel-related costs and $9.9 million for external costs. For the six months ended June 30, 2022, the amount of net reimbursement from us to Biogen was $0.3 million for personnel-related costs and the amount of net reimbursement from Biogen to us was $4.6 million for external costs. The primary reason for the decrease in net reimbursement was an increase in the collaboration costs incurred by Biogen in anticipation of a potential commercialization of ZURZUVAE.

Interest Income, Net and Other Income, Net

Interest income, net, and other income, net, for the six months ended June 30, 2023 and 2022 were $18.8 million and $3.3 million, respectively. The primary reason for the increase was the increase in interest rates from the six months ended June 30, 2022 to the six months ended June 30, 2023.

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. 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. As of June 30, 2023, we had an accumulated deficit of $2.3 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 June 30, 2023, 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 in the sale of shares of our common stock to Biogen in connection with the Biogen Collaboration Agreement, which we refer to as the Biogen Equity Purchase. We also received $1.0 billion in upfront payments under our collaborations with Biogen and Shionogi.

As of June 30, 2023, our primary sources of liquidity were our cash, cash equivalents and marketable securities, which totaled $1.0 billion. We invest our cash in money market funds, U.S. government securities, corporate bonds, commercial paper, certificates of deposit and municipal securities, 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 six months ended June 30, 2023 and 2022:

	Six Months Ended June 30,	
	2023	2022
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (285,200)	$ (214,239)
Investing activities	240,460	124,704
Financing activities	3,519	1,812
	$ (41,221)	$ (87,723)

Operating Activities

During the six months ended June 30, 2023, net cash used in operating activities primarily resulted from our net loss of $307.2 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 $2.8 million, partially offset by $24.7 million of non-cash items.

During the six months ended June 30, 2022, net cash used in operating activities primarily resulted from our net loss of $248.3 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 $4.3 million, partially offset by $38.4 million of non-cash items.

Investing Activities

During the six months ended June 30, 2023 and 2022, net cash provided by investing activities was $240.5 million and $124.7 million, respectively. During the six months ended June 30, 2023 and 2022, we purchased marketable securities and had sales and maturities of our marketable securities as part of managing our cash and investments portfolio.

Financing Activities

During the six months ended June 30, 2023 and 2022, net cash provided by financing activities was $3.5 million and $1.8 million, respectively. The increase was mainly due to an increase of proceeds from the purchase of shares under the Employee Stock Purchase Plan.

Operating Capital Requirements

We anticipate that we will continue to generate losses for the foreseeable future as we commercialize ZURZUVAE for the treatment of women with PPD in the U.S.; review feedback from the FDA and evaluate next steps with respect to the CRL regarding zuranolone for the treatment of MDD, and potentially advance work to support regulatory approval of zuranolone for the treatment of MDD, including potentially conducting one or more additional clinical trials in patients with MDD; 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 commercialization of product candidates beyond ZULRESSO and ZURZUVAE that are successfully developed and approved, including engaging in pre-launch and launch-readiness activities; begin to commercialize any such products, if 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, ZURZUVAE, and any other 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 estimates, we expect that our existing cash, cash equivalents and marketable securities as of June 30, 2023, in addition to anticipated funding from our ongoing collaborations and potential revenue, will enable us to

support our operations into 2025. Additionally, given recent developments, we are currently evaluating resource allocation, including pipeline prioritization and a workforce reorganization, with a goal of extending our cash runway. As a result, we expect that our operating expenses will decrease in 2024 as compared to 2023. We expect to continue to incur operating expenses as we prepare for the planned launch and commercialization of ZURZUVAE in the U.S. for the treatment of women with PPD in the fourth quarter of 2023 following DEA scheduling, which is anticipated to be completed within 90 days after FDA approval. These costs will include the expenses associated with engagement in permitted pre-launch and launch-planning activities; advancement of our planned and ongoing clinical trials for SAGE-718 and SAGE-324; depending on the outcome of our ongoing evaluation of resource allocation and pipeline prioritization efforts, continuing our various research activities; and pursuing 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:

- our ability, with our collaborator Biogen, to successfully commercialize ZURZUVAE for the treatment of women with PPD in the U.S., the costs associated with permitted pre-launch and launch-readiness activities and commercial launch; the timing and amount of any revenues from sales of ZURZUVAE; the level of reimbursement for ZURZUVAE both by commercial and government payors, and the nature of any potential limitations on coverage and reimbursement; and the degree of market acceptance of ZURZUVAE by healthcare providers and women with PPD;
- our ability, with Biogen, to evaluate and conduct next steps with respect to the CRL regarding zuranolone for the treatment of MDD, and potentially advance work to support regulatory approval of zuranolone for the treatment of MDD, including the potential to conduct additional clinical trials of zuranolone in patients with MDD, and the associated expense of such trials, if conducted;
- the outcome of our ongoing evaluation of resource allocation and pipeline prioritization;
- the timing and amount 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; and the number of healthcare professionals willing to prescribe ZULRESSO and women with PPD who agree to be treated with ZULRESSO;
- the timing and amount of costs associated with our commercialization of ZULRESSO;
- the initiation, progress, completion, timing, costs, and results of ongoing, planned and future non-clinical studies and clinical trials for our other 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;
- general macroeconomic and geopolitical conditions, including any capacity and resource constraints at our vendors and clinical trial sites on initiation and conduct of our clinical trials or on our supply chain;
- the ability of SAGE-324, SAGE-718 and our other clinical-stage product candidates to progress through clinical development successfully and on the timelines we expect; 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 profit-sharing, cost-sharing, development, regulatory, and sales milestones, and royalty payments;
- the size of the markets for our products and product candidates in the indications we are pursuing or plan to study; the portion of the population in the approved indications for our products are actually prescribed; and the rate and degree of market acceptance, pricing, and availability and level of reimbursement for our products and product candidates, if successfully developed and approved;
- 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.

We have the potential to earn a milestone payment of $75.0 million from Biogen related to the first commercial sale of zuranolone for the treatment of PPD. Until such time, if ever, as we can generate substantial product revenue and/or collaboration revenue and achieve sustained 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, licensing arrangements or other agreements 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 as a result of macroeconomic or geopolitical conditions, result in an economic recession, a decrease in corporate and consumer expenditures, prolonged unemployment, or other circumstances that could negatively impact general economic conditions. 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.

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.

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.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

We had cash, cash equivalents and marketable securities of $1.0 billion as of June 30, 2023. 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 and Canada. 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 that are in excess of federally insured limits at one or more financial institutions.

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 six months ended June 30, 2023 and 2022.

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 June 30, 2023, 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 June 30, 2023, 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

We may from time to time become involved in legal proceedings relating to claims arising from our ordinary course of business, including claims related to contracts, employment arrangements, operating activities, intellectual property or other matters. We are not currently subject to any legal proceeding that we believe would have a material adverse impact on our financial position, results of operations or cash flows or other material legal proceeding.

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

Our future business prospects depend heavily on our ability, with our collaboration partner, Biogen MA Inc., and Biogen International GmbH, or together, Biogen, to successfully commercialize ZURZUVAE™ (zuranolone) for the treatment of women with postpartum depression, or PPD, in the U.S. There is no assurance that our commercialization efforts in the U.S. with respect to ZURZUVAE for the treatment of women with PPD will be successful or that we will be able to generate revenues at the levels or on the timing we expect or at levels or on the timing necessary to support our goals.

Our second product, ZURZUVAE, was approved by the FDA on August 4, 2023 as a treatment for adults with PPD in the U.S. ZURZUVAE is expected to commercially launch in the U.S. for the treatment of women with PPD in the fourth quarter of 2023, following controlled substance scheduling by the U.S. Drug Enforcement Administration, or DEA, which is anticipated to be completed within 90 days after FDA approval. ZURZUVAE is the first oral, once-daily, 14-day treatment specifically indicated for adults with PPD. ZURZUVAE includes a boxed warning that instructs healthcare providers to advise patients that ZURZUVAE causes driving impairment due to central nervous system depressant effects, and that people who take ZURZUVAE should not drive a motor vehicle or engage in other potentially hazardous activities requiring complete mental alertness until at least 12 hours after ZURZUVAE administration for the duration of the 14-day treatment course, which could decrease willingness to prescribe or use ZURZUVAE. The label also includes information about adverse events and other warnings and precautions. Our business currently depends heavily on our ability to successfully commercialize ZURZUVAE in the U.S. as a treatment for women with PPD. We may never be able to launch or successfully commercialize ZURZUVAE or meet our expectations with respect to revenues or profits from sales. There is no guarantee that the infrastructure, systems, processes, policies, relationships and materials we and Biogen have built for the commercialization of ZURZUVAE for the treatment of women with PPD in the U.S. will be sufficient for us to achieve success. Even if we are successful in launching ZURZUVAE for the treatment of women with PPD in the U.S., it may not achieve the clinical benefit, clinical use or market acceptance we expect in women with PPD, including as a result of the boxed warning included in the ZURZUVAE label. The number of women with PPD, the unmet need for additional treatment options for women with PPD, and the potential market for ZURZUVAE may be significantly smaller than we expect, or we may encounter reimbursement-related or other market-related issues in the commercialization of ZURZUVAE for the treatment of women with PPD. In addition, controlled substance scheduling by the DEA may not be completed on the timelines we expect, which could delay or hamper our commercialization plans. Even if we are successful in launching and commercializing ZURZUVAE for the treatment of women with PPD, we expect the revenues from ZURZUVAE for the treatment of women with PPD to be significantly lower than if we had received regulatory approval in major depressive disorder, or MDD.

Our future business prospects depend heavily on our ability, with Biogen, to evaluate the FDA's feedback in the Complete Response Letter, or CRL, related to the New Drug Application, or NDA, for zuranolone in the treatment of MDD and find a pathway to regulatory approval for zuranolone for the treatment of MDD. The FDA has taken the position that one or more additional clinical trials of zuranolone are required to support approval in MDD and even if we were to seek to appeal this in the future, the FDA may not change their position; such trial or trials could be time-consuming, significantly increase our expenses, and may not be feasible; even if we conduct such clinical trials, they may not be successful. Even if we conduct additional trials in MDD, there is no guarantee that the design and results of any additional clinical trials we conduct will be sufficient to obtain such regulatory approval. We may never obtain regulatory approval of zuranolone for the treatment of MDD. Even if we receive regulatory approval of zuranolone for the treatment of MDD, our commercialization efforts with respect to zuranolone for the treatment of MDD may not be successful.

On August 4, 2023, the FDA issued a CRL relating to the NDA for zuranolone for the treatment of MDD in the U.S. The CRL stated that the NDA did not provide substantial evidence of effectiveness to support the approval of zuranolone for the treatment of MDD and that one or more additional clinical trials will be needed. We and Biogen are reviewing the feedback from the FDA and evaluating next steps. Our future business prospects depend heavily on our ability, with Biogen, to address the CRL and find a pathway to regulatory approval for zuranolone for the treatment of MDD in the U.S. There is no assurance that we will be successful in our efforts to find a path to regulatory approval for zuranolone for the treatment of MDD. The FDA has taken the position that an additional clinical trial or clinical trials of zuranolone are required to support approval in MDD and even if we were to seek to appeal this in the future, the FDA may not change their position. If, following our assessment of the FDA's feedback, we conduct one or more additional clinical trials to support approval of zuranolone in MDD, such trials could be time-consuming, significantly increase our expenses, and may not be successful. The FDA may find deficiencies in the conduct of any additional clinical trials or nonclinical studies we and Biogen conduct in patients with MDD or in the preparation, collection or analysis of data from clinical trials or non-clinical studies submitted to the FDA in support of regulatory approval for zuranolone for the treatment of MDD. In addition, if we conduct additional clinical trials to support approval of zuranolone in MDD, we may encounter delays in initiation, conduct, completion of enrollment or completion of any such clinical trials, including as a result of slower than expected site initiation, slower than expected enrollment, the need or decision to expand the trials or other changes, that may impact our ability to meet our expected timelines and increase our costs. Even if we are able to provide additional clinical trial data in support of regulatory approval for zuranolone for the treatment of MDD, the FDA may not accept such data or additional information as complete or as sufficient for approval. If in the future an advisory committee of the FDA meets to review our NDA for zuranolone for the treatment of MDD, 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.

Even if the FDA eventually approves zuranolone for the treatment of MDD, the FDA may approve it only for the treatment of a specific subset of patients with MDD, or may impose other restrictions, such as limitations or restrictions in the approved label such as a boxed warning, contraindications or a Risk Evaluation and Mitigation Strategy, or REMS, program requirement. For example, ZURZUVAE includes a boxed warning that instructs healthcare providers to advise patients that ZURZUVAE causes driving impairment due to central nervous system depressant effects, and that people who take ZURZUVAE should not drive a motor vehicle or engage in other potentially hazardous activities requiring complete mental alertness until at least 12 hours after ZURZUVAE administration for the duration of the 14-day treatment course. The FDA may not meet expected timelines or may elect to extend the timeframe for their review of any additional information or work we submit, or there may be delays at any point in the regulatory review cycle that negatively impact our plans and expectations with respect to zuranolone. 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 in the treatment of MDD, if approved. Even if zuranolone is approved for the treatment of MDD, it may not have the profile or market acceptance we expect in clinical practice after launch for MDD; the unmet need for new treatment options in MDD may not be as significant as we expect or we may encounter reimbursement-related or other market-related issues in the commercialization of zuranolone for MDD. Even if we and Biogen are able to obtain regulatory approval of zuranolone for the treatment of MDD, we and Biogen may never be able to successfully

commercialize zuranolone in MDD, if approved, or record any revenues or achieve profits from sales of zuranolone in MDD, if approved.

Our future business prospects depend heavily on our ability, alone or through our collaborations, to successfully develop, gain regulatory approval of and commercialize our current and future product candidates beyond zuranolone. 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, or that the results of our clinical trials or other activities under our development programs will be positive. We cannot be certain that we or our collaborators will be able to advance such product candidates into additional trials or to successfully develop, obtain regulatory approval for, or successfully commercialize any of our such product candidates, if approved.

Our future business prospects depend heavily on our ability, alone or through our collaborations, to successfully develop and gain regulatory approval of our current and future product candidates beyond 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, as applicable, may not be able to demonstrate the efficacy and safety of any of our other 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, in our ongoing dose-ranging study of SAGE-324, the KINETIC 2 Study, we are evaluating multiple doses, including the same maximum dose of SAGE-324 that we evaluated in prior studies. 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 activation 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, there are existing therapies, where other companies are running large clinical trials, or where relevant clinical sites or our vendors are experiencing healthcare staffing shortages or significant turnover. 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.

Our ongoing and planned development activities may be negatively impacted by a number of factors. Widespread healthcare and vendor staffing shortages and increased competition for patients and clinical sites may make it difficult to enroll patients in our clinical trials and/or identify and activate participating clinical sites for our trials, may cause other delays at clinical trial sites and/or vendors, and may increase the rates of patients withdrawing from our clinical trials following enrollment. Some clinical sites may decline or delay participation in our trials due to capacity and resource constraints. These factors may substantially slow clinical site identification and activation and enrollment in our clinical trials, or cause us to pause trials, which may, in each case, significantly impact our ability to meet our expected timelines, budgets, or other plans.

In response to these challenges during the COVID-19 pandemic, we or our clinical sites implemented measures 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, and some clinical sites 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 restrictions and limitations could be implemented again in the future, including possibly in response to any future pandemic. 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, as was the case with the CRL that the FDA issued related to the NDA for zuranolone for the treatment of MDD.

Even if we or a collaborator of ours gains approval of any of our current or future product candidates, we and our collaborator may never be able to successfully commercialize such new product in the approved indications or meet our expectations with respect to timing and revenues or profits from sales of such product.

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 FDA in March 2019 as a treatment for PPD in adults, and was made commercially available in June 2019. Our revenues from sales of ZULRESSO have been negatively impacted by significant barriers arising from the complex requirements for treatment and, historically, by the impacts of the COVID-19 pandemic. Some or all of 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 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. These barriers were compounded by the COVID-19 pandemic, its related disruptive effects on the U.S. healthcare system, and other changes to the macroeconomic environment.

Our commercial efforts for ZULRESSO, including our account management field-based team and sales representatives, are primarily focused on geographies that have existing, active ZULRESSO treating sites. We expect that this approach will 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, is also expected to 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, including staffing shortages. Healthcare settings that are active treating sites may also limit capacity used for ZULRESSO infusions.

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

- Some women with PPD who need treatment 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 REMS process or may be concerned about the risk of excessive sedation and sudden loss of consciousness.
- 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 compete with lower cost antidepressants.
- Given the mode of administration, the nature of the REMS and the current 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.
- ZURZUVAE, if successfully launched and commercialized for the treatment of women with PPD, could further limit our commercial opportunity for ZULRESSO.

We also expect to 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 encounter states that impose significant coverage restrictions or lengthy delays on reimbursement of ZULRESSO. Similarly, certain healthcare settings or patients may determine that the financial burdens of treatment are not acceptable. 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.

ZULRESSO, ZURZUVAE, our current products if approved in additional indications, 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, in clinical trials at any stage of development of our product candidates, as part of an expanded access program, if initiated for any of our products or product candidates, in commercial use or in post-approval studies of any approved product. 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, ZURZUVAE, any other 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, ZURZUVAE, any current product if approved in additional indication(s), any other existing or future product candidate, or any future approved product:

- regulatory authorities may withdraw, withhold 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 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;
- 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 any of 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. For example, on August 4, 2023, the FDA issued a CRL related to the NDA for zuranolone for the treatment of MDD. The CRL stated that the NDA did not provide substantial evidence of effectiveness to support the approval of zuranolone for the treatment of MDD and that one or more additional clinical trials will be needed. 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, as has been the case to date with respect to the NDA for zuranolone for the treatment of MDD;
- 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 or may impose other limitations or restrictions, like a boxed warning, as was the case with ZURZUVAE;

- 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 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 and ZURZUVAE. For ZURZUVAE, the FDA is requiring two post-marketing studies: a pharmacokinetic and safety study in adolescent females who have completed puberty and an embryofetal toxicity study in a second species. We may not be able to fulfill these obligations in accordance with the FDA's timelines, or at all. The FDA has recommended scheduling with respect to ZURZUVAE, which is anticipated to be completed within 90 days after FDA approval, and the FDA may recommend scheduling with respect to any of our other current or future product candidates, if approved. In such event, as was the case with ZULRESSO, prior to a product launch, the 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 would delay our ability to market any product candidate that is successfully developed and approved. For example, ZURZUVAE is expected to commercially launch in the U.S. for the treatment of women with PPD in the fourth quarter of 2023, after the DEA scheduling period. There is no guarantee that the DEA scheduling period will be completed for ZURZUVAE on the timelines we expect. Any delay in the completion of the DEA scheduling period could delay our planned commercial launch of ZURZUVAE.

We may seek priority review of future NDA submissions with the FDA, if our development efforts with respect to other product candidates are successful, but the FDA may not grant such priority review. Even if the FDA grants priority review for an NDA, the FDA may not meet the applicable review timelines or may elect to extend the timeframe for their review. Delays, resource constraints, and other 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, the U.S. government has shut down several times in recent history and certain regulatory agencies, including the FDA, 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. For example, the FDA issued a CRL related to the NDA for zuranolone for the treatment of MDD after previously granting both Fast Track and Breakthrough Therapy designations to zuranolone for MDD. 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 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.

There is no precise method of establishing in any geography over any period of time the actual number of patients with the diseases and disorders for which our products are indicated and our product candidates are targeted. With respect to women with PPD, in the case of ZULRESSO and ZURZUVAE, additional indications for which we are pursuing or may pursue regulatory approval for our products, like MDD in the case of zuranolone, or any of the indications for 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 women with PPD or any other indication for which we are pursuing or may 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 potential market for ZURZUVAE for the treatment of women with PPD, the market for ZULRESSO, and our other 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 for the treatment of 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, in our ongoing dose-ranging study of SAGE-324, we are evaluating multiple doses, including the same maximum dose of SAGE-324 that we evaluated in prior studies. 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, enrollment 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, enrollment 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;
- delay or inability to satisfy the requirements for clinical trials conducted in the EU, if applicable, pursuant to Regulation (EU) No 536/2014, or the EU Clinical Trials Regulation;
- 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;
- challenges in qualifying and activating clinical trial sites, including due to capacity and resource constraints and attrition at sites, and potential delays at clinical trial sites;
- general political and economic conditions, including as a result of bank failures;
- 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.

Finally, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. For example, in December 2022, with the passage of Food and Drug Omnibus Reform Act, Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Similarly, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the EU Clinical Trials Directive required a separate clinical trial application to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. If we are not able to fulfill these new requirements, our ability to conduct clinical trials may be delayed or halted.

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 completely on third-party suppliers to manufacture commercial supplies of ZULRESSO and ZURZUVAE, and clinical drug supplies for our product candidates, and we intend to rely on third parties to produce commercial supplies of zuranolone for the treatment of MDD, if approved, and 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 ZURZUVAE or ZULRESSO for commercial use, including if we eventually obtain regulatory approvals in additional indications, or 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 ZURZUVAE to manufacture commercial supplies of active drug substance, finished drug product and packaged and labeled product. We also rely on our contract manufacturers to manufacture sufficient quantities of our 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, depending on the outcome of our pipeline prioritization and 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. Contract manufacturers are subject to inspections by the FDA. If the FDA were to identify deficiencies in connection with the inspections of our contract manufacturers for our products or any of our product candidates, if successfully developed and approved, the FDA could issue a Form 483 documenting these deficiencies and require that we provide and comply with a corrective action plan, which could impact our ability to supply product or any of our product candidates, if successfully developed and approved. 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, on the timelines we expect or at all, 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 a long-term supply agreement with our contract manufacturer for ZURZUVAE drug product, and we intend to enter into a long-term supply agreement at the appropriate time with at least one of our contract manufacturing organizations, or CMOs, for ZURZUVAE drug substance. 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 have arrangements in place for either long-term supply or redundant supply of drug substance or drug product for SAGE-324 or SAGE-718. Each batch of drug substance and drug product for our product candidates is individually contracted through a purchase order governed by master service and quality agreements.

If our existing CMOs 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 and gain approval. 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.

ZURZUVAE or any of our other current or future products or product candidates, 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 sales.

The commercial success of ZURZUVAE in the U.S. for the treatment of women with PPD, or, if approved, for the treatment of patients with MDD, or of any of our current or future products or product candidates, if successfully developed and approved by the FDA or other applicable regulatory authorities, will depend upon the awareness and acceptance among healthcare professionals, patients, policy-makers 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 & 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 for any of our products, including ZURZUVAE, such as requiring patients to try other lower cost therapies prior to reimbursing 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 ZURZUVAE, or any of our product candidates, if successfully developed and approved. 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. Regulatory approvals, pricing and reimbursement for drug products vary widely from country to country.

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 ZURZUVAE for the treatment of women with PPD, or if approved, for the treatment of patients with MDD, 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. 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 plan to pursue a value-based agreement strategy with payors for ZURZUVAE for the treatment of women with PPD in the U.S.. Payors may not be receptive to the use of value-based agreements or may not agree with our approach and such a strategy may not increase market acceptance or access. Even if payors agree to our value-based agreement approach, they may still impose restrictions such as requiring patients to try other lower cost therapies to treat PPD prior to reimbursing ZURZUVAE, requiring patients to meet severity or other criteria more restrictive than the approved label for our product, or requiring prior authorizations, and such restrictions or requirements may be more onerous than we expect. If we believe a value-based agreement strategy will not be successful we may change our approach. We cannot be sure that adequate coverage or reimbursement will be available for ZURZUVAE or any other product candidate that we or our collaborators commercialize or that coverage will be available on reasonable terms.

Market acceptance with respect to ZURZUVAE in the U.S. for the treatment of women with PPD, or any of our product candidates that we successfully develop, including zuranolone for the treatment of adults with MDD, 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 ZURZUVAE for the treatment of women with PPD, 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, such as the boxed warning for ZURZUVAE related to driving impairment;
- 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, including ZURZUVAE for the treatment of women with PPD, and if approved in the future, zuranolone for the treatment of adults with MDD, may require significant resources and may never be successful. ZURZUVAE, or any of our other current or future products or product candidates, if successfully developed and approved by the FDA or other applicable regulatory authorities, 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 to the degree or 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 ZURZUVAE, and we may encounter issues or delays in the conduct of these post-marketing commitments or we may generate unexpected results. For ZURZUVAE, the FDA is requiring two post-marketing studies: a pharmacokinetic and safety study in adolescent females who have completed puberty and an embryofetal toxicity study in a second species.

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. For example, the FDA recommended controlled substance scheduling for ZURZUVAE, which is expected to launch and be commercially available in the U.S. for the treatment of women with PPD in the fourth quarter of 2023 after the DEA scheduling period, which is anticipated to be completed within 90 days after FDA approval. 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 and ZURZUVAE are, 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, ZURZUVAE, or any of our other 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. For example, even if we are successful in our efforts to find a path to regulatory approval of zuranolone for the treatment of MDD, the FDA may require additional trials or data to support approval of zuranolone as a treatment

for MDD, may not meet expected review timelines or may elect to extend the timeframe for their review, or there may be delays at any point in the regulatory review cycle, any of which could allow time for our competitors to establish a market position that could reduce or eliminate our commercial opportunity for zuranolone in the treatment of MDD.

Currently, there are no pharmacological therapies specifically approved for the treatment of PPD other than ZURZUVAE and 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. If ZURZUVAE is successfully launched and commercialized for the treatment of women with PPD, it could further limit our commercial opportunity for ZULRESSO. In addition, ZULRESSO and ZURZUVAE may also face competition for the treatment of PPD from LPCN 1154, an oral formulation of the neuroactive steroid brexanolone under development by Lipocine, Inc. under the 505(b)(2) regulatory pathway.

If approved in the future, zuranolone may also face competition for the treatment of MDD. Patients with MDD are typically treated with a variety of low-cost antidepressant medications, including SSRIs, SNRIs and atypical antipsychotics. Zuranolone, if approved for the treatment of MDD in the U.S., may face competition for the treatment of MDD from AXS-05, a combination formulation of an NMDA receptor antagonist, dextromethorphan, with bupropion, an FDA-approved antidepressant affecting norepinephrine and dopamine, which such combination formulation was approved in August 2022 by the FDA for the treatment of MDD in adults. Zuranolone, if approved for the treatment of MDD in the U.S., may also face competition from esketamine, which is approved for the treatment of treatment-resistant depression and depressive symptoms in adults with MDD with acute suicidal ideation or behavior, and from cariprazine, which was recently approved for the adjunctive treatment of MDD in patients who are receiving ongoing antidepressant therapy. A number of other companies are developing product candidates intended for the treatment of MDD.

In the field of neuroactive steroids focused specifically on modulation of $GABA_A$ receptors, we also face competition from a number of companies, including Marinus Pharmaceuticals, Inc., or Marinus. In March 2022, Marinus announced that the FDA had approved ganaxolone, a known $GABA_A$ positive allosteric modulator neuroactive steroid, to treat seizures associated with CDKL5 deficiency disorder, a rare, genetic epilepsy. Other $GABA_A$ competitors include darigabat, which is being developed by Cerevel Therapeutics, Inc. for the treatment of epilepsy and panic disorder.

SAGE-324, a novel $GABA_A$ receptor positive allosteric modulator, is in Phase 2 development for essential tremor. If successfully developed and approved as a treatment for essential tremor, SAGE-324 will face competition from current first-line treatments which include β-adrenergic blocker propranolol and anticonvulsant primidone. Other companies are also developing potential treatments for essential tremor, including a T-type calcium channel modulator that Jazz Pharmaceuticals, Inc. is currently evaluating in Phase 2b development and a Phase 2 T-type calcium channel modulator being developed by Praxis.

A number of companies are working to develop products designed to modulate the NMDA receptor. Novartis AG, following its acquisition of Cadent Therapeutics, Inc., is developing its own NMDA receptor positive allosteric modulator, CAD-9303, which is currently being investigated in cognitive impairment associated with schizophrenia. In addition, Vaccinex, Inc. is evaluating VX15/2503, a monoclonal antibody against the protein semaphorin 4D (SEMA4D), as a treatment for cognitive impairment in Huntington's disease. Prilenia Therapeutics, B.V. is also assessing pridopidine, a sigma-1 receptor (S1R) agonist, in a Phase 3 clinical trial as a treatment for Huntington’s disease. Several companies have developed or are developing products for the treatment of Alzheimer'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 regulatory or development strategy or appropriate program spending, that may hamper or delay our development and commercialization efforts or increase our costs. Our business may be adversely affected and we may be subject to delays, disputes, or litigation if we and any of our collaborators disagree significantly, if any of our collaborators fails to perform its obligations or terminates our collaboration in whole or in part, 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, the planned commercialization of ZURZUVAE for the treatment of women with PPD, and any 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 solely 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 to jointly develop and commercialize ZURZUVAE, other products containing 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. For example, while ZURZUVAE was approved for the treatment of adults with PPD in the U.S., the FDA issued a CRL to the NDA for zuranolone for the treatment of MDD in the U.S. While we expect to earn a potential milestone payment of $75.0 million from Biogen related to the first commercial sale of ZURZUVAE for the treatment of PPD, we may never earn the $150.0 milestone payment from Biogen related to the first commercial sale of zuranolone for the treatment of MDD.

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 or commercialization of a product, if approved, 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 or regulatory or development strategy, 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 for certain products 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. Further, even if we generate new compounds in areas of interest, we may determine that those compounds are not worth pursuing for strategic reasons, including new legislation that may impact the viability of commercializing such compounds, if approved.

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.

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 and shortages, attrition of experienced staff, and other resource constraints;
- 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 changes to the macroeconomic and geopolitical environment, and the downstream effects of these changes.

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 and ZURZUVAE, if successfully launched and commercialized, could be delayed.

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, commercialization activities, 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, ZURZUVAE, if successfully launched and commercialized, 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, ZURZUVAE, 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, ZURZUVAE, 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, 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, or, if we fail to comply with 340B program requirements, the Health Resources and Services Administration, or HRSA, could decide to terminate our 340B program participation agreement. In the event that CMS terminates our rebate agreement or HRSA terminates our 340B program participation agreement, no federal payments would be available under Medicaid or Medicare Part B for our covered outpatient drugs. We are also subject to civil monetary and other penalties applicable to the drug pricing negotiation program and Part B and Part D inflation rebate programs, as discussed further below under the risk factor entitled

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

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 currently or may in the future 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 ZURZUVAE, and will play a similar role with respect to any of our other future product candidates, 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 ZURZUVAE or 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 privacy, security and breach reporting obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission 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 were extended 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. We may also be substantially negatively impacted if governmental authorities conclude that the business practices of one of our collaborators does not comply with applicable laws. 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 and have an active compliance program, 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. Compliance with these regulations can be time-consuming and onerous. If we are found to have improperly handled personal information, we may become subject to fines and penalties, litigation and reputational harm.

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, to the extent applicable to our business activities, HIPAA imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. 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.

We plan to enroll subjects in our ongoing or future clinical trials in the European Union, or EU, or other countries. When we do so, 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. The United Kingdom's, or UK's, exit from the EU, often referred to as Brexit, has created uncertainty with regard to future data protection regulation in the United Kingdom. The European Commission has adopted an adequacy decision concerning the level of data protection in the UK. Personal data may now flow freely from the EEA to the UK; however, the European Commission may suspend the adequacy decision if it decides that the UK no longer provides for an adequate level of data protection. 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 that went into effect on January 1, 2023. In November 2020, California voters approved the California Privacy Rights Act, or CPRA, ballot initiative which introduced significant amendments to the CCPA and established and funded a dedicated California privacy regulator, the California Privacy Protection Agency, or the CPPA. New implementing regulations will be issued under the CPRA that may lead to new or additional obligations for us. Failure to comply with the CCPA may result in, among other things, significant civil penalties and injunctive relief, or statutory or actual damages. In addition, California residents have the right to bring a private right of action in connection with certain types of incidents. These claims may result in significant liability and damages. In addition to California, at least eleven other states have passed comprehensive privacy laws similar to the CCPA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering comprehensive privacy laws during the 2023 legislative sessions that will go into effect in 2024 and beyond, including New York and New Jersey. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, Washington state recently passed a health privacy law that will regulate the collection and sharing of health information, and the law also has a private right of action. Connecticut and Nevada have also passed similar laws regulating consumer health data.

In addition, there are substantial efforts at the federal level to pass a national data privacy law that may impact our business activities. The uncertainty, ambiguity, complexity and potential inconsistency surrounding the implementation and interpretation of CCPA and other enacted or potential laws in other states and at the federal level 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. We may be subject to fines, penalties, or private actions in the event of non-compliance with such laws. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. We have implemented processes to manage compliance with the CCPA and continue to assess the impact of the CPRA, and other federal and state legislation, on our business as additional information and guidance becomes available.

In addition to the foregoing, any breach of privacy laws or data security laws, particularly resulting in a significant security incident or breach involving the misappropriation, loss or other unauthorized use or disclosure of sensitive or confidential patient or consumer information, could have a material adverse effect on our business, reputation and financial condition. As a data controller, we will be accountable for any third-party service providers we engage to process personal data on our behalf, including our CROs. There is no assurance that privacy and security-related safeguards we implement will protect us from all risks associated with the third-party processing, storage and transmission of such information. In certain situations, both in the U.S. and in other countries, we also may be obligated as a result of a security breach to notify individuals and/or government entities about these breaches.

Additionally, in October 2022, President Joe Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The European Union initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022 and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision will permit U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the European Union to the United States. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. It is unclear if and when the framework will be finalized and whether it will be challenged in court. It is unclear if and when the framework will be finalized and whether it will be challenged in court. The uncertainty around this issue may impact our activities with companies in the EU, and any potential future business operations in the EU.

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 unapproved, or "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. For example, ZURZUVAE is approved in the U.S. for the treatment of adults with PPD only and may not be promoted for any uses that are not approved by the FDA, including MDD. 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 taken steps to restrict promotional activities of those companies. Pharmaceutical companies have also been prosecuted and incurred significant civil, criminal and administrative penalties, damages, fines under the False Claims Act in connection with their alleged off-label promotion of drugs. Any promotion of the off-label use of ZULRESSO, ZURZUVAE, or any of our other 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 in foreign markets is subject to foreign governmental control. 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 and administrative policies and proposals signal a desire to lower drug prices in the U.S. As a result, we or our collaborators outside the U.S. in the future may be limited in 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 $GABA_A$ positive allosteric modulator compounds, asserting a lack of novelty and non-obviousness. We are in the process of appealing the rejection, 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, ZURZUVAE, 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, ZURZUVAE, and our other product candidates, if successfully developed and 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, ZURZUVAE, 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 or revocation 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 2022 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 products, 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 the relevant 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 Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as 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 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 May 2023, the Supreme Court, in Amgen Inc. v. Sanofi, et al., held that claims to a functionally-defined genus of monoclonal antibodies were invalid due to a lack of enablement, as they failed to provide adequate guidance for making and using the claimed antibodies. The Court noted that the general principle remains that all claims must be enabled to their "full scope" and that broader claims require more enablement.

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.

With passage of the CREATES Act, we are exposed to possible litigation and damages by competitors. In addition, existing statutes, including the CREATES Act, and proposed legislation in Congress, if passed into law, could limit the patent exclusivity on our products or facilitate earlier entry of generic competition.

Under the CREATES Act, legislation intended to facilitate the development of generic and biosimilar products, we are exposed to possible litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of their ANDAs and 505(b)(2) applications. Such litigation would subject us to additional litigation costs, damages and reputational harm, which could lead to lower revenues. Increased risk of generic competition with ZULRESSO,

ZURZUVAE, and any of our product candidates, if approved, including as a result of the CREATES Act, could impact our ability to maximize product revenue.

In addition, 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, ZURZUVAE, 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 operations.

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 cost containment measures, drug pricing controls or other reforms could have an adverse effect on our revenue from ZULRESSO, ZURZUVAE, or from the sales of any other products that are successfully developed and approved, including zuranolone if eventually approved for the treatment of MDD, 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 (subsequently modified by the IRA, as discussed below).

In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031. Pursuant to the Coronavirus Aid, Relief and Economic Security Act and subsequent legislation, these Medicare sequester reductions were reduced and suspended, with the full 2% cut resuming in July 2022. These and other laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our products or product candidates for which we may obtain regulatory approval or the frequency with which any such product is prescribed or used. For example, the Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010 (PAYGO) sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Act’s health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Certain provisions of the ACA have been subject to judicial challenges as well as efforts to modify them or to alter their interpretation or implementation. For example, the U.S. Tax Cuts and Jobs Act of 2017, signed into law in December 2017, included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." We expect that the ACA, its implementation, efforts to challenge or modify the ACA or its implementing regulations, or portions thereof, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to commercialize our product candidates, if approved.

There has been increasing legislative and enforcement interest in the U.S. with respect to drug pricing practices. Specifically, there have been several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs, including under Medicare and Medicaid, which may potentially impact negotiations on pricing and discounts with commercial payers, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. There have been multiple Congressional and administrative efforts to address drug pricing, including the Inflation Reduction Act of 2022, or IRA. It is unclear whether any other legislation or public policy will come to pass, and if so, what effect it could have on our business.

The IRA was signed into law by President Biden in August 2022. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for certain outpatient prescription drug coverage, as well as Medicare Part B. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare, with negotiated prices subject to a cap and first set to take effect in 2026; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (the first Part B inflation rebate period is in first quarter 2023; the first Part D inflation rebate period is fourth quarter 2022 through third quarter 2023); and replaces the Part D coverage gap discount program with a new Part D discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years of these programs. Manufacturers may be subject to civil monetary penalties for certain violations of the negotiation and inflation rebate provisions and an excise tax during a noncompliance period under the negotiation program.

Several pharmaceutical companies, as well as the U.S. Chamber of Commerce, and the Pharmaceutical Research and Manufacturers of America have filed lawsuits against HHS and CMS asserting that, among other things, the IRA's drug price negotiation program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the U.S. Constitution. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

Specifically, with respect to price negotiations, Congress authorized CMS to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. Drugs may be selected for negotiation only once they are at least seven years post-approval (such that they will be nine years post-approval when first subject to the maximum negotiated price) and biologics may be selected for negotiation 11 years post approval (such that they will be 13 years post-approval when first subject to the maximum negotiated price). It does not apply to drugs and biologics that have been approved for a single rare disease or condition. We could be at risk of government action if, in the future, any of our products are the subject of Medicare price negotiations. In that event, the outcome of the Medicare price negotiations, which will be made publicly available, may also impact negotiations on pricing and discounts with commercial payers.

These risks as to pricing may further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if the pricing of any of our products are the subject of Medicare price negotiations. For example, even if we successfully find a path to regulatory approval of zuranolone for the treatment of MDD, the IRA may negatively impact our potential future revenues. As a result, these risks may also impact the development decisions we make with respect to our products and product candidates, including zuranolone.

Further, the IRA subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the IRA by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The IRA also requires manufacturers to pay rebates for drugs reimbursed under Medicare Part D whose price increases exceed inflation and caps Medicare out-of-pocket drug costs beginning in 2025, at $2,000 a year, subject to an adjustment for inflation thereafter. Drug manufacturers may also be subject to civil monetary penalties with respect to their compliance with these programs. In addition, the IRA potentially raises risks related to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by eliminating the coverage gap starting in 2025, reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and imposing price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

It is unclear how the IRA will be implemented. We further cannot predict with certainty what impact the IRA or any other federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition. There may be additional Congressional and administrative efforts to address drug pricing.

At the state level, legislatures have increasingly passed legislation and agencies have 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, ZURZUVAE, or 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 measures discussed above, 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 and ZURZUVAE, successfully commercialize any other products if approved in the future, and achieve profitability.

Our internal computer systems or networks, or cloud platforms or those of our collaborators, our third-party CROs or our other contractors, consultants or service providers, may fail or suffer security breaches, which could result in a material disruption of our development programs, compromise personal or sensitive information related to our business, or cause us to incur significant liabilities which could adversely impact our business.

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business, and despite the implementation of security measures, our internal computer systems and those of our collaborators, our third-party CROs and our other contractors, consultants and service providers are vulnerable to cyber security threats, including damage from unauthorized access, theft, natural disasters, terrorism, war, telecommunication and electrical failures, and system malfunction, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, viruses, worms, denial-of-service attacks, supply chain attacks, social engineering schemes and other means to affect service reliability and threaten the confidentiality, integrity and availability of information). 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 or cloud platforms. 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 acts or practices in violation of Section 5(a) of the Federal Trade Commission Act, or the FTC Act. The Federal Trade Commission, or the FTC, expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. The guidance of the FTC for appropriately securing consumers' personal information is similar to what is required by the HIPAA Security Rule, which establishes national standards for covered entities to protect individuals' electronic personal health information. The HIPAA Security Rule requires covered entities to have appropriate administrative, physical and technical safeguards to help ensure the confidentiality, integrity, and security of electronic protected health information. With respect to privacy, the FTC also sets expectations that companies honor the privacy promises made to individuals about how the company handles consumers' personal information. Any failure to honor promises, such as the statements made in a privacy policy or on a website, may also constitute unfair or deceptive acts or practices in violation of the FTC Act. While we do not intend to engage in unfair or deceptive acts or practices, the FTC has the power to enforce promises as it interprets them, and events that we cannot fully control, such as data breaches, may be result in FTC enforcement. Enforcement by the FTC under the FTC Act can result in civil penalties or enforcement actions.

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, we cannot guarantee that our, or our third-party CROs' or our other contractors', consultants' or service providers' security measures will be sufficient to prevent data loss and other security breaches. 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, including security breaches that may remain undetected for extended periods of time, which can substantially increase the potential for a material adverse impact resulting from the breach.

Risks Related to Our Financial Position and Need for Capital

We are a biopharmaceutical company that has 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 only one approved product, and only began generating revenue from product sales in the second quarter of 2019. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk.

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 June 30, 2023, 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 June 30, 2023, our cash, cash equivalents and marketable securities were $1.0 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 $307.2 million for the six months ended June 30, 2023, and our accumulated deficit was $2.3 billion as of June 30, 2023.

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. Given recent developments, we are currently evaluating resource allocation, including pipeline prioritization and a workforce reorganization, with a goal of extending our cash runway. As a result, we expect that our operating expenses will decrease in 2024 as compared to 2023. We expect to continue to incur operating expenses, particularly as we prepare for the planned launch and commercialization of ZURZUVAE in the U.S. for the treatment of women with PPD in the fourth quarter of 2023 following DEA scheduling. These costs include the expenses associated with engagement in permitted pre-launch and launch-readiness activities; the cost of any work we advance to support the regulatory approval of zuranolone for the treatment of MDD, if we decide to advance such work after evaluating the feedback from the FDA; and advancement of planned and ongoing clinical trials for SAGE-718 and SAGE-324. We expect to incur significant sales, marketing and outsourced-manufacturing expenses in connection with the recent marketing approval of ZURZUVAE for the treatment of adults with PPD, and will incur such expenses if we obtain marketing approval for any of our current or future product candidates beyond ZULRESSO and ZURZUVAE. We incur significant legal and accounting costs associated with operating as a public company. We expect to continue to incur additional significant and 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 and/or revenue from our collaborations on a sustained basis. 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 ZULRESSO, ZURZUVAE, and any future approved product depends on a number of factors, including, but not limited to:

- our ability to successfully launch and commercialize ZURZUVAE for the treatment of women with PPD in the U.S., including by developing and effectively deploying a sales force, and our ability to achieve market acceptance and satisfactory reimbursement of such product in the medical community, with patients and with third-party payors;
- after evaluating feedback from the FDA and deciding on next steps for zuranolone, our ability to advance additional work to support regulatory approval of zuranolone in the U.S. for MDD, and obtain such regulatory approval;

- 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 other product candidates; and our ability to file for and receive marketing approval to commercialize our product candidates, if successfully developed; and
- with respect to any product candidate potentially approved in the future, 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 and/or revenue from our collaborations on a sustained basis, we will not become profitable, and may be unable to continue operations without continued funding.

We may 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 preparing for the commercial launch of ZURZUVAE for the treatment of women with PPD in the U.S., and are advancing our product candidates, including SAGE-718 and SAGE-324, through non-clinical and clinical development. Commercializing products and developing additional small molecule products are expensive. We are currently evaluating resource allocation, including pipeline prioritization and a workforce reorganization, with a goal of extending our cash runway. As a result, we expect that our operating expenses will decrease in 2024 as compared to 2023. We expect to continue to incur operating expenses, particularly as we prepare for the planned launch and commercialization of ZURZUVAE in the U.S. for the treatment of women with PPD in the fourth quarter of 2023 following DEA scheduling. These anticipated operating expenses include costs associated with engagement in permitted pre-launch and launch-readiness activities, the cost of any work we advance to support the regulatory approval of zuranolone for the treatment of MDD, if we decide to advance such work after evaluating the feedback from the FDA, and the costs of planned and ongoing clinical trials for SAGE-718 and SAGE-324. 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 June 30, 2023, our cash, cash equivalents and marketable securities were $1.0 billion. Based on our current estimates, we expect that our existing cash, cash equivalents and marketable securities, in addition to anticipated funding from our ongoing collaborations and potential revenue, will be sufficient to support our operations into 2025. 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 not achieve milestones tied to cash payments to us from our collaboration partners on the timelines we expect or at all, generate revenues from ZURZUVAE for the treatment of women with PPD at the levels we expect, or generate revenues from zuranolone for the treatment of MDD, if approved, or any other of our products that may be successfully developed, at the levels we expect. We may use available capital resources sooner than we expect under our current operating plan, including as a result of unexpected events or changes in plans. 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, licensing arrangements and arrangements involving other rights or a combination of these or other 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 current or future economic conditions impact capital markets 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. Any time we encounter a major setback in our development or regulatory activities, as is the case with the CRL issued by the FDA to our NDA for zuranolone for the treatment of MDD, or in our commercialization efforts, or receive negative data from a key clinical program, 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. In addition, future global economic uncertainty, reduced liquidity, capital market disruptions, and other macroeconomic or geopolitical conditions may potentially make it more difficult for us to raise additional funds on favorable terms. 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 cause our stock price, and the value of an investment in our stock, to fluctuate.

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 launch and commercialization efforts with respect to ZURZUVAE in the U.S. as a treatment for women with PPD, and our ability to attain commercial success;
- our ability to receive FDA approval of zuranolone for the treatment of MDD, without significant restrictions or limitations, or at all;
- 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 other existing or future product candidates beyond zuranolone;

- 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;
- the impact of macroeconomic and geopolitical conditions;
- 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 purchased by BIMA were subject to an 18-month lockup period, which expired on June 30, 2022, after which BIMA is able to sell a certain amount of its shares, subject to certain sales and volume limitations, or, if BIMA requests registration of its shares pursuant to its registration rights, without such sales and volume limitations. Following a second 18-month period, which expires December 31, 2023, BIMA will be able to sell shares without limitation.

Item 5. Other Information

None of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K) during the quarterly period covered by this Quarterly Report on Form 10-Q.

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
3.1	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-36544), filed on June 16, 2023)
10.1*	2014 Employee Stock Purchase Plan, as amended
10.2*#	Supply Agreement by and between the Registrant and CyDex Pharmaceuticals, Inc., dated December 13, 2012, as amended August 21, 2013 and April 30, 2014
10.3*#	Amendment No. 3 to Supply Agreement, by and between the Registrant and CyDex Pharmaceuticals, Inc., dated September 25, 2015
10.4*#	Commercial License Agreement by and between the Registrant and CyDex Pharmaceuticals, Inc., dated August 21, 2013, as amended April 30, 2014
10.5*#	Non-Exclusive License Agreement by and between the Registrant and the Regents of University of California, dated October 23, 2013, as amended May 14, 2014
10.6*#	Exclusive License Agreement by and between the Registrant and Washington University, dated November 11, 2013
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1+	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
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 and contained in Exhibits 101.*)

* Filed herewith.

\# Filed with this Quarterly Report on Form 10-Q solely for the purpose of transitioning these previously-filed exhibits, which are the subject of expiring confidential treatment orders, to the rules governing the filing of redacted exhibits under Regulation S-K Item 601(b)(10)(iv) pursuant to the SEC's CF Disclosure Guidance: Topic 7. Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

+ The certifications furnished in Exhibit 32.1 hereto are deemed to accompany this Quarterly Report on Form 10-K and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

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.

August 7, 2023

By: /s/ Barry E. Greene

Barry E. Greene

Chief Executive Officer, President and Director

(Principal Executive Officer)

August 7, 2023

By: /s/ Kimi Iguchi

Kimi Iguchi

Chief Financial Officer

(Principal Financial and Accounting Officer)

EXHIBIT 10.1

SAGE THERAPEUTICS, INC.

2014 EMPLOYEE STOCK PURCHASE PLAN, AS AMENDED

The purpose of the Sage Therapeutics, Inc. 2014 Employee Stock Purchase Plan ("the Plan") is to provide eligible employees of Sage Therapeutics, Inc. (the "Company") and each Designated Subsidiary (as defined in Section 11) with opportunities to purchase shares of the Company's common stock, par value $0.0001 per share (the "Common Stock"). 1,082,000 shares of Common Stock in the aggregate have been approved and reserved for this purpose. The Plan is intended to constitute an "employee stock purchase plan" within the meaning of Section 423(b) of the Internal Revenue Code of 1986, as amended (the "Code"), and shall be interpreted in accordance with that intent.

1. Administration. The Plan will be administered by the person or persons (the "Administrator") appointed by the Company's Board of Directors (the "Board") for such purpose. The Administrator has authority at any time to: (i) adopt, alter and repeal such rules, guidelines and practices for the administration of the Plan and for its own acts and proceedings as it shall deem advisable; (ii) interpret the terms and provisions of the Plan; (iii) make all determinations it deems advisable for the administration of the Plan; (iv) decide all disputes arising in connection with the Plan; and (v) otherwise supervise the administration of the Plan. All interpretations and decisions of the Administrator shall be binding on all persons, including the Company and the Participants. No member of the Board or individual exercising administrative authority with respect to the Plan shall be liable for any action or determination made in good faith with respect to the Plan or any option granted hereunder.

2. Offerings. The Company will make one or more offerings to eligible employees to purchase Common Stock under the Plan ("Offerings"). Unless otherwise determined by the Administrator, an Offering will begin on the first business day occurring on or after each January 1st and July 1st and will end on the last business day occurring on or before the following June 30th and December 31st, respectively. The Administrator may, in its discretion, designate a different period for any Offering, provided that no Offering shall exceed 12 months in duration or overlap any other Offering.

3. Eligibility. All individuals classified as employees on the payroll records of the Company and each Designated Subsidiary are eligible to participate in any one or more of the Offerings under the Plan, provided that (i) as of the first day of the applicable Offering (the "Offering Date") they are customarily employed by the Company or a Designated Subsidiary for more than 20 hours a week, and (ii) they were employees of the Company on the first day of the month preceding the Offering Date (i.e., employment status determined as of June 1 for the Offering commencing on July 1 and determined as of December 1 for the Offering commencing on January 1). Notwithstanding any other provision herein, individuals who are not contemporaneously classified as employees of the Company or a Designated Subsidiary for purposes of the Company's or applicable Designated Subsidiary's payroll system are not considered to be eligible employees of the Company or any Designated Subsidiary and shall not be eligible to participate in the Plan. In the event any such individuals are reclassified as employees of the Company or a Designated Subsidiary for any purpose, including, without limitation, common law or statutory employees, by any action of any third party, including, without limitation, any government agency, or as a result of any private lawsuit, action or administrative proceeding, such individuals shall, notwithstanding such reclassification, remain ineligible for participation. Notwithstanding the foregoing, the exclusive means for individuals who are not contemporaneously classified as employees of the Company or a Designated Subsidiary on the Company's or Designated Subsidiary's payroll system to become eligible to participate in this Plan is through an amendment to this Plan, duly executed by the Company, which specifically renders such individuals eligible to participate herein.

4. Participation.

(a) Participants in Offering. An eligible employee who is not a Participant on any Offering Date may participate in such Offering by submitting an enrollment form to his or her appropriate payroll location at least 15 business days before the Offering Date (or by such other deadline as shall be established by the Administrator for the Offering).

(b) Enrollment. The enrollment form will (a) state a whole percentage to be deducted from an eligible employee's Compensation (as defined in Section 11) per pay period, (b) authorize the purchase of Common Stock in each Offering in accordance with the terms of the Plan and (c) specify the exact name or names in which shares of Common Stock purchased for such individual are to be issued pursuant to Section 10. An employee who does not enroll in accordance with these procedures will be deemed to have waived the right to participate. Unless a Participant files a new enrollment form or withdraws from the Plan, such Participant's deductions and purchases will continue at the same percentage of Compensation for future Offerings, provided he or she remains eligible.

(c) Notwithstanding the foregoing, participation in the Plan will neither be permitted nor be denied contrary to the requirements of the Code.

5. Employee Contributions. Each eligible employee may authorize payroll deductions at a minimum of one percent (1%) up to a maximum of ten percent (10%) of such employee's Compensation for each pay period. The Company will maintain book accounts showing the amount of payroll deductions made by each Participant for each Offering. No interest will accrue or be paid on payroll deductions.

6. Deduction Changes. Except as may be determined by the Administrator in advance of an Offering, a Participant may not increase or decrease his or her payroll deduction during any Offering, but may increase or decrease his or her payroll deduction with respect to the next Offering (subject to the limitations of Section 5) by filing a new enrollment form at least 15 business days before the next Offering Date (or by such other deadline as shall be established by the Administrator for the Offering). The Administrator may, in advance of any Offering, establish rules permitting a Participant to increase, decrease or terminate his or her payroll deduction during an Offering.

7. Withdrawal. A Participant may withdraw from participation in the Plan by delivering a written notice of withdrawal to his or her appropriate payroll location. The Participant's withdrawal will be effective as of the next business day. Following a Participant's withdrawal, the Company will promptly refund such individual's entire account balance under the Plan to him or her (after payment for any Common Stock purchased before the effective date of withdrawal). Partial withdrawals are not permitted. Such an employee may not begin participation again during the remainder of the Offering, but may enroll in a subsequent Offering in accordance with Section 4.

8. Grant of Options. On each Offering Date, the Company will grant to each eligible employee who is then a Participant in the Plan an option ("Option") to purchase on the last day of such Offering (the "Exercise Date"), at the Option Price (as defined herein) for, the lowest of (a) a number of shares of Common Stock determined by dividing such Participant's accumulated payroll deductions on such Exercise Date by the Option Price (as defined herein), (b) 2,500 shares; or (c) such other lesser maximum number of shares as shall have been established by the Administrator in advance of the Offering; provided, however, that such Option shall be subject to the limitations set forth below. Each Participant's Option shall be exercisable only to the extent of such Participant's accumulated payroll deductions on the Exercise Date. The purchase price for each share purchased under each Option (the "Option Price") will be eighty-five percent (85%) of the Fair Market Value of the Common Stock on the Offering Date or the Exercise Date, whichever is less.

Notwithstanding the foregoing, no Participant may be granted an Option hereunder if such Participant, immediately after the Option was granted, would be treated as owning stock possessing five percent (5%) or more of the total combined voting power or value of all classes of stock of the Company or any Parent or Subsidiary (as defined in Section 11). For purposes of the preceding sentence, the attribution rules of Section 424(d) of the Code shall apply in determining the stock ownership of a Participant, and all stock which the Participant has a contractual right to purchase shall be treated as stock owned by the Participant. In addition, no Participant may be granted an Option which permits his or her rights to purchase stock under the Plan, and any other employee stock purchase plan of the Company and its Parents and Subsidiaries, to accrue at a rate which exceeds $25,000 of the fair market value of such stock (determined on the Option grant date or dates) for each calendar year in which the Option is outstanding at any time. The purpose of the limitation in the preceding sentence is to comply with Section 423(b)(8) of the Code and shall be applied taking Options into account in the order in which they were granted.

9. Exercise of Option and Purchase of Shares. Each employee who continues to be a Participant in the Plan on the Exercise Date shall be deemed to have exercised his or her Option on such date and shall acquire from the

Company such number of whole shares of Common Stock reserved for the purpose of the Plan as his or her accumulated payroll deductions on such date will purchase at the Option Price, subject to any other limitations contained in the Plan. Any amount remaining in a Participant's account at the end of an Offering solely by reason of the inability to purchase a fractional share will be carried forward to the next Offering; any other balance remaining in a Participant's account at the end of an Offering will be refunded to the Participant promptly.

10. Issuance of Certificates. Certificates representing shares of Common Stock purchased under the Plan may be issued only in the name of the employee, in the name of the employee and another person of legal age as joint tenants with rights of survivorship, or in the name of a broker authorized by the employee to be his, her or their, nominee for such purpose.

11. Definitions.

The term "Compensation" means the amount of base pay, prior to salary reduction pursuant to Sections 125, 132(f) or 401(k) of the Code, but excluding overtime, commissions, incentive or bonus awards, allowances and reimbursements for expenses such as relocation allowances or travel expenses, income or gains on the exercise of Company stock options, and similar items.

The term "Designated Subsidiary" means any present or future Subsidiary (as defined below) that has been designated by the Board to participate in the Plan. The Board may so designate any Subsidiary, or revoke any such designation, at any time and from time to time, either before or after the Plan is approved by the stockholders.

The term "Fair Market Value of the Common Stock" on any given date means the fair market value of the Common Stock determined in good faith by the Administrator; provided, however, that if the Common Stock is admitted to quotation on the NASDAQ Capital Market, the NASDAQ Global Market, the NASDAQ Global Select Market or another national securities exchange, the determination shall be made by reference to the closing price on such date. If there is no closing price for such date, the determination shall be made by reference to the last date preceding such date for which there is a closing price.

The term "Initial Public Offering" means the consummation of the first underwritten firm commitment public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, covering the offer and sale by the Company of its Common Stock.

The term "Parent" means a "parent corporation" with respect to the Company, as defined in Section 424(e) of the Code.

The term "Participant" means an individual who is eligible as determined in Section 3 and who has complied with the provisions of Section 4.

The term "Subsidiary" means a "subsidiary corporation" with respect to the Company, as defined in Section 424(f) of the Code.

12. Rights on Termination of Employment. If a Participant's employment terminates for any reason before the Exercise Date for any Offering, no payroll deduction will be taken from any pay due and owing to the Participant and the balance in the Participant's account will be paid to such Participant or, in the case of such Participant's death, to his or her designated beneficiary as if such Participant had withdrawn from the Plan under Section 7. An employee will be deemed to have terminated employment, for this purpose, if the corporation that employs him or her, having been a Designated Subsidiary, ceases to be a Subsidiary, or if the employee is transferred to any corporation other than the Company or a Designated Subsidiary. An employee will not be deemed to have terminated employment for this purpose, if the employee is on an approved leave of absence for military service or sickness or for any other purpose approved by the Company, if the employee's right to reemployment is guaranteed either by a statute or by contract or under the policy pursuant to which the leave of absence was granted or if the Administrator otherwise provides in writing.

13. Special Rules. Notwithstanding anything herein to the contrary, the Administrator may adopt special rules applicable to the employees of a particular Designated Subsidiary, whenever the Administrator determines that such rules are necessary or appropriate for the implementation of the Plan in a jurisdiction where such Designated Subsidiary has employees; provided that such rules are consistent with the requirements of Section 423(b) of the Code. Any special rules established pursuant to this Section 13 shall, to the extent possible, result in the employees subject to such rules having substantially the same rights as other Participants in the Plan.

14. Optionees Not Stockholders. Neither the granting of an Option to a Participant nor the deductions from his or her pay shall constitute such Participant a holder of the shares of Common Stock covered by an Option under the Plan until such shares have been purchased by and issued to him or her.

15. Rights Not Transferable. Rights under the Plan are not transferable by a Participant other than by will or the laws of descent and distribution, and are exercisable during the Participant's lifetime only by the Participant.

16. Application of Funds. All funds received or held by the Company under the Plan may be combined with other corporate funds and may be used for any corporate purpose.

17. Adjustment in Case of Changes Affecting Common Stock. In the event of a subdivision of outstanding shares of Common Stock, the payment of a dividend in Common Stock or any other change affecting the Common Stock, the number of shares approved for the Plan and the share limitation set forth in Section 8 shall be equitably or proportionately adjusted to give proper effect to such event.

18. Amendment of the Plan. The Board may at any time and from time to time amend the Plan in any respect, except that without the approval within 12 months of such Board action by the stockholders, no amendment shall be made increasing the number of shares approved for the Plan or making any other change that would require stockholder approval in order for the Plan, as amended, to qualify as an "employee stock purchase plan" under Section 423(b) of the Code.

19. Insufficient Shares. If the total number of shares of Common Stock that would otherwise be purchased on any Exercise Date plus the number of shares purchased under previous Offerings under the Plan exceeds the maximum number of shares issuable under the Plan, the shares then available shall be apportioned among Participants in proportion to the amount of payroll deductions accumulated on behalf of each Participant that would otherwise be used to purchase Common Stock on such Exercise Date.

20. Termination of the Plan. The Plan may be terminated at any time by the Board. Upon termination of the Plan, all amounts in the accounts of Participants shall be promptly refunded.

21. Governmental Regulations. The Company's obligation to sell and deliver Common Stock under the Plan is subject to obtaining all governmental approvals required in connection with the authorization, issuance, or sale of such stock.

22. Governing Law. This Plan and all Options and actions taken thereunder shall be governed by, and construed in accordance with, the laws of the State of Delaware, applied without regard to conflict of law principles.

23. Issuance of Shares. Shares may be issued upon exercise of an Option from authorized but unissued Common Stock, from shares held in the treasury of the Company, or from any other proper source.

24. Tax Withholding. Participation in the Plan is subject to any minimum required tax withholding on income of the Participant in connection with the Plan. Each Participant agrees, by entering the Plan, that the Company and its Subsidiaries shall have the right to deduct any such taxes from any payment of any kind otherwise due to the Participant, including shares issuable under the Plan.

25. Notification Upon Sale of Shares. Each Participant agrees, by entering the Plan, to give the Company prompt notice of any disposition of shares purchased under the Plan where such disposition occurs within two years after the date of grant of the Option pursuant to which such shares were purchased.

26. Effective Date and Approval of Shareholders. The Plan shall take effect on the date of the Company's Initial Public Offering, subject to approval by the holders of a majority of the votes cast at a meeting of stockholders at which a quorum is present or by written consent of the stockholders.

DATE APPROVED BY BOARD OF DIRECTORS: July 2, 2014

DATE APPROVED BY STOCKHOLDERS: July 2, 2014

AMENDED BY BOARD OF DIRECTORS: June 7, 2017

AMENDED BY BOARD OF DIRECTORS: December 15, 2021

AMENDED BY STOCKHOLDERS: June 16, 2022

AMENDED BY BOARD OF DIRECTORS: February 6, 2023

AMENDED BY STOCKHOLDERS: June 15, 2023

EXHIBIT 10.2

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. […***…] denotes omissions.

SUPPLY AGREEMENT

THIS SUPPLY AGREEMENT (this "**Agreement**") is made this 13th day of December, 2012 (the "**Effective Date**") between:

CYDEX PHARMACEUTICALS, INC., a Delaware corporation with offices at 11119 North Torrey Pines Road, Suite 200, La Jolla, California 92037 ("**CyDex**"); and

SAGE THERAPEUTICS INC., a Delaware corporation with offices at 29 Newbury Street, Suite 301, Boston, Massachusetts 02116 ("**Sage**").

RECITALS

WHEREAS, CyDex and Sage are also parties to that certain Commercial License Agreement of even date herewith (the "**Commercial License Agreement**") and that certain License Agreement dated October 13, 2011 (the "**License Agreement**"); and

WHEREAS, CyDex desires to sell Captisol® to Sage or its Contract Manufacturers (defined below), and Sage desires to obtain supplies of Captisol® from CyDex, for use in the Licensed Product, in accordance with the terms and conditions contained herein.

NOW, THEREFORE, in consideration of the following mutual promises and other good and valuable consideration, the receipt and sufficiency of which are acknowledged, the parties, intending to be legally bound, agree as follows:

1. Definitions.

For the purposes of this Agreement, defined terms shall have the meanings defined in the Commercial License Agreement or as defined elsewhere in this Agreement. For reference purposes, "**Affiliate**", "**Captisol**", "**Claim**", "**Clinical Grade Captisol**", "**Commercial Grade Captisol**", "**Commercial Launch Date**", "**Commercially Reasonable Efforts**", "**Compound**", "**Contract Manufacturer**", "**FDA**", "**Field**", "**Licensed Product**", "**NDA**", "**Pfizer**" "**Specifications**", and "**Sublicensees**" are defined in the Commercial License Agreement.

2. Purchase and Supply of Captisol.

2.1 **Clinical Quantities**. Sage shall have, subject to the terms and conditions of this Agreement, the right to purchase Clinical Grade Captisol and/or Commercial Grade Captisol from CyDex, at the purchase prices specified in Exhibit A hereto, as may be increased pursuant to Section 4.1(a); such purchase prices are EXW (Incoterms 2010) CyDex's production point or storage facilities.

2.2 **Purchase Commitment**. Subject to the provisions of this Agreement and during the Term of this Agreement, Sage agrees that Sage and its Affiliates and Sublicensees and their Contract Manufacturers shall purchase 100% of their requirements for Captisol for use in the formulation of Licensed Product exclusively from CyDex. Sage shall not itself, and will not permit its Affiliates and Sublicensees to, make, sell, offer to sell or import bulk Captisol. This Agreement and the Commercial License Agreement do not grant Sage, its Affiliates or Sublicensees or their Contract Manufacturers the right to manufacture (or have manufactured on their behalf) Captisol, without CyDex's prior written consent. Sage covenants and agrees that it and its Affiliates, Sublicensees and Contract Manufacturers shall not re-sell any Captisol purchased pursuant to this Agreement (except as incorporated into the Licensed Product in and for the Field), and shall not use any Captisol purchased pursuant to this Agreement except in connection with the Licensed Product in and for the Field. Before entering into an agreement with any Sublicensees or Contract Manufacturers, Sage shall advise such Sublicensee or Contract Manufacturer of the foregoing restrictions and shall obtain such Sublicensee's or Contract Manufacturer's written agreement to observe and be bound thereby. Sage shall be responsible and liable for any actions by its Affiliates, Sublicensees and Contract Manufacturers which would have violated this Section 2.2 if committed by Sage itself.

2.3 **Supply Commitment**. CyDex agrees that CyDex shall produce (or have produced for it) and sell to Sage and its Affiliates and Sublicensees and their Contract Manufacturers 100% of Sage's and its Affiliates' and Sublicensees' and their Contract Manufacturers' requirements for Captisol for use in the formulation of Licensed Product in and for the Field, during the Term and subject to the provisions of this Agreement; *provided* that, and notwithstanding anything to the contrary in this Agreement, in no event shall CyDex be obligated to supply to Sage or its Affiliates or Sublicensees or their Contract Manufacturers more than an aggregate quantity of […***…] kilograms of Captisol per year pursuant to this Agreement.

2.4 **Third-Party Manufacturers**. Without limiting CyDex's responsibility under this Agreement, CyDex shall have the right at any time to satisfy its supply obligations to Sage hereunder either in whole or in part through arrangements with third parties engaged by CyDex to perform services or supply facilities or goods in connection with the manufacture or testing of Captisol (each, a "**Third- Party Manufacturer**"). CyDex shall give Sage no less than 12 month's prior written notice of any such arrangement. The parties hereby agree that The Hovione Group is a Third-Party Manufacturer as of the Effective Date of this Agreement.

3. Supply Terms.

3.1 **Orders**. During the Term and subject to the provisions of this Agreement, Sage may place orders in customary form (or, to the extent so required by Section 3.2(d), in Section 3.2(d) form) for Captisol on behalf of its Affiliates and Sublicensees; *provided, however*, that: (a) Sage shall instruct CyDex as to the location for the shipment thereof; (b) Sage shall guarantee payment to CyDex of all amounts payable with respect thereto; and (c) if Sage requests that CyDex deliver such orders to Sage for re-delivery thereof by Sage to its Affiliates or Sublicensees, Sage shall comply with all applicable laws, rules and regulations applicable to the transportation of Captisol from Sage to its Affiliates and Sublicensees.

3.2 **Supply Terms**.

(a) **Long-term Forecast**. No later than 12 months before the anticipated Commercial Launch Date, Sage shall provide CyDex with a good-faith forecast setting forth Sage's estimate of the required quantities of Commercial Grade Captisol for each of the following three years. Such long-term forecast shall thereafter be updated by Sage at least once every 12 months. Such long-term forecasts shall not be binding and shall be for planning purposes only.

(b) **Detailed Forecast**. At least 4 months before the first order of Commercial Grade Captisol, Sage shall deliver to CyDex a detailed good-faith rolling forecast setting forth Sage's requirements and anticipated delivery schedules for Commercial Grade Captisol for the 12 month period following such first order (the "**Initial Detailed Forecast**"). The Initial Detailed Forecast shall thereafter be updated by Sage quarterly (each a "**Detailed Forecast**"), no later than the first day of each calendar quarter, so that each quarter CyDex shall have been provided with a rolling Detailed Forecast for each quarter during the 12-month period commencing on the first day of the next calendar quarter following the date on which such Detailed Forecast is submitted. Before the third anniversary of the Commercial Launch Date, the first 6 months of each Detailed Forecast shall be firm and binding on both parties, subject to the permissible variances set forth in Section 3.2(c)(i) below, while the final 6 months of each Detailed Forecast shall not be binding and shall be for planning purposes only. After the third anniversary of the Commercial Launch Date, the entire Detailed Forecast shall be firm and binding on both parties, subject to the permissible variances set forth in Section 3.2(c)(ii) below. If Sage fails to provide any updated Detailed Forecast in accordance with this Section 3.2(b), the Detailed Forecast last provided by Sage shall be deemed to be resubmitted as Sage's binding Detailed Forecast for the next succeeding 12-month period, and with the same quantity and timing as had been forecasted (or deemed to be forecasted) for the fourth quarter of the prior Detailed Forecast being repeated as the forecasted quantity and timing for the new Detailed Forecast's fourth quarter.

(c) **Detailed Forecast Variances**.

(i) Until the 3rd anniversary of the first Commercial Launch Date, each updated Detailed Forecast may modify the amount of Commercial Grade Captisol estimated in the previous Detailed Forecast and the corresponding delivery timing in accordance with the following limitations (the "**Purchase Volume Limitations**"):

(1) for the first through third calendar months covered by such updated Detailed Forecast, there shall be no change in excess of a percentage to be agreed upon at a later date such that volume increases or decreases per month from the prior Detailed Forecast may be made without the prior express written consent of CyDex;

(2) for the fourth through sixth calendar months covered by such updated Detailed Forecast, there shall be no change in excess of a percentage to be agreed upon at a later date such that volume increases or decreases per month from the prior Detailed Forecast may be made without the prior express written consent of CyDex;

(3) for the third calendar quarter covered by such updated Detailed Forecast, there shall be no change in excess of a percentage to be agreed upon at a later date such that volume increases or decreases from the prior Forecast may be made without the prior express written consent of CyDex; and

(4) for the fourth calendar quarter covered by such updated Detailed Forecast, there shall be no change in excess of a percentage to be agreed upon at a later date such that volume increases or decreases from the prior Forecast may be made without the prior express written consent of CyDex.

(ii) After the 3rd anniversary of the Commercial Launch Date, the Purchase Volume Limitations shall be deemed modified as follows:

(1) for the first calendar quarter covered by such updated Detailed Forecast, there shall be no change in excess of a percentage to be agreed upon at a later date such that volume increases or decreases per month from the prior Detailed Forecast may be made without the prior express written consent of CyDex;

(2) for the second calendar quarter covered by such updated Detailed Forecast, there shall be no change in excess of a percentage to be agreed upon at a later date such that volume increases or decreases from the prior Detailed Forecast may be made without the prior express written consent of CyDex;

(3) for the third calendar quarter covered by such updated Detailed Forecast, there shall be no change in excess of a percentage to be agreed upon at a later date such that volume increases or decreases from the prior Forecast may be made without the prior express written consent of CyDex; and

(4) for the fourth calendar quarter covered by such updated Detailed Forecast, there shall be no change in excess of a percentage to be agreed upon at a later date such that volume increases or decreases from the prior Forecast may be made without the prior express written consent of CyDex.

(d) **Purchase Orders**. Together with each Detailed Forecast provided under Section 3.2(b) above, Sage shall place a firm purchase order with CyDex in a form mutually agreed upon by the parties, for Sage's order of Commercial Grade Captisol for the first calendar quarter of the Detailed Forecast for delivery consistent with the Detailed Forecast. Detailed Forecasts deemed delivered pursuant to the last sentence of Section 3.2(b) shall also be deemed to be accompanied by corresponding firm purchase orders for the first calendar quarter. Each purchase order, for all grades of Captisol, shall specify: (i) the grade of Captisol ordered (*i.e.*, Commercial Grade Captisol or Clinical Grade Captisol); (ii) quantities; (iii) delivery dates; and (iv) reasonable shipping instructions. CyDex shall comply with Sage's requested delivery dates if the firm purchase order date is at least 90 days before the stipulated delivery date and is made in accordance with the quantities set forth in the latest Detailed Forecast. Any such firm purchase order for Commercial Grade Captisol provided by Sage, to the extent such order is in the form mutually agreed upon by the parties and does not request more or less than the Purchase Volume Limitations, shall be deemed accepted by CyDex upon receipt by CyDex. With respect to any quantities ordered under such purchase order that exceed the Purchase Volume Limitations, CyDex shall not be obligated to accept such orders but nevertheless shall use good faith efforts to fill such orders for such excess quantities from available supplies. If CyDex, despite the use of good faith efforts, is unable to supply such quantities that exceed the Purchase Volume Limitations to Sage, such inability to supply shall not be deemed to be a breach of this Agreement by CyDex or a failure by CyDex to supply for any purpose. CyDex shall use reasonable efforts to notify Sage as soon as possible, but no less than within 30 days, after its receipt of Sage's purchase order of its ability to fill any amounts of such order that are in excess of the Purchase Volume Limitations. If any purchase order or other document submitted by Sage hereunder or any other document passing between the parties contains terms or conditions in addition to or inconsistent with the terms of this Agreement, the terms of this Agreement shall control and prevail and the parties hereby agree that such additional or inconsistent terms shall simply be ignored and deemed not to exist, unless they are handwritten and expressly identified as being additional to or inconsistent with this Section 3.2(d) and are signed by officers of both parties next to the handwriting.

3.3 **Delivery**. Sage acknowledges the inherent risk that a batch of Captisol may be lost in production or shipment, and Sage shall use commercially reasonable efforts to maintain a sufficient inventory of Captisol in the event of late delivery by CyDex. Quantities actually delivered to Sage or Sage's designee pursuant to an accepted purchase order may vary from the quantities reflected in such purchase order by up to 10% and still be deemed to be in compliance with such purchase order; *provided, however*, that Sage shall only be invoiced and required to pay for the quantities of Captisol that Sage actually ordered and CyDex actually delivered to Sage or Sage's designee. CyDex shall use Commercially Reasonable Efforts to include, in the next shipment of Captisol to Sage, any quantities ordered pursuant to an accepted purchase order but not delivered.

3.4 **Modified Specifications**. CyDex shall have the right to change the Specifications from time to time during the Term; *provided* that any change to the Specifications that would require Sage to (i) conduct additional process validation or (ii) comply with additional clinical study requirements from the FDA or other major-market regulatory agencies that would be beyond that required for the Licensed Product formulated with Captisol meeting the unmodified Specifications, will require Sage's prior written consent. In the event that CyDex desires to change the Specifications, CyDex shall give Sage at least 3 months' notice. If CyDex desires to change the Specifications or a regulatory agency requires a change to the Specifications where such change is generally applicable to Captisol, CyDex shall reimburse Sage for any Captisol purchased hereunder which is rendered unusable in all major markets by such change in Specifications. CyDex shall use Commercially Reasonable Efforts to cooperate with Sage to, if necessary, have any change approved by the FDA and other regulatory agencies having jurisdiction. CyDex will continue to provide Captisol with the unmodified Specifications under the terms of this Agreement until such time that Sage has obtained any required approvals for the Specification change by the FDA and other applicable major-market regulatory agencies. In the event that the FDA or another applicable major- market regulatory agency having jurisdiction requires Sage to implement any changes to the Specifications, CyDex shall use all

reasonable efforts to make such changes. CyDex shall promptly advise Sage as to any lead-time changes or other terms that may result from a change to the Specifications. Sage shall bear the costs CyDex actually incurred for materials already purchased expressly for Sage, its Affiliates or Sublicensees and rendered unusable by a change in Specifications requested by Sage and agreed to by CyDex. If a regulatory agency requires a change to the Specifications where such change is not generally applicable to Captisol but is specific to the Licensed Product, or if Sage requests a change to the Specifications which CyDex agrees to, then Sage shall be responsible for the documented, reasonable costs incurred to generate such unique, modified Specifications. In all other instances, CyDex shall bear all costs associated with any change to the Specifications.

3.5 **Inability to Supply**.

(a) **Notice**. CyDex shall notify Sage if CyDex is unable to supply the quantity of (i) Commercial Grade Captisol ordered by Sage within the Purchase Volume Limitations set forth in Section 3.2(c) or (ii) Clinical Grade Captisol ordered by Sage as set forth in Section 2.1 above: (1) as soon as possible but no less than within 15 days after CyDex's receipt of a purchase order from Sage; or (2) immediately upon becoming aware of an event of *force majeure* or any other event including, but not limited to, CyDex's failure to pass any regulatory inspections or as a result of modified Specifications that would render CyDex unable to supply to Sage the quantity of Captisol that CyDex is required to supply hereunder.

(b) **Allocation**. If CyDex is unable to supply to Sage the quantity of Captisol that CyDex is required to supply hereunder, CyDex (i) shall allocate its available Captisol among Sage and any other purchasers of Captisol with which CyDex then has an on- going contractual relationship, in proportion to the quantity of Captisol for which each of them has orders pending at such time and (ii) shall take all reasonable steps necessary to minimize supply delays. The supply allocation provided in this Section 3.5(b) and the alternate suppliers provisions of Section 3.5(c) shall be CyDex's sole obligation and Sage's sole and exclusive remedy for any supply shortage.

(c) **Alternate Suppliers**. If CyDex fails to supply to Sage, or if CyDex will be unable to supply Sage with 80% (*i.e.*, maximum shortfall of 20%) of the quantity of Captisol properly forecasted and ordered by Sage (and provided such order was within the Purchase Volume Limitations) in accordance with this Agreement, for a period of three consecutive months or longer or if any such failure occurs three or more times during any twelve month period ("**Supply Interruption**") then CyDex shall immediately provide written notice to Sage of the Supply Interruption. In the event of a Supply Interruption:

(i) *Additional Site*. CyDex shall negotiate with its Third-Party Manufacturer for such Third-Party Manufacturer to validate and qualify an additional site for the manufacture of Captisol as soon as practicable, but in any event within 90 days from the first day of the Supply Interruption.

(ii) *Additional Manufacturer*. If an additional site pursuant to Section 3.5(c)(i) does not resolve the Supply Interruption, then CyDex shall use its good faith efforts to qualify one or more alternate suppliers for the manufacture of Captisol as soon as practicable, but in any event within 90 days from the first day of the Supply Interruption.

(iii) *Alternate Supply*. In the event of a Supply Interruption, Sage shall be permitted to purchase Captisol from any Third-Party Manufacturer on the terms provided hereunder until CyDex provides reasonably acceptable assurances to Sage that the cause of the Supply Interruption has been resolved.

3.6 **Control; Acceptance and Rejection**.

(a) **Quality Control**. CyDex shall conduct or have conducted quality control testing of Captisol before shipment in accordance with the Specifications and other CyDex-approved quality control testing procedures that shall be set forth in the Specifications (the "**Testing Methods**"). CyDex shall retain or have retained accurate and complete records pertaining to such testing as well as samples (equal to at least twice the amount required to perform the full suite of Testing Methods) from each lot of Captisol shipped to Sage, for at least through the expiration date of such Captisol plus six months or longer if required by law. Each shipment of Captisol hereunder shall be accompanied by a certificate of analysis for each lot of Captisol therein.

(b) **Acceptance Testing**. Sage shall have a period of 45 days from the date of receipt to test or cause to be tested Captisol supplied under this Agreement. Sage or its designee shall have the right to reject any shipment of Captisol that does not conform in all respects with the Specifications at the time of delivery when tested in accordance with the Testing Methods. All shipments of Captisol shall be deemed accepted by Sage unless CyDex receives written notice of rejection from Sage within such 45-day period, describing the reasons for the rejection in reasonable detail. Once a delivery of Captisol is accepted or deemed accepted hereunder, Sage shall have no recourse against CyDex in the event Captisol is subsequently deemed unsuitable for use for any reason, except as provided in Section 10 below and except for Captisol that is not fit for use after the acceptance has occurred due to a defect in the Captisol that could not be detected through the performance of the Testing Method.

(c) **Confirmation**. After its receipt of a notice of rejection from Sage pursuant to Section 3.6(b) above, CyDex shall notify Sage as soon as reasonably practical whether it accepts Sage's basis for rejection and Sage shall cooperate with CyDex in determining whether such rejection was necessary or justified. If the parties are unable to agree as to whether a shipment of Captisol supplied by

CyDex or its Third-Party Manufacturer hereunder meets the Specifications, such question shall be submitted to an independent quality control laboratory mutually agreed upon by the parties. The findings of such independent laboratory shall be binding upon the parties. The cost of the independent quality control laboratory shall be borne by the party whose results are shown by such laboratory to have been incorrect.

(d) **Return or Destruction of Rejected Shipments**. Sage may not return or destroy any batch of Captisol until it receives written notification from CyDex that CyDex does not dispute that the batch fails to meet the Specifications. CyDex will indicate in its notice either that Sage is authorized to destroy the rejected batch of Captisol or that CyDex requires return of the rejected Captisol. Upon written authorization from CyDex to do so, Sage shall promptly destroy the rejected batch of Captisol and provide CyDex with written certification of such destruction. Upon receipt of CyDex's request for return, Sage shall promptly return the rejected batch of Captisol to CyDex. In each case, CyDex will reimburse Sage for the documented, reasonable costs associated with the destruction or return of the rejected Captisol.

(e) **Refund or Replacement**. Sage shall not be required to pay any invoice with respect to any shipment of Captisol properly rejected pursuant to this Section 3.6. Notwithstanding the foregoing, Sage shall be obligated to pay in full for any rejected shipment of Captisol that is not returned or destroyed in accordance with Section 3.6(d) above and that is subsequently determined to meet the Specifications in all material respects, irrespective of whether Sage has already paid CyDex for a replacement shipment. If Sage pays in full for a shipment of Captisol and subsequently properly rejects such shipment in accordance with this Section 3.6, Sage shall be entitled, upon confirmation that such shipment failed to meet the Specifications in all material respects, either, at Sage's option: (i) to a refund or credit equal to the purchase price paid with respect to such rejected shipment (including without limitation, taxes paid and shipping expenses); or (ii) to require CyDex to promptly replace and deliver to Sage an amount of Captisol that conforms to the requirements of this Agreement to replace such rejected shipment at no additional cost to Sage. Sage acknowledges and agrees that, except for the indemnification obligations set forth in Section 10 below, Sage's rights to a refund or credit for or to receive replacement of properly rejected shipments of Captisol hereunder shall be Sage's sole and exclusive remedy, and CyDex's sole obligation, with respect to non-conforming Captisol delivered hereunder.

(f) **Exceptions**. Sage's rights of rejection, return, refund and replacement set forth in this Section 3.6 shall not apply to any Captisol that is non-conforming due to damage (i) caused by Sage, its Affiliates or Sublicensees or their respective employees or agents, including but not limited to, misuse, neglect, improper storage, transportation or use beyond any dating provided or (ii) that occurs after delivery of such Captisol to the carrier at the point of origin, including but not limited to any damage caused thereafter by accident, fire or other hazard and CyDex shall have no liability or responsibility to Sage with respect thereto.

(g) **Inspections**. Authorized representatives of Sage shall be permitted to inspect those portions of all CyDex and Third- Party Manufacturer facilities that are used to manufacture, prepare, process, store or conduct testing of Captisol on an annual basis (scheduled at least 90 days in advance) during the term of this Agreement. Such representatives shall comply with the applicable rules and regulations for workers at such facilities and shall enter into reasonable confidentiality and non-use agreements if so requested by CyDex. Such audits shall be conducted in a manner that is intended to minimize any disruption to the operations at such facilities. CyDex shall promptly address and correct any deficiencies from cGMP's identified in connection with such inspections.

3.7 **Incoterms Delivery**. All Captisol shall be delivered EXW (Incoterms 2010) CyDex's production point or storage facilities.

4. Compensation.

4.1 **Pricing**.

(a) **Captisol Purchase Price Increases and Quanta**. CyDex reserves the right to increase such purchase prices set forth in Exhibit A on each January 1 during the Term, upon no less than 180 days' written notice to Sage, by a percentage equal to the aggregate percentage increase, if any, in the […***…], U.S. Department of Labor, for the 12-month period ending March 31 of the prior year (or any applicable successor index). Ordered quantities of Commercial Grade Captisol shall be specified in multiples of […***…] kilograms, subject to a minimum order quantity of […***…] kilograms.

(b) **Shortfall Reimbursement (Take or Pay)**. If Sage fails to order for the first calendar quarter of any Detailed Forecast (a "**Q1**") a quantity of Commercial Grade Captisol to be delivered during such Q1 (or within 100 days after the firm purchase order is placed) that is equal to or greater than the quantity of Commercial Grade Captisol Sage is obligated to purchase pursuant to the applicable Detailed Forecast (the difference between the quantity of Commercial Grade Captisol Sage is obligated to purchase in Q1 pursuant to the applicable Detailed Forecast and the amount of Commercial Grade Captisol that Sage actually orders for delivery in Q1 (or within 60 days after the firm purchase order is placed), the "**Shortfall**"), then Sage shall pay CyDex 60% of the purchase price hereunder for the Shortfall amount and shall not be entitled to receive delivery of such Shortfall amount. This Section 4.1(b) is based on the time stated for delivery in the original order, as opposed to the time delivery is actually made.

(c) **Compound Supplies**. For clarity, Sage or its Contract Manufacturers shall at their cost arrange for supplies of the Compound and for all other items and services needed in connection with the manufacture and commercial delivery of Licensed Products.

4.2 **Invoicing; Payment**. CyDex shall invoice Sage upon shipment of each order of Captisol. All invoices shall be sent to the address specified in the applicable purchase order, and each invoice shall state the purchase price for Captisol in such shipment, plus any insurance, taxes, shipping costs or other costs incidental to such purchase or shipment initially paid by CyDex but to be borne by Sage hereunder; *provided, however*, that if such insurance, taxes, shipping costs or other costs incidental to such purchase or shipment initially paid by CyDex but to be borne by Sage are not known at the time CyDex invoices Sage for the purchase price for the Captisol ordered by Sage, CyDex may invoice such costs at a later date.

4.3 **Payments**. All amounts due hereunder are stated in, and shall be paid in, U.S. dollars. Payment of CyDex's invoices shall be made within 30 days of Sage's receipt of such invoices except in the event of a good faith rejection of a shipment of Captisol in accordance with this Agreement, in which event payment shall be made promptly after such shipment is determined to comply with the requirements of this Agreement, if applicable. Unpaid balances shall accrue interest, from due date until paid, at a rate equal to the prime rate, as reported in *The Wall Street Journal*, Eastern U.S. Edition, on the date such payment is due (or the last previous publication date if such date is not a publication date), plus an additional 200 basis points. If any amount due hereunder or under the Commercial License Agreement and not subject to a reasonable, good-faith dispute by Sage remains outstanding for more than 45 days after its due date, CyDex may, in addition to any other rights or remedies it may have, refuse to ship Captisol hereunder except upon payment by Sage in advance.

4.4 **Taxes**. All amounts due hereunder exclude all applicable sales, use, and other taxes, and Sage will be responsible for payment of all such taxes (other than taxes based on CyDex's income), fees, duties, and charges, and any related penalties and interest, arising from the payment of amounts due under this Agreement. Sage shall make all payments to CyDex under this Agreement free and clear of, and without reduction for, any withholding taxes; any such taxes imposed on payments of amounts to CyDex hereunder will be Sage's sole responsibility. Sage shall indemnify and hold CyDex harmless from any and all such taxes and any actions brought against CyDex by any taxing authority with respect to such taxes. The parties agree to cooperate with one another and use reasonable efforts to avoid or reduce tax withholding or similar obligations in respect of payments made by Sage to CyDex under this Agreement. To the extent Sage is required to withhold taxes on any payment to CyDex, Sage shall pay the amounts of such taxes to the proper governmental authority in a timely manner and promptly transmit to CyDex official receipts issued by the appropriate taxing authority and/or an official tax certificate, or such other evidence as CyDex may reasonably request, to establish that such taxes have been paid. CyDex shall provide Sage any tax forms that may be reasonably necessary in order for Sage to not withhold tax or to withhold tax at a reduced rate under an applicable bilateral income tax treaty. CyDex shall use reasonable efforts to provide any such tax forms to Sage at least 30 days before the due date for any payment for which CyDex desires that Sage apply a reduced withholding rate. Each party shall provide the other with reasonable assistance to enable the recovery, as permitted by applicable law, of withholding taxes, value added taxes, or similar obligations resulting from payments made under this Agreement, such recovery to be for the benefit of the party bearing such withholding tax or value added tax.

5. Representations and Warranties.

5.1 **Limited Warranty**. CyDex warrants solely to Sage that all Captisol sold to Sage pursuant to this Agreement (a) shall conform to the respective Specifications (as applicable for Clinical Grade Captisol or Commercial Grade Captisol) in all respects at the time of delivery, (b) shall have been manufactured, stored, packaged and (to the extent CyDex is responsible for shipping) shipped in accordance with cGMP's and all other applicable laws and regulations, (c) shall be delivered with good and marketable title, free and clear of any liability, pledge, lien, restriction, claim, charge, security interest or other encumbrance and (d) shall have not less than 75% of the remaining shelf life on the date of delivery. CyDex's sole obligation, and Sage's sole and exclusive remedies, for any breach of such warranty, shall be (i) for a refund or credit equal to the purchase price paid with respect to such rejected shipment, or for CyDex to replace such rejected shipment at no additional cost to Sage; and (ii) indemnification pursuant to Section 6.1 (Indemnification by CyDex) hereof. The term "**cGMP's**" shall mean current good manufacturing practices for the methods to be used in, and the facilities and controls to be used for, the manufacture, preparation, packing and holding of pharmaceutical excipients, all as set forth from time to time by the U.S. Pharmacopoeia General Chapter <1078> Good Manufacturing Practices For Bulk Excipients and International Pharmaceutical Excipients Council's IPEC/PQG GMP Guide For Pharmaceutical Excipients, and any successors thereto.

5.2 **Representations and Warranties**. The provisions of Section 9.1 (Mutual Representations and Warranties) and Section 9.2 (CyDex Representation) of the Commercial License Agreement are incorporated herein by reference as if fully set forth herein, with references therein to "this Agreement" being understood to refer to this Supply Agreement rather than to the Commercial License Agreement.

5.3 **Disclaimer**. The warranties set forth in this Section 5 are provided in lieu of, and each party hereby disclaims, all other warranties, express and implied, relating to the subject matter of this Agreement or Captisol, including but not limited to the implied warranties of merchantability and fitness for a particular purpose, title and non-infringement of third party rights.

6. CONFIDENTIALITY.

6.1 **Definition**. Sage and CyDex each recognizes that, during the Term, it may be necessary for a party (the "**Disclosing Party**") to provide Confidential Information (as defined herein) to the other party (the "**Receiving Party**") that is highly valuable, the disclosure of which would be highly prejudicial to such party. The disclosure and use of Confidential Information will be governed by the provisions of this Section 6. Neither Sage nor CyDex shall use the other's Confidential Information except as expressly permitted in this Agreement. For purposes of this Agreement, "**Confidential Information**" means all information disclosed by the Disclosing Party to the Receiving Party and which is obviously Confidential Information, or which is designated in writing by the Disclosing Party as "Confidential" (or equivalent), or which when disclosed orally is declared to be confidential by the Disclosing Party and confirmed in a writing delivered to the Receiving Party within 30 days of such disclosure, including but not limited to product specifications, data, know-how, formulations, product concepts, sample materials, business and technical information, financial data, batch records, trade secrets, processes, techniques, algorithms, programs, designs, drawings, and any other information related to a party's present or future products, sales, suppliers, customers, employees, investors or business. Without limiting the generality of the foregoing, CyDex's Confidential Information includes all materials provided as part of the Captisol Data Package, and Sage's Confidential Information includes Sage Patents and Sage Know-How.

6.2 **Obligation**. CyDex and Sage agree that they will disclose Confidential Information received from the other to its (or its respective parent's) own officers, employees, consultants and agents only if and to the extent necessary to carry out their respective responsibilities under this Agreement or in accordance with the exercise of their rights under this Agreement, and such disclosure shall be limited to the maximum extent possible consistent with such responsibilities and rights. Neither party shall disclose Confidential Information of the other to any Third Party without the other's prior written consent, and any such disclosure to a Third Party shall be pursuant to the terms of a non-disclosure agreement no less restrictive than this Section 6. The party which disclosed Confidential Information of the other to any Third Party shall be responsible and liable for any disclosure or use by such Third Party (or its disclosees) which would have violated this Agreement if committed by the party itself. Neither party shall use Confidential Information of the other except as expressly allowed by and for the purposes of this Agreement. Each party shall take such action to preserve the confidentiality of each other's Confidential Information as it would customarily take to preserve the confidentiality of its own Confidential Information (but in no event less than a reasonable standard of care). Unless otherwise specified in this Agreement and subject to terms and conditions in this Agreement, if so requested by the other party a party shall promptly return all relevant records and materials in its possession or control containing or embodying the other party's Confidential Information (including all copies and extracts of documents); *provided, however*, that each party may retain one archival copy (and such electronic copies that exist as part of the party's computer systems, network storage systems and electronic backup systems) of such records and materials solely to be able to monitor its obligations that survive under this Agreement.

6.3 **Exceptions**. The use and non-disclosure obligations set forth in this Section 6 shall not apply to any Confidential Information, or portion thereof, that the Receiving Party can demonstrate by appropriate documentation:

(i) at the time of disclosure is in the public domain;

(ii) after disclosure, becomes part of the public domain, by publication or otherwise, through no fault of the Receiving Party or its disclosees;

(iii) is independently developed by Receiving Party personnel with no reference or access to the Confidential Information; or

(iv) is made available to the Receiving Party by an independent third party without obligation of confidentiality; *provided, however*, that to the Receiving Party's knowledge, such information was not obtained by said third party, directly or indirectly, from the Disclosing Party hereunder.

In addition, the Receiving Party may disclose information that is required to be disclosed by law, by a valid order of a court or by order or regulation of a governmental agency including but not limited to, regulations of the Securities and Exchange Commission, or in the course of litigation; *provided* that in all cases the Receiving Party shall give the other party prompt notice of the pending disclosure and make a reasonable effort to obtain, or to assist the Disclosing Party in obtaining, a protective order or confidential- treatment order preventing or limiting (to the greatest possible extent and for the longest possible period) the disclosure and/or requiring that the Confidential Information so disclosed be used only for the purposes for which the law or regulation required, or for which the order was issued.

6.4 **Injunction**. Each party agrees that should it breach or threaten to breach any provisions of this Section 6, the Disclosing Party will suffer irreparable damages and its remedy at law will be inadequate. Upon any breach or threatened breach by the Receiving Party of this Section 6, the Disclosing Party shall be entitled to seek temporary, preliminary and/or permanent injunctive relief in addition to any other remedy which it may have, without need to post any bond or security, in addition to any and all other legal and equitable rights and remedies available to the Disclosing Party.

6.5 **Third Party Information**. The parties acknowledge that the defined term "Confidential Information" shall include not only a disclosing party's own Confidential Information but also Confidential Information of a Third Party which is in the possession of a disclosing party.

Sage acknowledges that CyDex's Confidential Information includes information developed by Pfizer that is confidential to both CyDex and Pfizer. In so far as Confidential Information of Pfizer is disclosed, Pfizer is a third-party beneficiary of this Section 6 of this Agreement and may enforce it or seek remedies pursuant to it in accordance with its terms.

Sage agrees not to disclose to CyDex any Confidential Information of a Third Party which is in the possession of Sage, unless CyDex has given an express prior written consent (which specifies the owner of such Confidential Information) to receive such particular Confidential Information. If CyDex refuses to provide such consent, then any obligation of Sage to provide such information to CyDex under this Agreement shall be deemed waived by CyDex.

6.6 **Public Announcements**. The parties will mutually agree on a press release to be issued upon execution of this Agreement or reasonably soon thereafter. Neither party shall make any subsequent public announcement concerning this Agreement or the terms hereof not previously made public without the prior written approval of the other party with regard to the form, content, and precise timing of such announcement, except as may be required to be made by either party in order to comply with applicable Law, regulations, court orders, or tax, securities filings, financing arrangements, acquisitions, or sublicenses. Such consent shall not be unreasonably withheld or delayed by such other party. Before any such public announcement, the party wishing to make the announcement will submit a draft of the proposed announcement to the other party in sufficient time to enable such other party to consider and comment thereon.

7. Indemnification.

7.1 **By CyDex**. CyDex shall defend, indemnify and hold Sage and its Affiliates and Sublicensees, and each of their respective directors, officers, agents and employees, harmless from and against any and all losses, judgments, damages, liabilities, settlements, penalties, fines, costs and expenses (including the reasonable costs and expenses of attorneys and other professionals) (collectively "**Losses**") incurred by Sage as a result of any claim, demand, action or other proceeding (each, a "**Claim**") by a Third Party, to the extent such Losses arise out of: (a) the manufacture, use, handling, promotion, marketing, distribution, importation, sale or offering for sale of Captisol by CyDex and its Affiliates (including without limitation, the sale of Captisol by CyDex to Sage hereunder); (b) infringement of any person's intellectual property rights in Captisol *per se*; (c) CyDex's breach of this Agreement, including without limitation any of its representations and warranties set forth in Sections 5.1 and 5.2 and (d) CyDex's negligence or misconduct.

7.2 **By Sage**. Sage shall defend, indemnify and hold CyDex and its Affiliates, and each of their respective directors, officers, agents and employees, harmless from and against any and all Losses incurred by CyDex as a result of any Claim by a Third Party, to the extent such Losses arise out of: (a) the manufacture, use, handling, promotion, marketing, distribution, importation, sale or offering for sale of the Licensed Product by Sage, its Affiliates and Sublicensees; (b) any acts or omissions by Sage in connection with pre-clinical studies and clinical studies of actual or potential Licensed Products; (c) infringement of any person's intellectual property rights in connection with the subject matter of this Agreement (other than intellectual property rights in Captisol *per se*); (d) Sage's breach of this Agreement, including without limitation any of its representations and warranties set forth in Section 5.2 and (e) Sage's negligence or misconduct.

7.3 **Expenses**. As the parties intend complete indemnification, all costs and expenses of enforcing any provision of this Section 7 shall also be reimbursed by the Indemnifying Party.

7.4 **Procedure**.

(a) The person intending to claim indemnification under this Section 7 (an "**Indemnified Party**") shall promptly notify the other party (the "**Indemnifying Party**") of any Claim in respect of which the Indemnified Party intends to claim such indemnification, and a reasonable explanation of the basis for the Claim and the amount of alleged Losses to the extent of the facts then known by the Indemnified Party. (Notwithstanding the foregoing, no delay or deficiency on the part of the Indemnified Party in so notifying the Indemnifying Party will relieve the Indemnifying Party of any liability or obligation under this Agreement except to the extent the Indemnifying Party has suffered actual prejudice directly caused by the delay or other deficiency.) The Indemnifying Party shall assume the defense thereof whether or not such Claim is rightfully brought; *provided, however*, that if the Indemnifying Party assumes the defense, the Indemnified Party shall have the right to employ counsel separate from counsel employed by the Indemnifying Party in any such action and to participate in the defense thereof, but the fees and expenses of such counsel employed by the Indemnified Party shall be at the sole cost and expense of the Indemnified Party unless the Indemnifying Party consents to the retention of such counsel or unless the named parties to any action or proceeding include both the Indemnifying Party and the Indemnified Party and a representation of both the Indemnifying Party and the Indemnified Party by the same counsel would be inappropriate due to the actual or potential differing interests between them. And *provided further* that, if the Indemnifying Party shall fail to assume the defense of

and reasonably defend such Claim, the Indemnified Party shall have the right to retain or assume control of such defense and the Indemnifying Party shall pay (as incurred and on demand) the fees and expenses of counsel retained by the Indemnified Party.

(b) The Indemnifying Party shall not be liable for the indemnification of any Claim settled (or resolved by consent to the entry of judgment) without the written consent of the Indemnifying Party. Also, if the Indemnifying Party shall control the defense of any such Claim, the Indemnifying Party shall have the right to settle such Claim; *provided*, that the Indemnifying Party shall obtain the prior written consent (which shall not be unreasonably withheld or delayed) of the Indemnified Party before entering into any settlement of (or resolving by consent to the entry of judgment upon) such Claim unless (A) there is no finding or admission of any violation of law or any violation of the rights of any Person by an Indemnified Party, no requirement that the Indemnified Party admit fault or culpability, and no adverse effect on any other claims that may be made by or against the Indemnified Party and (B) the sole relief provided is monetary damages that are paid in full by the Indemnifying Party and such settlement does not require the Indemnified Party to take (or refrain from taking) any action.

(c) Regardless of who controls the defense, the other party hereto shall reasonably cooperate in the defense as may be requested. Without limitation, the Indemnified Party, and its directors, officers, advisers, agents and employees, shall cooperate fully with the Indemnifying Party and its legal representatives in the investigations of any Claim.

8. Limitation of Liability.

EXCEPT FOR DAMAGES FOR WHICH A PARTY IS RESPONSIBLE PURSUANT TO ITS INDEMNIFICATION OBLIGATIONS SET FORTH IN SECTION 7 ABOVE, EACH PARTY SPECIFICALLY DISCLAIMS ALL LIABILITY FOR AND SHALL IN NO EVENT BE LIABLE FOR ANY INCIDENTAL, SPECIAL, INDIRECT OR CONSEQUENTIAL DAMAGES, EXPENSES, LOST PROFITS, LOST SAVINGS, INTERRUPTIONS OF BUSINESS OR OTHER DAMAGES OF ANY KIND OR CHARACTER WHATSOEVER ARISING OUT OF OR RELATED TO THIS AGREEMENT OR RESULTING FROM THE MANUFACTURE, HANDLING, MARKETING, SALE, DISTRIBUTION OR USE OF LICENSED PRODUCT OR USE (PURSUANT TO OR IN CONNECTION WITH THE RIGHTS GRANTED UNDER THIS AGREEMENT) OF THE LICENSED PATENTS AND CAPTISOL DATA PACKAGE, REGARDLESS OF THE FORM OF ACTION, WHETHER IN CONTRACT, TORT, STRICT LIABILITY OR OTHERWISE, EVEN IF SUCH PARTY WAS ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. EXCEPT WITH RESPECT TO THE INDEMNIFICATION SPECIFICALLY PROVIDED IN SECTION 7 ABOVE, IN NO EVENT SHALL EITHER PARTY'S TOTAL AGGREGATE LIABILITY FOR ALL CLAIMS ARISING OUT OF OR RELATED TO THIS SUPPLY AGREEMENT, OR RESULTING FROM THE MANUFACTURE, HANDLING, MARKETING, SALE, DISTRIBUTION OR USE OF LICENSED PRODUCT OR USE OF THE LICENSED PATENTS AND CAPTISOL DATA PACKAGE PURSUANT TO OR IN CONNECTION WITH THE RIGHTS GRANTED UNDER THIS AGREEMENT, EXCEED THE GREATER OF (I) $250,000 AND (II) THE TOTAL AMOUNTS ACTUALLY PAID BY SAGE TO CYDEX UNDER THIS AGREEMENT AS OF THE DATE SUCH CLAIMS ARISE; *PROVIDED*, THAT THE FOREGOING LIMITATIONS SHALL NOT LIMIT CYDEX'S RIGHT TO TAKE ACTION TO ENFORCE THIS SUPPLY AGREEMENT TO COLLECT AMOUNTS THAT ARE PROPERLY DUE AND OWING UNDER ARTICLE 4 HEREOF. NO ACTION, REGARDLESS OF FORM, ARISING OUT OF OR RELATED TO THIS AGREEMENT MAY BE BROUGHT BY EITHER PARTY MORE THAN TWO YEARS AFTER SUCH PARTY HAS KNOWLEDGE OF THE LEGAL AND FACTUAL BASIS FOR SUCH CAUSE OF ACTION OR AFTER EXPIRATION OF THE APPLICABLE STATUTORY LIMITATIONS PERIOD, WHICHEVER IS SOONER. FOR AVOIDANCE OF DOUBT, THE PARTIES' RESPECTIVE RIGHTS AND OBLIGATIONS WITH RESPECT TO ANY LIABILITY THAT MAY ACCRUE UNDER THE LICENSE AGREEMENT, ANY COMMERCIAL LICENSE AGREEMENT OR ANY SUPPLY AGREEMENT (OTHER THAN THIS AGREEMENT) OR IN CONNECTION WITH ACTIVITIES CONDUCTED PURSUANT TO OR CONTEMPLATED BY ANY SUCH AGREEMENTS SHALL BE DETERMINED PURSUANT TO THE TERMS OF THOSE AGREEMENTS AND NOT BY THE TERMS AND CONDITIONS SET FORTH IN THIS AGREEMENT.

9. Term and Termination.

9.1 **Term**. The term of this Agreement (the "**Term**") shall commence on the Effective Date and shall continue in effect unless and until terminated as set forth herein.

9.2 **Termination for Breach**.

(a) **Notice**. If either party believes that the other is in material breach of this Agreement, then the party holding such belief (the "**Non-breaching Party**") may deliver notice of such breach to the other party (the "**Notified Party**"). The Notified Party shall have […***…] days to cure such breach to the extent involving non-payment of amounts due hereunder, and […***…] days to either cure such breach for all other material breaches, or, if cure of such breach other than nonpayment cannot reasonably be effected within such […***…] day period, to deliver to the Non-breaching Party a plan reasonably calculated to cure such breach within a timeframe that is reasonably prompt in light of the circumstances then prevailing but in no event in excess of an additional […***…] day period. Following delivery of such a plan, the Notified Party shall diligently carry out the plan and cure the breach and the cure period shall be

extended by the time period provided in such plan but in no event to exceed […***…] days from the date of any initial breach notice delivered under this Section 9.2.

(b) Failure to Cure. If the Notified Party fails to cure a material breach of this Agreement as provided for in Section 9.2, then the Non-Breaching Party may terminate this Agreement upon written notice to the Notified Party.

9.3 **Termination with Commercial License Agreement**. This Agreement shall automatically terminate upon the termination, for whatever reason, of the Commercial License Agreement.

9.4 **Survival**. Notwithstanding any other provisions of this Agreement, any liability or obligation of either party to the other for acts or omissions before the termination of this Agreement shall survive the termination of this Agreement, including Sage's obligation to pay CyDex sums due in respect of Captisol shipped before termination of this Agreement. And, such termination shall not relieve either party from obligations that are expressly indicated to survive termination of this Agreement. Sections 2.2 (Purchase Commitment) (final two sentences only), 3.4 (Modified Specifications) (final two sentences only), 3.6 (Control; Acceptance and Rejection), 4.1(b) (Shortfall Reimbursement (Take or Pay)), 4.3 (Payments), 4.4 (Taxes), 5.3 (Disclaimer), 6 (Confidentiality), 7 (Indemnification), 8 (Limitation of Liability), 9.4 (Survival), and 10 (General Provisions) shall survive termination of this Agreement. […***…].

10. General Provisions.

10.1 **Non-Solicitation**. During the Evaluation Period and for a period of one year thereafter, neither party shall solicit any employee of the other party to terminate his or her employment with such other party or to breach any other obligation to such other party. This section is not meant to encompass general solicitations such as may be found in newspaper advertisements and the like.

10.2 **Relationship of Parties**. Each of the parties hereto is an independent contractor and nothing in this Agreement is intended or shall be deemed to constitute a partnership, agency, employer-employee or joint venture relationship between the parties. No party shall have the right to, and each party agrees not to purport to, incur any debts or make any commitments or contracts for the other.

10.3 **Compliance with Law**. Each of the parties shall comply with all applicable international, federal, state and local laws, rules and regulations, including, but not limited to, import/export restrictions, laws, rules and regulations governing product quality and safety and patent, copyright and trade secret protection.

10.4 **Arbitration**.

(a) **Procedure**. Any and all disputes or controversies arising out of or relating to this Agreement shall be exclusively and finally resolved by binding arbitration in accordance with the commercial arbitration rules of the American Arbitration Association then in effect, in Boston, Massachusetts. The arbitration shall be conducted by an arbitrator reasonably knowledgeable about the pharmaceutical industry and acceptable to CyDex and Sage. If CyDex and Sage cannot agree on a single arbitrator within 30 days after a demand for arbitration has been made, CyDex shall appoint an arbitrator, Sage shall appoint an arbitrator, the two arbitrators shall appoint a third arbitrator, and the three arbitrators shall hear and decide the issue in controversy. If either party fails to appoint an arbitrator within 45 days after service of the demand for arbitration, then the arbitrator appointed by the other party shall arbitrate any controversy in accordance with this Section 10.4(a). Except as to the selection of arbitrators, the arbitration proceedings shall be conducted promptly and in accordance with the rules of the American Arbitration Association then in effect. The expenses of any arbitration, including the reasonable attorney fees of the prevailing party, shall be borne by the party deemed to be at fault or on a pro-rata basis should the arbitration conclude in a finding of mutual fault.

(b) **Confidentiality of Proceedings**. All arbitration proceedings hereunder shall be confidential and the arbitrator(s) shall issue appropriate protective orders to safeguard each party's Confidential Information. Except as required by law, no party shall make (or instruct the arbitrator(s) to make) any public announcement with respect to the proceedings or decision of the arbitrator(s) without prior written consent of the other party.

(c) **Interim Equitable Relief**. Notwithstanding Section 10.4(a), but subject to the limitations set forth in Article 8, each party shall not be precluded from seeking equitable relief (including but not limited to interim injunctive relief) in any court having jurisdiction to protect its interests.

(d) **Binding Effect**. The provisions of this Section 10.4 shall survive any termination of this Agreement, and shall be severable and binding on the parties hereto, notwithstanding that any other provision of this Agreement may be held or declared to be invalid, illegal or unenforceable.

10.5 **Costs and Expenses**. Except as otherwise expressly provided in this Agreement, each party shall bear all costs and expenses associated with the performance of such party's obligations under this Agreement.

10.6 **Force Majeure**. Neither party shall be liable for failure to perform, or delay in the performance of, its obligations under this Agreement (other than payment obligations) when such failure or delay is caused by an event of force majeure. For purposes of this Agreement, an event of force majeure means any event or circumstance beyond the reasonable control of the affected party, including but not limited to, war, insurrection, riot, fire, flood or other unusual weather condition, explosion, act of God, peril of the sea, strike, lockout or other industrial disturbance, sabotage, accident, embargo, breakage of machinery or apparatus, injunction, act of governmental authority, compliance with governmental order or national defense requirements, or inability to obtain fuel, power, raw materials, labor or transportation facilities. If, due to any event of force majeure, either party shall be unable to fulfill its obligations under this Agreement (other than payment obligations), the affected party shall immediately notify the other party of such inability and of the period during which such inability is expected to continue and the time for performance shall be extended for a number of days equal to the duration of the force majeure.

10.7 **Notices**. Any notice, request, or communication under this Agreement shall be effective only if it is in writing and personally delivered; sent by certified mail, postage pre-paid; facsimile with receipt confirmed; or by nationally recognized overnight courier with signature required, addressed to the parties at the addresses stated below or such other persons and/or addresses as shall be furnished in writing by any party in accordance with this Section 10.7. Unless otherwise provided, all notices shall be sent:

If to CyDex, to:

CyDex Pharmaceuticals, Inc.
11119 North Torrey Pines Road, Suite 200
La Jolla, CA 92037
Attention: President
Fax: (858) 550-7272

With a copy to: General Counsel
Ligand Pharmaceuticals Incorporated
11085 North Torrey Pines Road, Suite 200
La Jolla, CA 92037
Fax: (858)550-7272

If to Sage, to:

Sage Therapeutics, Inc.
29 Newbury Street, Suite 301
Boston, MA 02116
Attention: President
Fax: (617) 859-2891

With a copy to:
Goodwin Procter LLP
Exchange Place
Boston, MA 02109
Attention: Christopher Denn
Fax: (617)523-1231

If sent by facsimile transmission, the date of transmission shall be deemed to be the date on which such notice, request or communication was given. If sent by overnight courier, the next business day after the date of deposit with such courier shall be deemed to be the date on which such notice, request or communication was given. If sent by certified mail, the third business day after the date of mailing shall be deemed the date on which such notice, request or communication was given.

10.8 **Use of Name; Publicity**. No party shall use the name, trademark, trade name or logo of the other party, its Affiliates or their respective employee(s) in any publicity, promotion, news release or public disclosure relating to this Agreement or its subject matter, without the prior express written permission of the other party, except as may be required by law or the rules of NASDAQ. The parties agree that a party may disclose this Agreement's existence and terms, and material developments or material information generated under this Agreement, in (i) securities filings with the Securities and Exchange Commission (or equivalent foreign agency) to the extent required by law, or (ii) under conditions of confidentiality/nonuse in connection with investment and similar corporate transactions. Notwithstanding the above, once a public announcement has been made, either party shall be free to disclose to third parties any information contained in said public announcement. In the event of a required public announcement, the party making such announcement shall provide the other party with a copy of the proposed text before such announcement sufficiently in advance of the

scheduled release of such announcement to afford such other party a reasonable opportunity to review and comment upon the proposed text and the timing of such disclosure.

10.9 **Governing Law**. This Agreement shall be governed by and construed in accordance with the internal laws of the State of California (without giving effect to any conflicts of law principles that require the application of the law of a different state).

10.10 **Entire Agreement; Amendment**. The Supply Agreement and all Exhibits attached hereto contain the entire agreement of the parties relating to the subject matter hereof and thereof and supersede any and all prior or contemporaneous agreements, written or oral, between CyDex (and/or any of its Affiliates) and Sage (and/or any of its Affiliates) relating to the subject matter hereof and thereof; *provided*, that any confidentiality/nonuse provisions of any prior agreement are not superseded and will remain in effect in addition to the confidentiality/nonuse provisions hereof. This Agreement cannot be amended except by way of an express writing signed by both parties.

10.11 **Binding Effect**. This Agreement shall be binding upon, and the rights and obligations hereof shall apply to, CyDex and Sage and any successor(s) and permitted assigns. The name of a party appearing herein shall be deemed to include the names of such party's successors and permitted assigns to the extent necessary to carry out the intent of this Agreement.

10.12 **Waiver**. The rights of either party under this Agreement may be exercised from time to time, singularly or in combination, and the exercise of one or more such rights shall not be deemed to be a waiver of any one or more of the others. No waiver of any breach of a term, provision or condition of this Agreement shall be deemed to have been made by either party unless such waiver is addressed in writing and signed by an authorized representative of that party. The failure of either party to insist upon the strict performance of any of the terms, provisions or conditions of this Agreement, or to exercise any option contained in this Agreement, shall not be construed as a waiver or relinquishment for the future of any such term, provision, condition or option or the waiver or relinquishment of any other term, provision, condition or option.

10.13 **Severability**. If any provision of this Agreement is determined by a final and binding court or arbitration judgment to be invalid, illegal or unenforceable to any extent, such provision shall not be not affected or impaired up to the limits of such invalidity, illegality or unenforceability; the validity, legality and enforceability of the remaining provisions of this Agreement shall not be affected or impaired in any way; and the parties agree to negotiate in good faith to replace such invalid, illegal and unenforceable provision (or portion of provision) with a valid, legal and enforceable provision that achieves, to the greatest lawful extent under this Agreement, the economic, business and other purposes of such invalid, illegal or unenforceable provision (or portion of provision). This Agreement shall not be invalidated by any future determination that any or all of the Licensed Patents have expired or been invalidated.

10.14 **Assignment**. Sage may not assign its rights or delegate its obligations under this Agreement, in whole or in part, by operation of law or otherwise, to any third party without the prior written consent of CyDex, which consent shall not be unreasonably withheld. Notwithstanding the foregoing, Sage may assign its rights and delegate its obligations under this Agreement to an Affiliate or to a third party successor, whether by way of merger, sale of all or substantially all of its assets, sale of stock or otherwise, without CyDex's prior written consent. As a condition to any permitted assignment hereunder, the assignor must guarantee the performance of any assignee to the terms and obligations of this Agreement. Any assignment by Sage not in accordance with this Section 10.14 shall be void. CyDex has the right to assign its rights or delegate its obligations under this Agreement, in whole or in part, by operation of law or otherwise, to any third party, without any requirement for consent of Sage; *provided* that CyDex also assigns all of its right, title and interest in all assets, including without limitation, intellectual property rights, pertaining to its Captisol business to the same third party contemporaneous with the assignment of this Agreement.

10.15 **Third Party Beneficiaries**. Except for the rights of Indemnified Parties pursuant to Section 7 hereof, and subject to Section 6.5 hereof, the terms and provisions of this Agreement are intended solely for the benefit of each party hereto and their respective successors or permitted assigns and it is not the intention of the parties to confer third-party beneficiary rights upon any other person, including without limitation Sublicensees. The enforcement of any obligation of CyDex under this Agreement shall only be pursued by Sage or such Indemnified Party, and not Sublicensees.

10.16 **Remedies Cumulative**. Subject to the limitations set forth in Article 8 and Section 10.4, any enumeration of a party's rights and remedies in this Agreement is not intended to be exclusive, and a party's rights and remedies are intended to be cumulative to the extent permitted by law and include any rights and remedies authorized in law or in equity.

10.17 **Headings**. The descriptive headings of this Agreement are for convenience only, and shall be of no force or effect in construing or interpreting any of the provisions of this Agreement.

10.18 **Interpretation**. The language used in this Agreement is the language chosen by the parties to express their mutual intent, and no provision of this Agreement will be interpreted for or against any party because that party or its attorney drafted the provision.

10.19 **Counterparts**. This Agreement may be executed in counterparts, each of which shall constitute an original document, but both of which shall constitute one and the same instrument.

[Remainder of this page left blank intentionally]

IN WITNESS WHEREOF, the parties have executed this Supply Agreement as of the Effective Date.

CYDEX PHARMACEUTICALS, INC.

By: /s/ Charles Berkman

Name: Charles Berkman

Title: VP and Secretary

SAGE THERAPEUTICS, INC.

By: /s/ Kiran Reddy

Name: Kiran Reddy

Title: Chief Business Officer

AMENDMENT TO SUPPLY AGREEMENT

THIS AMENDMENT TO SUPPLY AGREEMENT (this "**Amendment**") is made this "21th day of August, 2013 (the **"Amendment Effective Date")** between **CYDEX PHARMACEUTICALS, INC.**, a Delaware corporation **("CyDex")** and **SAGE THERAPEUTICS, INC.**, a Delaware corporation **("Sage")**.

1. This Amendment amends the Supply Agreement dated December 13, 2012 between CyDex and Sage (the **"Agreement")**.

2. On page 1 of the Agreement, the first recital is hereby amended and replaced in its entirety with the following:

WHEREAS, CyDex and Sage are also parties to that certain Commercial License Agreement of December 13, 2012 (the **"Old Agreement")** which the parties are terminating as of the Amendment Effective Date, that Commercial License Agreement of August 21, 2013 (the **"Commercial License Agreement")** and that certain License Agreement dated October 13, 2011 (the **"License Agreement")**; and.

3. Except as expressly set forth herein, the Agreement remains unchanged and in full force and effect.

IN WITNESS WHEREOF, the parties have executed this Agreement to Supply Agreement as of the date first above written.

CYDEX PHARMACEUTICALS, INC.

By: /s/ Charles Berkman
Name: Charles Berkman
Title: VP and Secretary

SAGE THERAPEUTICS, INC.

By: /s/ Kimi Iguchi
Name: Kimi Iguchi
Title: CFO

August 21, 2013

AMENDMENT NO. 2 TO SUPPLY AGREEMENT

THIS AMENDMENT NO. 2 TO SUPPLY AGREEMENT (this "**Amendment**") is made this 30th day of April, 2014 (the "**Amendment Effective Date**") between:

CYDEX PHARMACEUTICALS, INC., a Delaware corporation ("**CyDex**"); and

SAGE THERAPEUTICS INC., a Delaware corporation ("**Sage**").

RECITALS

WHEREAS, CyDex and Sage entered into a Supply Agreement as of December 13, 2012, as amended on August 21, 2013, (the "**Agreement**");

WHEREAS, CyDex and Sage wish to amend the Agreement in accordance with Section 10.10 thereof;

NOW, **THEREFORE**, in consideration of the following mutual promises and other good and valuable consideration, the receipt and sufficiency of which are acknowledged, the parties, intending to be legally bound, agree as follows:

1. DEFINITIONS. All terms used, but not defined, in this Amendment shall have the meaning set forth in the Agreement.

2. PURCHASE VOLUME LIMITATIONS. Section 3.2(c) of the Agreement is hereby amended to read as follows:

(c) Detailed Forecast Variances.

(i) Until the […***…] anniversary of the first Commercial Launch Date, each updated Detailed Forecast may modify the amount of Commercial Grade Captisol estimated in the previous Detailed Forecast and the corresponding delivery timing in accordance with the following limitations (the "**Purchase Volume Limitations**"):

(1) for the first through third calendar months covered by such updated Detailed Forecast, no change in excess of a […***…]% volume increase or decrease per month from the prior Detailed Forecast may be made without the prior express written consent of CyDex; and

(2) for the fourth through sixth calendar months covered by such updated Detailed Forecast, no change in excess of a […***…]% volume increase or decrease per month from the prior Detailed Forecast may be made without the prior express written consent of CyDex.

(3) for the third calendar quarter covered by such updated Detailed Forecast, no change in excess of a […***…]% volume increase or decrease from the prior Forecast may be made without the prior express written consent of CyDex; and

(4) for the fourth calendar quarter covered by such updated Detailed Forecast, no change in excess of a […***…]% volume increase or decrease from the prior Forecast may be made without the prior express written consent of CyDex.

(ii) After the […***…] anniversary of the Commercial Launch Date, the Purchase Volume Limitations shall be deemed modified as follows:

(1) for the first calendar quarter covered by such updated Detailed Forecast, no change in excess of a […***…]% volume increase or decrease per month from the prior Detailed Forecast may be made without the prior express written consent of CyDex;

(2) for the second calendar quarter covered by such updated Detailed Forecast, no change in excess of a […***…]% volume increase or decrease from the prior Detailed Forecast may be made without the prior express written consent of CyDex;

(3) for the third calendar quarter covered by such updated Detailed Forecast, no change in excess of a […***…]% volume increase or decrease from the prior Forecast may be made without the prior express written consent of CyDex; and

(4) for the fourth calendar quarter covered by such updated Detailed Forecast, no change in excess of a […***…]% volume increase or decrease from the prior Forecast may be made without the prior express written consent of CyDex.

3. PRICING.

3.1 The first sentence of section 4.1(a) is hereby amended to read:

CyDex reserves the right to increase such purchase prices set forth in Exhibit A on each January 1 during the Term, upon no less than 180 days' written notice to Sage, by a percentage equal to the aggregate percentage increase, if any, in the […***…] as reported by the Bureau of Labor Statistics, U.S. Department of Labor, for the 12-month period ending March 31 of the prior year (or any applicable successor index); provided, however, that […***…].

3.2 Exhibit A of the Agreement is hereby amended to read:

[…***…]

Portion of Cumulative Amount of Commercial Grade Captisol Purchased by Sage	**Price per kilogram**
[…***…]	$[…***…]
[…***…]	$[…***…]
[…***…]	$[…***…]
[…***…]	$[…***…]
[…***…]	$[…***…]

[…***…]

4. NOTICES. Sage's address is hereby revised to read:

If to Sage, to:
Sage Therapeutics, Inc.
215 First Street
Cambridge, Massachusetts 02142
Attention: President
Fax: (617) 299-8379

5. INTERPRETATION. The following sentence is added to the end of Section 10.18 of the Agreement:

Except as the context otherwise requires, (a) the word "including" or correlatives thereof, means "including without limitation," and (b) the word "or" means "and/or."

6. ENTIRE AGREEMENT/AMENDMENTS. Except as amended by this Amendment, the Agreement shall remain in full force and effect. After the Amendment Effective Date, every reference in the Agreement to the "Agreement" shall mean the Agreement as amended by this Amendment.

7. Counterparts. This Amendment may be executed in counterparts, each of which shall constitute an original document, but both of which shall constitute one and the same instrument.

[Remainder of this page left blank intentionally]

IN WITNESS WHEREOF, the parties have executed this Amendment No. 2 to Supply Agreement as of the Amendment Effective Date.

CYDEX PHARMACEUTICALS, INC.

By: /s/ Charles Berkman
Name: Charles Berkman
Title: VP and Secretary

SAGE THERAPEUTICS, INC.

By: /s/ Jeffrey Jonas
Name: Jeffrey Jonas
Title: CEO

EXHIBIT 10.3

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. […***…] denotes omissions.

AMENDMENT NO. 3 TO SUPPLY AGREEMENT

THIS AMENDMENT NO. 3 TO SUPPLY AGREEMENT (this "**Amendment**") is entered into on this 25th day of September, 2015 (the "**2015 Date**"), with retroactive effect to April 30, 2014 (the "**Amendment Effective Date**") between:

CYDEX PHARMACEUTICALS, INC., a Delaware corporation ("**CyDex**"); and

SAGE THERAPEUTICS, INC., a Delaware corporation ("**Sage**").

RECITALS

WHEREAS, CyDex and Sage entered into a Supply Agreement as of December 13, 2012, as amended on August 21, 2013 and April 30, 2014 (as so amended, the "**Agreement**" or, in certain contexts, this "**Supply Agreement**");

WHEREAS, CyDex and Sage wish to amend the Agreement in accordance with Section 10.10 thereof; and

WHEREAS, CyDex and Sage were also parties to a Commercial License Agreement dated December 13, 2012 (the "**Original Agreement**") and are parties to a Commercial License Agreement dated August 21, 2013, as amended on April 30, 2014, and as now further amended and restated by an Amended and Restated Commercial License Agreement, dated on the 2015 Date with retroactive effect to April 30, 2014 (the "**2013-2015 Agreement**"; the Original Agreement and the 2013-2015 Agreement are hereinafter referred to together in the singular (but each with regard to its respective applicable term) as the "**Commercial License Agreement**").

NOW, THEREFORE, in consideration of the following mutual promises and other good and valuable consideration, the receipt and sufficiency of which are acknowledged, the parties, intending to be legally bound, agree as follows:

1. DEFINITIONS. All terms used, but not defined, in this Amendment shall have the meaning set forth in the Agreement or (if not defined in the Agreement) in the Commercial License Agreement.

2. LICENSED PRODUCTS. The parties agree and acknowledge that, except as expressly set forth in the Agreement, as hereby amended, (a) the Agreement, as hereby amended, shall apply to any and all of the Licensed Products, (b) the Agreement, as hereby amended, shall permit Sage to order and purchase Clinical Grade Captisol and Commercial Grade Captisol for use in the formulation of any of the Licensed Products and (c) such Captisol orders and purchases shall be aggregated for purposes of the Agreement, including Section 3.2(c), Section 3.5(b) and Exhibit A of the Agreement.

3. COMMERCIAL LAUNCH DATE. The reference to "Commercial Launch Date" in Sections 3.2 and 4.1(a) of the Agreement shall mean the "first Commercial Launch Date of any Licensed Product" (*e.g.*, if the Commercial Launch Date of an Allo Licensed Product is earlier than the Commercial Launch Date of the SAGE-689 Licensed Products, then the Commercial Launch Date of such Allo Licensed Product will be used to measure the timeframes in Sections 3.2 and 4.1(a) of the Agreement).

4. SUPPLY AND PURCHASE OBLIGATIONS.

4.1 Section 2.2 of the Agreement is amended to read:

"**2.2 Purchase Commitment**. Subject to the provisions of this Agreement and during the Term of this Agreement, Sage agrees that Sage and its Affiliates and Sublicensees and their Contract Manufacturers shall purchase exclusively from CyDex 100% of their requirements for Captisol for use in the preparation, formulation and production of Licensed Products. Sage shall not itself, and will not permit its Affiliates and Sublicensees to, make, sell or offer to sell bulk Captisol during the Term of this Agreement (provided, that Sage and its Affiliates, Sublicensees and Contract Manufacturers may re-sell any Captisol purchased pursuant to this Agreement to Sage's Affiliates or Sublicensees for or as incorporated into the Licensed Products in and for the Field), and shall not use any Captisol purchased pursuant to this Agreement except in connection with the Licensed Products in and for the Field; provided, however, that Sage may transfer any Captisol purchased pursuant to this Agreement to any Sublicensee, or any researcher or research

institution solely for research or development of a Licensed Product, including for any investigator-initiated study of any Licensed Product. This Agreement and the Commercial License Agreement do not grant Sage, its Affiliates or Sublicensees or their Contract Manufacturers the right to manufacture (or have manufactured on their behalf) Captisol, without CyDex's prior written consent. Before entering into an agreement with any Sublicensees or Contract Manufacturers, Sage shall advise such Sublicensee or Contract Manufacturer of the foregoing restrictions and shall obtain such Sublicensee's or Contract Manufacturer's written agreement to observe and be bound thereby. Sage shall be responsible and liable for any actions by its Affiliates, Sublicensees and Contract Manufacturers which would have violated this Section 2.2 if committed by Sage itself."

4.2 Section 2.3 of the Agreement is hereby amended by adding the following sentence to the end of such Section; "CyDex shall supply only Branded Captisol to Sage, its Affiliates and Sublicensees and their Contract Manufacturers to fulfill the orders for Captisol placed with CyDex hereunder."

4.3 The following sentence is added to the end of Section 4.1(b) of the Agreement: "This Section 4.1(b) shall not apply with respect to the period of any Supply Interruption or (to the extent it causes a shortfall) other CyDex inability to supply Captisol."

5. WARRANTIES. The following provision is added to the end of Section 5.2 of the Agreement: "CyDex hereby represents and warrants that neither it, nor any of its past or present employees or suppliers, is debarred under subsections 306(a) or (b) of the Federal Food, Drug, and Cosmetic Act and covenants that it shall notify Sage if it becomes aware that it or any of its past or present employees or suppliers becomes debarred."

6. CONFIDENTIALITY. The provisions of Section 6 of the Agreement are hereby amended to conform with the provisions of Section 8 of the Commercial License Agreement, with references to the "Agreement" meaning this Supply Agreement as hereby amended, not the Commercial License Agreement, and with references to Section 8 or subsection thereof meaning Section 6 of this Supply Agreement as hereby amended, not Section 8 of the Commercial License Agreement.

7. INDEMNIFICATION. The word "and" between clauses (c) and (d) of Section 7.1 of the Agreement and between clauses (d) and (e) of Section 7.2 of the Agreement is hereby changed to the word "or". The clause "(other than to the extent arising primarily from the manufacture, use, handling, promotion, marketing, distribution, importation, sale or offering for sale of Captisol by CyDex and its Affiliates (including without limitation, the sale of Captisol by CyDex to Sage hereunder))" is hereby added to the end of clauses (a) and (b) of Section 7.2 of the Agreement.

8. LIMITATION OF LIABILITY. Section 8 of the Agreement is amended to read:

"EXCEPT FOR DAMAGES FOR WHICH A PARTY IS RESPONSIBLE PURSUANT TO (A) ITS BREACH OF SECTION 6 ABOVE, OR (B) ITS INDEMNIFICATION OBLIGATIONS SET FORTH IN SECTION 7 ABOVE, EACH PARTY SPECIFICALLY DISCLAIMS ALL LIABILITY FOR AND SHALL IN NO EVENT BE LIABLE FOR ANY INCIDENTAL, SPECIAL, INDIRECT OR CONSEQUENTIAL DAMAGES, EXPENSES, LOST PROFITS, LOST SAVINGS, INTERRUPTIONS OF BUSINESS OR OTHER DAMAGES OF ANY KIND OR CHARACTER WHATSOEVER ARISING OUT OF OR RELATED TO THIS AGREEMENT OR RESULTING FROM THE MANUFACTURE, HANDLING, MARKETING, SALE, DISTRIBUTION OR USE OF ANY LICENSED PRODUCT OR USE (PURSUANT TO OR IN CONNECTION WITH THE RIGHTS GRANTED UNDER THIS AGREEMENT) OF THE LICENSED PATENTS AND CAPTISOL DATA PACKAGE, REGARDLESS OF THE FORM OF ACTION, WHETHER IN CONTRACT, TORT, STRICT LIABILITY OR OTHERWISE, EVEN IF SUCH PARTY WAS ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. EXCEPT WITH RESPECT TO (A) A PARTY'S BREACH OF SECTION 6 ABOVE, OR (B) THE INDEMNIFICATION SPECIFICALLY PROVIDED IN SECTION 7 ABOVE, TN NO EVENT SHALL EITHER PARTY'S TOTAL AGGREGATE LIABILITY FOR ALL CLAIMS ARISING OUT OF OR RELATED TO THIS SUPPLY AGREEMENT, OR RESULTING FROM THE MANUFACTURE, HANDLING, MARKETING, SALE, DISTRIBUTION OR USE OF ANY LICENSED PRODUCT OR USE OF THE LICENSED PATENTS AND CAPTISOL DATA PACKAGE PURSUANT TO OR IN CONNECTION WITH THE RIGHTS GRANTED UNDER THIS AGREEMENT, EXCEED THE GREATER OF (I) $250,000 AND (II) THE TOTAL AMOUNTS ACTUALLY PAID BY SAGE TO CYDEX UNDER THIS AGREEMENT AS OF THE DATE SUCH CLAIMS ARISE; PROVIDED, THAT THE FOREGOING LIMITATIONS SHALL NOT LIMIT CYDEX'S RIGHT TO TAKE ACTION TO ENFORCE THIS SUPPLY AGREEMENT TO COLLECT AMOUNTS THAT ARE PROPERLY DUE AND OWING UNDER ARTICLE 4 HEREOF. NO ACTION, REGARDLESS OF FORM, ARISING OUT OF OR RELATED TO THIS AGREEMENT MAY BE BROUGHT BY EITHER PARTY MORE THAN TWO YEARS AFTER

SUCH PARTY HAS KNOWLEDGE OF THE LEGAL AND FACTUAL BASIS FOR SUCH CAUSE OF ACTION OR AFTER EXPIRATION OF THE APPLICABLE STATUTORY LIMITATIONS PERIOD, WHICHEVER IS SOONER. FOR AVOIDANCE OF DOUBT, THE PARTIES' RESPECTIVE RIGHTS AND OBLIGATIONS WITH RESPECT TO ANY LIABILITY THAT MAY ACCRUE UNDER THE LICENSE AGREEMENT, THE COMMERCIAL LICENSE AGREEMENT OR ANY SUPPLY AGREEMENT (OTHER THAN THIS AGREEMENT) OR IN CONNECTION WITH ACTIVITIES CONDUCTED PURSUANT TO OR CONTEMPLATED BY ANY SUCH AGREEMENTS SHALL BE DETERMINED PURSUANT TO THE TERMS OF THOSE AGREEMENTS AND NOT BY THE TERMS AND CONDITIONS SET FORTH IN THIS AGREEMENT."

9. TERMINATION WITH COMMERCIAL LICENSE AGREEMENT. Section 9.3 of the Agreement is hereby amended to read: "This Agreement shall automatically terminate upon the termination, for whatever reason, of the Commercial License Agreement in its entirety. For clarity, if the Commercial License Agreement is permissibly terminated with respect to one or more of the Licensed Products and not in its entirety, then this Agreement shall remain in effect with respect to the other Licensed Products."

10. SURVIVAL. Section 9.4 of the Agreement is hereby amended to read: "**SURVIVAL**. Notwithstanding any other provisions of this Agreement, any liability or obligation of either party to the other for acts or omissions before the termination of this Agreement shall survive the termination of this Agreement, including Sage's obligation to pay CyDex sums due in respect of Captisol shipped before termination of this Agreement. And, such termination shall not relieve either party from obligations that are expressly indicated to survive termination of this Agreement. Sections 2.2 (Purchase Commitment) (final two sentences only), 3.4 (Modified Specifications) (final two sentences only, with respect to Specifications modified during the Term), 3.6 (Control; Acceptance and Rejection), 4.1(b) (Shortfall Reimbursement (Take or Pay)) (with respect to Shortfalls during the Term, prior to a Failure to Supply, for which the relevant payment in Section 4.1(b) was not made prior to termination), 4.3 (Payments) (to the extent owed but unpaid as of the date of termination of this Agreement), 4.4 (Taxes), 5.3 (Disclaimer), 6 (Confidentiality), 7 (Indemnification), 8 (Limitation of Liability), 9.4 (Survival), and 10 (General Provisions) shall survive termination of this Agreement. […***…]. For clarity, if this Agreement is terminated with respect to one or more of the Licensed Products and not in its entirety, then this Agreement shall terminate only with respect to such terminated Licensed Products and shall remain in effect with respect to the other Licensed Products and all outstanding Captisol orders properly made before and pending at the time of termination shall remain in full force and effect."

11. NON-SOLICITATION. Section 10.1 of the Agreement is hereby deleted in its entirety and replaced with "[Intentionally Omitted.]".

12. CONFIDENTIALITY OF PROCEEDINGS. The second sentence of Section 10.4(b) of the Agreement is amended to read: "Except as required by law, no party shall make (or instruct the arbitrator(s) to make) any public announcement with respect to the arbitration proceedings or decision of the arbitrators) without prior written consent of the other party."

13. NOTICES. Section 10.7 is hereby amended to read:

"**Notices**. Any notice, request, or communication under this Agreement shall be effective only if it is in writing and personally delivered, or sent by certified mail, postage pre-paid, or by nationally recognized overnight courier (for next-business-day delivery) with signature required, in each case addressed to the applicable party at the addresses stated below or such other persons and/or addresses as shall be furnished in writing by any party in accordance with this Section 10.7. Unless otherwise provided, all notices shall be sent:

If to CyDex, to:

CyDex Pharmaceuticals, Inc.
11119 North Torrey Pines Road
Suite 200
La Jolla, CA 92037
Attention: President

With a copy to:

General Counsel
Ligand Pharmaceuticals Incorporated
11119 North Torrey Pines Road
Suite 200
La Jolla, CA 92037

If to Sage, to:

Sage Therapeutics, Inc.

215 First Street
Cambridge, Massachusetts 02142
Attention: President

With a copy to:

Sage Therapeutics, Inc.
215 First Street
Cambridge, Massachusetts 02142
Attention: Senior Vice President, General Counsel

If sent by overnight courier, the next business day after the date of deposit with such courier (by the courier's stated time for enabling next-business-day delivery) shall be deemed to be the date on which such notice, request or communication was given. If sent by certified mail, the third business day after the date of mailing shall be deemed the date on which such notice, request or communication was given."

14. USE OF NAME; PUBLICITY. Section 10.8 of the Agreement is hereby deleted in its entirety and replaced with "[Intentionally Omitted.]".

15. GOVERNING LAW. The following sentence is added to the end of Section 10.9 of the Agreement: "The parties agree that the United Nations Convention on Contracts for the International Sale of Goods shall be inapplicable to this Agreement and the Commercial License Agreement and transactions hereunder and thereunder."

16. ASSIGNMENT. Section 10.14 of the Agreement is amended to read:

"Sage may not assign its rights or delegate its obligations under this Agreement, in whole or in part, by operation of law or otherwise, to any third party without the prior written consent of CyDex, which consent shall not be unreasonably withheld. Notwithstanding the foregoing, Sage may assign its rights and delegate its obligations under this Agreement to an Affiliate or to a third party successor, whether by way of merger, sale of all or substantially all of its assets, sale of stock or otherwise, without CyDex's prior written consent. As a condition to any permitted assignment hereunder, if such assignment is (a) to an Affiliate, the assignor must guarantee the performance of any assignee to the terms and obligations of this Agreement or (b) to a Third Party successor, such successor shall agree for the express benefit of CyDex to comply with the terms and conditions of this Agreement. Any assignment by Sage not in accordance with this Section 10.14 shall be void. CyDex has the right to assign its rights or delegate its obligations under this Agreement, in whole or in part, by operation of law or otherwise, to any third party, either (y) without any requirement for consent of Sage; provided that (i) CyDex also assigns all of its right, title and interest in all operating assets, including without limitation, intellectual property rights, pertaining to its Captisol business to the same third party contemporaneous with the assignment of this Agreement, and (ii) if such assignment is (A) to an Affiliate, the assignor must guarantee the performance of any assignee to the
terms and obligations of this Agreement or (B) to a Third Party successor, such successor shall agree for the express benefit of Sage to comply with the terms and conditions of this Agreement; or (z) with the prior written consent of Sage, which consent shall not be unreasonably withheld. Any assignment by CyDex not in accordance with this Section 10.14 shall be void. For clarity, each party may sublicense its rights, and use its Affiliates and Third Parties to perform its obligations or exercise its rights, under this Agreement to the extent permitted by and in accordance with the express terms and conditions of this Agreement."

17. ENTIRE AGREEMENT. This Agreement as amended hereby contains the entire agreement of the parties relating to the subject matter hereof and supersede any and all prior or contemporaneous agreements, written or oral, between CyDex (and/or any of its Affiliates) and Sage (and/or any of its Affiliates) relating to the subject matter thereof and hereof. Provided, that (a) any confidentiality nonuse provisions of any pre-Agreement agreement are not superseded and will remain in effect in addition to the confidentiality/nonuse provisions hereof, and (b) the Commercial License Agreement, as amended through and including the 2015
Date, is not superseded and remains in full force and effect as so amended.

18. COUNTERPARTS. This Amendment may be executed in counterparts, each of which shall constitute an original document, but both of which shall constitute one and the same instrument.

19. EFFECT ON AND OF SUPPLY AGREEMENT. The parties intend (a) that the changes made to the Commercial License Agreement by the 2015 Date-dated Amended and Restated Commercial License Agreement (*i.e.*, in definitions) shall flow through to and thereby be deemed to amend, as of the Amendment Effective Date, the Agreement; (b) that except as expressly set forth in this Amendment and to the extent of such express flow-through, the Agreement remains unchanged and in full force and effect; (c) that every reference in the Agreement to the "Commercial License Agreement" shall mean the Commercial License Agreement (as defined in the recitals of this Amendment); (d) that for acts and omissions after the Amendment Effective Date, every reference in the Agreement to the Agreement (*i.e.*, the Supply Agreement) shall mean the Agreement as amended by this Amendment and as deemed

to be amended by such express flow-through; and (e) that after the Amendment Effective Date, every reference in the Commercial License Agreement to the Agreement (*i.e.*, the Supply Agreement) shall mean the Agreement as amended by this Amendment and as deemed to be amended by such express flow-through.

[Remainder of this page left blank intentionally]

IN WITNESS WHEREOF, the parties have executed this Amendment No. 3 to Supply Agreement as of the 2015 Date.

CYDEX PHARMACEUTICALS, INC.

By: /s/ Charles Berkman

Charles Berkman
Vice President and Secretary

SAGE THERAPEUTICS, INC.

By: /s/ Anne Marie Cook

Anne Marie Cook
Senior Vice President, General Counsel

EXHIBIT 10.4

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. […***…] denotes omissions.

COMMERCIAL LICENSE AGREEMENT

This **COMMERCIAL LICENSE AGREEMENT** (this "**Agreement**") is made this 21st day of August, 2013 (the "**Effective Date**") between:

CYDEX PHARMACEUTICALS, INC., a Delaware corporation with offices at 11119 North Torrey Pines Road, Suite 200, La Jolla, California 92037 ("**CyDex**"); and

SAGE THERAPEUTICS INC., a Delaware corporation with offices at 29 Newbury Street, Suite 301, Boston, Massachusetts 02116 ("**Sage**").

RECITALS

WHEREAS, CyDex is engaged in the business of developing and commercializing novel drug delivery technologies designed to enhance the solubility and effectiveness of existing and development-stage drugs;

WHEREAS, CyDex is the exclusive supplier of Captisol®, a patented drug formulation system designed to enhance the solubility and stability of drugs;

WHEREAS, Sage has developed or obtained certain rights related to the Compound (defined below);

WHEREAS, Sage desires to obtain a license to use Captisol together with the Compound for the development and commercialization of the Licensed Product (defined below) and the conduct of the Probe Studies and CyDex is willing to grant such license to Sage under the terms and conditions set forth herein;

WHEREAS, CyDex and Sage entered into a Commercial License Agreement with an effective Date of December 13, 2012 (the "**Old Agreement**" and such effective date, the "**Old Agreement Effective Date**"), which the parties are terminating as of the Effective Date; AND

WHEREAS, on or about December 13, 2012, CyDex and Sage entered into a Supply Agreement, specifying the terms under which CyDex would sell Captisol to Sage or its Contract Manufacturers (defined below), and Sage would obtain supplies of Captisol from CyDex, for use in development of and in the Licensed Product (the "**Supply Agreement**").

NOW, THEREFORE, in consideration of the following mutual promises and other good and valuable consideration, the receipt and sufficiency of which are acknowledged, the parties, intending to be legally bound, agree as follows:

1. DEFINITIONS.

For the purposes of this Agreement, the following terms whether used in singular or plural form shall have the meanings as defined below:

"**Affiliate**" means, with respect to any party, any entity controlling, controlled by, or under common control with such party, during and for such time as such control exists. For these purposes, "control" shall refer to the ownership, directly or indirectly, of at least 50% of the voting securities or other ownership interest of the relevant entity.

"**Bankruptcy Code**" means title 11 of the United States Code.

"**Captisol**" means Captisol, also known scientifically as sulfobutylether β(beta) cyclodextrin, sodium salt, and any modified or improved form of Captisol®, including without limitation, any improved or modified form of sulfobutylether β(beta) cyclodextrin that is marketed with the use of the Captisol® trademark or a variation thereof.

"**Captisol Data Package**" means (a) all toxicology/safety and other relevant scientific data owned, licensed or developed by CyDex and its Affiliates relating to Captisol; and (b) all toxicology/safety and other relevant scientific data owned, licensed or developed by the licensees or sublicensees of CyDex or its Affiliates or other third parties (to the extent permitted in the applicable license or other agreements between CyDex and/or its Affiliates and such licensees, sublicensees or other third parties), in each case relating to Captisol alone (and not in conjunction with a product formulation).

"**Captisol Improvement**" means any modification or improvement of Captisol alone, whether or not patentable, that is developed by Sage or its Affiliates, solely or jointly with a third party. For clarity, Captisol Improvements shall not include technology or improvements which are related to the Compound and/or other non-Captisol components of the Licensed Product.

"**Captisol Patents**" means all patents and patent applications in the Territory which pertain to Captisol, other than the Licensed Product Patents, and which now or at any time during the Term are owned by or licensed to CyDex or any CyDex Affiliate with the right to sublicense, including any and all extensions, renewals, continuations, substitutions, continuations-in-part, divisions, patents- of-addition, reissues, reexaminations and/or supplementary protection certificates to any such patents. For avoidance of doubt, all intellectual property pertaining to the Licensed Product or the Probe Study Product generated by Sage or its Affiliates or their
Sublicensees during the Term of this Agreement or during the term of the Old Agreement shall be solely owned by Sage and shall not be part of the Captisol Patents. The Captisol Patents include the patents and patent applications set forth on Exhibit A attached hereto. Such Exhibit A may be updated by CyDex from time to time during the Term.

"**Claim**" has the meaning specified in Section 1.0.1.

"**Clinical Grade Captisol**" means Captisol which (a) has been manufactured under conditions of current good manufacturing practices for bulk excipients as set forth in U.S. Pharmacopoeia <1078> as of the Effective Date or any successor thereto, (b) is intended for use in humans, and (c) is intended for clinical trials for the Product.

"**Commercial Grade Captisol**" means Captisol which (a) has been manufactured under conditions of current good manufacturing practices for bulk excipients as set forth in U.S. Pharmacopoeia <1078> as of the Effective Date or any successor thereto, (b) is intended for use in humans, and (c) is intended for commercial sale of the Product.

"**Commercial Launch Date**" means the first commercial sale by Sage, its Affiliates or Sublicensees of the Licensed Product to a Third Party. For avoidance of doubt, any transfer of the Licensed Product to a Third Party for preclinical, clinical or regulatory purposes shall not be deemed as commercial launch.

"**Commercially Reasonable Efforts**" means those efforts consistent with the exercise of prudent scientific and business judgment as applied by a party to the development and commercialization of its own pharmaceutical products at a similar stage of development and with similar market potential.

"**Compound**" means that certain neuroactive steroid known as Allopregnanolone.
"**Confidential Information**" has the meaning specified in Section 8.1.
"**Contract Manufacturer**" has the meaning specified in Section 2.4.

"**Cover**" (including variations thereof such as "**Covered**," "**Coverage**," or "**Covering**") means that the manufacture, use, importation or sale of the applicable Licensed Product or Probe Study Product would infringe a Valid Claim of a specified patent in the absence of a grant of rights under such patent. The determination of whether an item or process is Covered by a Valid Claim shall be made on a country-by-country basis.

"**Disclosing Party**" has the meaning specified in Section 8.1 hereof.

"**DMF**" means a Drug Master File for Captisol, as filed as of the Effective Date, or as hereafter updated from time to time during the Term, by CyDex with the FDA.

"**FDA**" means the United States Food and Drug Administration, or any successor thereto.

"**Field**" means as applicable, either or both of the Epilepticus Field and the TBI Field, where the "**Epilepticus Field**" means the field of therapeutic use against status epilepticus in humans and "**TBI Field**" means the treatment of traumatic brain injury in humans.

"**Indemnified Party**" has the meaning specified in Section 10.4.

"**Indemnifying Party**" has the meaning specified in Section 10.4.

"**License Agreement**" means the License Agreement dated October 13, 2011 between CyDex and Sage.

"**Licensed Patents**" means, collectively, the Captisol Patents and the Licensed Product Patents.

"**Licensed Product**" means a pharmaceutical composition in and for the Field comprising the Compound combined with or formulated using Captisol that is Covered by the Licensed Patents or that is developed with the assistance of or incorporates any component of the Captisol Data Package. For clarity, the Licensed Product shall not include any product the composition of which includes the Compound and any other active pharmaceutical ingredient.

"**Licensed Product Patents**" means all patents and patent applications in the Territory which Cover the use of Captisol with the Compound, other than the Captisol Patents, and which now or at any time during the Term are owned by or licensed to CyDex or any CyDex Affiliate with the right to sublicense, including any and all extensions, renewals, continuations, substitutions, continuations-in- part, divisions, patents-of-addition, reissues, reexaminations and/or supplementary protection certificates to any such patents. Licensed Product Patents further include all other patents and patent applications, other than the Captisol Patents, which are owned or licensed by CyDex on the Effective Date or at any time during the Term of this Agreement, and which are necessary to develop, manufacture, and commercialize the Licensed Product, or which arc necessary to develop or manufacture the Probe Study Product or which are necessary for Sage to exercise its license under this Agreement. Set forth in Exhibit B attached hereto is a list of the Licensed Products Patents as of the Effective Date. Such Exhibit B may be updated by CyDex from time to time during the Term.

"**Losses**" has the meaning set forth in Section 10.1.

"**Marketing Approval**" means final approval of an NDA by the FDA for the United States, or final approval of a comparable document filed with an equivalent health regulatory authority in any other country or in the European Union (using the centralized process or mutual recognition).

"**NDA**" means a New Drug Application, as defined in the United States Federal Food, Drug and Cosmetic Act and the regulations promulgated thereunder, or similar application filed with an equivalent regulatory body in another country.

"**Net Sales**" means, with respect to a particular time period, the total gross amounts invoiced by Sage and its Affiliates and their Sublicensees for sales of the Licensed Product made during such time period to unaffiliated Third Parties, less the following deductions to the extent actually allowed or incurred with respect to such sales:

(a) reasonable and customary discounts (other than discounts which have already diminished the gross amount invoiced), including cash, trade and quantity discounts, fees for service, patient assistance discounts, administrative fees, and rebates granted to trade customers, government, and distributors; *provided* that such discounts shall be subject to audit pursuant to Section 5.3 below;

(b) credits or allowances granted for damaged, outdated, spoiled, returned or rejected products, including, without limitation, in connection with recalls;

(c) freight, postage, insurance and transportation charges (if separately identified on the invoice); and

(d) sales, use, value-added or excise taxes, tariffs, customs fees, duties or other governmental charges (other than income taxes) levied on, absorbed or otherwise imposed on sales of the Licensed Product (if separately identified on the invoice), as adjusted by any refunds.

Notwithstanding the foregoing, amounts invoiced by Sage and its Affiliates for the sale of the Licensed Product among Sage or its Affiliates for resale shall not he included in the computation of Net Sales. For purposes of determining Net Sales, a "**sale**" shall not include reasonable transfers or dispositions as samples for promotional purposes, or transfers or dispositions at no cost for preclinical, clinical or regulatory purposes.

"**Non-breaching Party**" has the meaning specified in Section 13.2.

"**Notified Party**" has the meaning specified in Section 13.2.

"**Pfizer**" has the meaning specified in Section 8.5.

"**Pre-Existing Agreement**" has the meaning ascribed to it in Sections 1.1 and 13 of the License Agreement.

"**Probe Condition**" mean any of the following: (a) […***…], (b) […***…], (c) […***…], (d) […***…], (e) […***…], or (f) […***…].

"**Probe Study**" means […***…].

"**Probe Study Product**" means […***…].

"**Receiving Party**" has the meaning specified in Section 8.1.

"**Regulatory Approval**" means, with respect to the Licensed Product in any country or jurisdiction, all approvals (including, where required, pricing and reimbursement approvals and the applicable Marketing Approval), registrations, licenses or authorizations from the relevant regulatory authority in a country or jurisdiction that is specific to the Licensed Product and necessary to market and sell such Licensed Product in such country or jurisdiction.

"**Sage Know-How**" means information or data owned, licensed or generated by Sage and its Affiliates, before and during the Term of this Agreement or the term of the Old Agreement. For clarity, Sage Know-How shall not include information within the Captisol Data Package; nor does Sage Know-How include any other information or data to which CyDex has obtained rights before the term of the Old Agreement, to the extent of such rights.

"**Sage Patents**" means all patents and patent applications owned now, licensed or developed during the Term of this Agreement or the term of the Old Agreement by Sage and its Affiliates, including any and all extensions, renewals, continuations, substitutions, continuations-in-part, divisions, patents-of-addition, reissues, reexaminations and/or supplementary protection certificates to any such patents. For clarity, Sage Patents shall not include Licensed Patents under this Agreement.

"**Specifications**" means the specifications for Captisol set forth in Exhibit C hereto, as such may be amended from time to time. "**Study**" has the meaning specified in Section 6.3.

"**Sublicensees**" has the meaning specified in Section 2.3.

"**Term**" has the meaning specified in Section 13.1.

"**Territory**" means the entire world.

"**Third Party**" means any person or entity or authority other than CyDex or Sage or an Affiliate of either of them.

"**Valid Claim**" means a claim in any unexpired, issued patent which has not been irrevocably abandoned or held to be invalid or unenforceable by a non-appealed or unappealable decision of a court or other authority of competent jurisdiction, which is not admitted to be invalid through disclaimer or dedication to the public, and which Covers the applicable Licensed Product or Probe Study Product.

2. GRANT OF RIGHTS.

2.1 **License Grants from CyDex to Sage**.

(a) **Field Licenses**.

(i) **Licensed Patents**. Subject to the terms and conditions of this Agreement, CyDex hereby grants to Sage an exclusive, nontransferable (except as provided in Section 14.14) license during the Term under the Licensed Patents, solely to research, develop, make, have made, import, use, offer for sale and sell the Licensed Product in the Territory in and for the Field. Notwithstanding the foregoing, to the extent that any Licensed Patents are licensed to CyDex or its Affiliates by a Third Party on a non-exclusive basis, the license granted to Sage in the foregoing sentence shall be exclusive as to CyDex but non-exclusive as to such Third Party and other persons whose rights derive from such Third Party. Sage may not sublicense the Licensed Patents, except as expressly set forth in Section 2.3 and Section 2.4 below.

(ii) **Know-How License**. Subject to the terms and conditions of this Agreement, CyDex hereby grants to Sage an exclusive, nontransferable (except with respect to the assignment provision in Section 14.14) license during the Term under CyDex's rights in and to the Captisol Data Package, solely to research, develop, make, have made, import, use, offer for sale and sell the Licensed Product in the Territory in and for the Field. Notwithstanding the foregoing, to the extent that any contents of the Captisol Data Package are licensed to CyDex or its Affiliates by a Third Party on a non-exclusive basis, the license granted to Sage in the foregoing sentence shall be exclusive as to CyDex but non-exclusive as to such Third Party and other persons whose rights derive from such Third Party. Sage may not sublicense its rights to the Captisol Data Package, except as expressly set forth in Section 2.3 and Section 2.4 below.

(b) **Probe Study Licenses.**

(i) **Licensed Patents**. Subject to the terms and conditions of this Agreement, CyDex hereby grants to Sage a non- exclusive, nontransferable (except as provided in Section 14.14) license during the Term under the Licensed Patents, solely to research, develop, make, have made, import and use the Probe Study Product in the Territory in and for the Probe Studies. Sage may not sublicense the Licensed Patents, except as expressly set forth in Section 2.3 and Section 2.4 below.

(ii) **Know-How License**. Subject to the terms and conditions of this Agreement, CyDex hereby grants to Sage a non-exclusive, nontransferable (except with respect to the assignment provision in Section 14.14) license during the Term under CyDex's rights in and to the Captisol Data Package, solely to research, develop, make, have made, import and use the Probe Study Product in the Territory in and for the Probe Studies. Sage may not sublicense its rights to the Captisol Data Package, except as expressly set forth in Section 2.3 and Section 2.4 below.

(iii) **Development and Commercialization License.** Sage shall notify CyDex if Sage wishes subsequent to a Probe Study to further develop a Probe Study Product for any Probe Condition for potential commercialization, in which event the parties shall negotiate in good faith a license agreement with commercially reasonable terms for a license of appropriate scope.

(c) **Scope of Licenses**. CyDex grants no licenses or rights to use other than as expressly set forth herein. Unless otherwise provided in this Agreement, CyDex grants no rights to Sage to manufacture, import, sell or offer for sale bulk Captisol. Sage acknowledges that not all rights of CyDex related to the manufacture of Captisol are included within the rights licensed hereunder, given that CyDex shall supply Sage's requirements of Captisol for the Licensed Product. Sage shall not attempt to reverse engineer, deconstruct or in any way determine the structure or composition of Captisol except as and to the extent reasonably required to determine an optimal formulation of the Licensed Product or Probe Study Product, and such structure and composition (as and if so determined) shall be considered Confidential Information of CyDex. Sage acknowledges and agrees that (i) CyDex shall not be required to obtain or maintain patent rights for the Licensed Patents, (ii) except as expressly provided herein, CyDex shall not be restricted in making sales of Captisol or licensing rights to other parties, and (iii) CyDex does not warrant or indemnify Licensee or its Affiliates and Sublicensees against the Licensed Product infringing third party rights.

(d) **Non-Suit**. During the term of this Agreement, neither CyDex nor any of its Affiliates shall sue or threaten to sue, or take any similar action against, or aid, abet or enable any third party to sue, threaten to sue or take any similar action against. Sage, or any Sublicensees, or any of their respective Affiliates, or any customers or end-users of any Licensed Products, or any users of any Probe Study Product, claiming that the manufacture, use, sale, offer for sale or importation of any Licensed Product, or the manufacture, use or importation of any Probe Study Product, infringes any patents or patent applications owned, licensed, sublicensed or otherwise controlled by, now or in the future, CyDex or any of its Affiliates.

(e) **Negative Covenant**. During the term of this Agreement, CyDex and its Affiliates shall not grant any rights to any Third Party that conflict with the exclusive rights granted herein to Sage or that conflict with or otherwise impair Sage's ability to conduct the activities described herein; *provided*, that, if CyDex negotiates toward and/or enters into a further agreement with a party to a Pre- Existing Agreement as expressly contemplated by such Pre-Existing Agreement (for example, upon the exercise by such party of an option granted in a Pre-Existing Agreement), such negotiation and/or agreement shall not be deemed to impermissibly conflict with the exclusive rights granted herein to Sage or to impermissibly conflict with or otherwise impair Sage's ability to conduct the activities described herein and such further agreement shall, from and after the date of execution and delivery, constitute a "Pre-Existing Agreement" for purposes of the definition of "Probe Condition" herein; *provided further* that CyDex shall provide notice to Sage of the terms and conditions included in any such further agreement prior to executing same, Without limiting the generality of the foregoing, in the event that CyDex or any of its Affiliates become aware that a Third Party is (other than as permitted by a Pre-Existing Agreement) conducting research, development or commercial activities using the Compound with Captisol, then CyDex shall take all reasonable measures to cease the supply of Captisol to such Third Party and to any other Third Party that is determined to be supplying Captisol to such Third Party. Sage hereby acknowledges that CyDex's performance of its obligations under any Pre-Existing Agreement, and the exercise by a Third Party of its rights under any Pre-Existing Agreement, are hereby deemed not to be a breach by CyDex or any of its Affiliates of this Section 2.1(e).

(f) **Bankruptcy Code**. All rights and licenses granted under or pursuant to this Agreement by CyDex to Sage are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the Bankruptcy Code, licenses of rights to "intellectual property" as defined under Section 101 of the Bankruptcy Code. The parties agree that Sage, as a licensee of such rights under this Agreement, shall retain and may fully exercise all of its rights and elections under the Bankruptcy Code.

2.2 **Grant of License from Sage to CyDex**. Sage hereby grants to CyDex a nonexclusive, transferable, perpetual, worldwide and royalty-free license, with the right to gran' sublicenses (through multiple tiers of sublicensees), under Sage's and its Affiliates' rights in and to Captisol Improvements to develop, make, have made, use, market, distribute, import, sell and offer for sale Captisol, any Captisol Improvement and products formulated with Captisol or any Captisol Improvement (in each case, other than the Compound, the Licensed Product and any other compound that is a "Compound" under any other Commercial License Agreement entered into by and between Sage and CyDex and any other product that is a "Licensed Product" under any other Commercial License Agreement entered into by and between Sage and CyDex). If during the Term any of (a) Sage, (b) Affiliates to whom Sage has provided rights under the licenses granted to Sage by CyDex pursuant to Section 2.1, or (c) Sublicensees pursuant to the practice of their respective sublicenses from Sage under Section 2.3, tile any patent application claiming Captisol anywhere in the world, CyDex shall be deemed automatically to have a nonexclusive, transferable, perpetual, worldwide and royalty-free license, with the right to grant sublicenses (through multiple tiers of sublicensees), under the claims relating specifically to Captisol to make, have made, use, market, distribute, import, sell, and offer for sale Captisol and all products formulated with Captisol (in each case, other than the Compound, the Licensed Product and any other compound that is a "Compound" under any other Commercial License Agreement entered into by and between Sage and CyDex and any other product that is a "Licensed Product" under any other Commercial License Agreement entered into by and between Sage and CyDex). Sage shall provide prompt notice of any Captisol Improvement, and shall notify and consult with CyDex at least 30 days before the filing of any patent application claiming Captisol or any Captisol Improvement. Sage grants no licenses or rights to use other than as expressly set forth herein.

All rights and licenses granted under or pursuant to this Agreement by Sage to CyDex are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the Bankruptcy Code, licenses of rights to "intellectual property" as defined under Section 101 of the Bankruptcy Code. The parties agree that CyDex, as a licensee of such rights under this Agreement, shall retain and may fully exercise all of its rights and elections under the Bankruptcy Code.

2.3 **Sublicensing**. Sage shall have the right to grant sublicenses to any Third Party (collectively "**Sublicensees**") under the licenses granted to Sage pursuant to Section 2.1; *provided* that Sage warrants and shall procure, as a condition precedent thereto, that each such Sublicensee shall first be advised of the restrictions set forth in this Agreement with respect to the transfer of the rights sublicensed to such Sublicensee and such Sublicensee shall enter into an agreement (in a form reasonably satisfactory to CyDex, with CyDex named as an intended third-party beneficiary) with Sage pursuant to which such Sublicensee shall acknowledge and agree to observe and be bound by the applicable restrictions set forth in this Agreement. Other than as specifically provided in this Section 2.3 and Section 2.4, Sage shall not have the right to grant sublicenses to any third party under the licenses granted pursuant to Section 2.1. Sage shall ensure that all of its Sublicensees will comply with the terms and conditions of this Agreement and shall remain fully responsible for the compliance by such Sublicensees with the terms and conditions of this Agreement as if such Sublicensees were Sage hereunder.

2.4 **Contracting**. Sage may manufacture the Licensed Product or the Probe Study Product (but not the bulk Captisol) or contract the manufacture of the Licensed Product or the Probe Study Product (but not the manufacture of bulk Captisol) with reputable FDA- inspected third party manufacturers (each a "**Contract Manufacturer**") upon notification to CyDex in writing of Sage's intent to do so (such notice to include the identity and location of the proposed Contract Manufacturers). To the extent necessary to engage a Contract Manufacturer for the Licensed Product or the Probe Study Product, Sage shall be permitted under this Agreement to grant any such Contract Manufacturer a sublicense under the licenses granted to Sage pursuant to Section 2.1 solely for such purposes; provided that Sage warrants and shall procure, as a condition precedent thereto, that (a) any such Contract Manufacturer shall first be advised of the restrictions set forth in this Agreement with respect to the transfer of the rights licensed to Sage mid its Sublicensees hereunder and (b) any such Contract Manufacturer shall enter into an agreement (in a form reasonably satisfactory to CyDex, with CyDex named as an intended third-party beneficiary) with Sage pursuant to which such Contract Manufacturer shall acknowledge and agree to observe and be bound by the applicable restrictions set forth in this Agreement. Sage shall ensure that all of its Contract Manufacturers will comply with the terms and conditions of this Agreement and shall remain fully responsible for the compliance by such Contract Manufacturers with the terms and conditions of this Agreement as if such Contract Manufacturers were Sage
hereunder.

2.5 **Technology Transfer**. CyDex shall, for a period of one year after the Old Agreement Effective Date, make its personnel available to Sage and its Contract Manufacturers to respond to informational inquiries and provide technical assistance related to the Captisol Data Package. Sage shall compensate CyDex at the rate of $150 per hour for the time of CyDex personnel incurred to provide such services. Such technology transfer shall not include information related to the manufacture of bulk Captisol.

2.6 **Negative Covenant by CyDex**. During the Term of this Agreement, CyDex and its Affiliates shall not develop or commercialize any pharmaceutical composition comprising the Compound in and for the Field, and shall not in any way assist any Third Party in developing or commercializing any pharmaceutical composition comprising the Compound (including without limitation by granting any license or similar rights under intellectual property) in and for the Field.

3. MANUFACTURE AND SUPPLY OF CAPTISOL.

The provisions of the Supply Agreement and any related quality agreement shall govern the manufacture and supply of Captisol for use in the formulation of the Licensed Product or Probe Study Product, and nothing in the Supply Agreement (including Section 2.2 thereof) shall limit Sage's right to use Probe Study Product in accordance with the terms of this Agreement.

4. COMPENSATION.

4.1 **Payments and Royalties for Licenses.**

(a) **One-Time Fees.**

(i) Upon the exercise of its option under the License Agreement to enter into the Old Agreement and the Supply Agreement, Sage has paid to CyDex a nonrefundable, one-time option exercise fee. Receipt of such fee is hereby acknowledged.

(ii) In consideration of CyDex entering into this Agreement, Sage agrees to pay to CyDex $300,000 by wire transfer on the Effective Date.

(b) **Milestone Payments.** Within ten (10) days following the occurrence of each of the milestone events listed below with respect to the Licensed Product, Sage shall provide written notice to CyDex of the achievement of such milestone event, and within twenty (20) days of the occurrence of each of the milestone events, pay to CyDex the applicable nonrefundable milestone fee listed next to each such event in further consideration of the rights granted Sage hereunder. The milestone payments (each payable only one time per Field regardless of the number of times achieved by the Licensed Product for the applicable Field; for the avoidance of doubt, if the same Licensed Product achieves one or more given milestones for both the Epilepticus Field and the TBI Field, then the milestone payment for that event must be paid twice) are as follows. If any such milestone is achieved before all prior sequential milestones have been actually achieved, then any and all prior sequential milestones which were not previously actually achieved shall be deemed to have thereby been achieved, and the milestone payments for such deemed-achieved milestones shall also be payable within such twenty (20) days.

	MILESTONE	MILESTONE PAYMENT	
(i)	[…***…]	$	[…***…]
(ii)	[…***…]	$	[…***…]
(iii)	[…***…]	$	750,000
(iv)	Upon receipt of the first Marketing Approval from the FDA for a Licensed Product	$	3,000,000

(c) **Royalties**. In addition to amounts payable pursuant to Sections 4.1(a) and 4.1(b) above, Sage shall make royalty payments to CyDex on a calendar quarterly basis, in amounts equal to […***…]% times the Net Sales during such quarter arising from the sale of Licensed Products in the Territory in the Field during the Term. All royalties payable to CyDex pursuant to this Section 4.1(c) shall be due and payable within 60 days after the conclusion of each calendar quarter.

All royalties payable to CyDex pursuant to this Section 4.1(c) shall be due and payable within 60 days after the conclusion of each calendar quarter. For avoidance of doubt, Net Sales under any other agreements entered into pursuant between the parties shall not be accumulated with Net Sales under this Commercial License Agreement for any purposes under this Agreement.

Following the expiration of the last to expire Valid Claim within the Licensed Patents Covering the manufacture, use, sale or importation of a Licensed Product in or into a given country of the Territory, Sage shall have the right to reduce by […***…]% the royalty payments which would otherwise thereafter be owed pursuant to the first paragraph of this Section 4.1(c) with respect to Net Sales arising from the sale of Licensed Product in such country.

For avoidance of doubt, the parties confirm that if different royalty rates could apply to Net Sales of a particular unit of Licensed Product (*e.g.*, manufactured in Country A but sold in Country B, and different royalty rates are then applicable to Country A than to Country B), the higher of the royalty rates shall apply to such unit of Licensed Product.

In establishing the royalty structure hereunder, the parties recognize, and Sage acknowledges, the substantial value of the various obligations being undertaken by CyDex under this Agreement, in addition to the grant of the licenses under the Captisol Data Package as well as under the Licensed Patents, to enable the rapid and effective market introduction of the Licensed Product. The parties have agreed to the payment structure set forth herein as a convenient and fair mechanism to compensate CyDex for these obligations.

(d) **Probe Study Milestone Payment.** Within ten (10) days following a new IND submission for a Probe Study or the first submission of an amendment to an existing/open 1ND for a Probe Study, Sage shall provide written notice to CyDex of the achievement of such milestone event, and within twenty (20) days after the occurrence of such milestone event, pay to CyDex $[… ***…]. Such milestone payment shall be payable only one time; *provided* that it is not achieved more than five (5) times by a Probe Study Product; and *provided* that no more than five (5) Probe Studies are performed.

4.2 **Currency**. All amounts due hereunder are stated in, and shall be paid in, U.S. dollars, Net Sales based on foreign revenue will be converted to U.S. dollars at the rate of exchange published in *The Wall Street Journal*, Eastern U.S. Edition on the last day of each calendar quarter (or the last previous publication date if such day is not a publication date). Sage shall provide CyDex, together with each royalty payment owed pursuant to Section 4.1(c) above, a schedule detailing the calculation of Net Sales resulting from the conversion of foreign revenue to U.S. dollars as set forth herein.

4.3 **Taxes.** All amounts due hereunder exclude all applicable sales, use, and other taxes, and Sage will be responsible for payment of all such taxes (other than taxes based on CyDex's income), fees, duties, and charges, and any related penalties and interest, arising from the payment of amounts due under this Agreement or the sublicense or license, as the case may be, under the Licensed Patents and Captisol Data Package under this Agreement. The parties agree to cooperate with one another and use reasonable efforts to avoid or reduce tax withholding or similar obligations in respect of royalties, milestone payments, and other payments made by Sage to CyDex under this Agreement. To the extent Sage is required to withhold taxes on any payment to CyDex, Sage shall pay the amounts of such taxes to the proper governmental authority in a timely manner and promptly transmit to CyDex official receipts issued by the appropriate taxing authority and/or an official tax certificate, or such other evidence as CyDex may reasonably request, to establish that such taxes have been paid. CyDex shall provide Sage any tax forms that may be reasonably necessary in order for Sage to not withhold tax or to withhold tax at a reduced rate under an applicable bilateral income tax treaty, CyDex shall use reasonable efforts to provide any such tax forms to Sage at least 30 days before the due date for any payment for which CyDex desires that Sage apply a reduced withholding rate. Each party shall provide the other with reasonable assistance to enable the recovery, as permitted by applicable law, of withholding taxes, value added taxes, or similar obligations resulting from payments made under this Agreement, such recovery to be for the benefit of the party bearing such withholding tax or value added tax.

4.4 **Late Payments.** Payments that are not made when due hereunder shall accrue interest, from due date until paid, at a rate equal to the prime rate, as reported in The Wall Street Journal, Eastern U.S. Edition, on the date such payment is due (or the last previous publication date if such day is not a publication date), plus an additional 200 basis points.

5. RECORDS; REPORTS; AUDIT.

5.1 **Records.** During the Term and for a period of three years thereafter, Sage shall, and shall require its Affiliates and Sublicensees to, maintain accurate records relating to clinical study subject enrollment for Studies of the Licensed Product and Net Sales of the Licensed Product.

5.2 **Reports**.

(a) **Quarterly Reports.** Within 30 calendar days following the conclusion of each calendar quarter during the Term, Sage shall provide CyDex with written reports with respect to such calendar quarter (with a monthly breakdown) that describe in reasonable detail Sage's progress made toward achievement of the milestones specified in Section 4.1(h) above during such calendar quarter, including without limitation Sage's then-current best estimate for the dates to achieve such milestones and the number of human subjects enrolled during such calendar quarter in a clinical study conducted by or on behalf of Sage, its Affiliates and Sublicensees to support Marketing Approval for the Licensed Product and that received Licensed Product during such calendar quarter. Within 60 calendar days following the conclusion of each calendar quarter during the Term, Sage shall provide CyDex with a written report with respect to such calendar quarter (with a monthly breakdown) that sets forth in reasonable detail complete and accurate records of Sage's, its Affiliates' and Sublicensees' Net Sales of the Licensed Product during such calendar quarter.

(b) **Annual Reports.** Annually, by February 1st of each calendar year during the Term, Sage shall provide CyDex with written reports that: (i) update CyDex regarding development and commercial activities with respect to the Licensed Product, (ii) describe in reasonable detail Sage's progress made toward achievement of the milestones specified in Section 4.1(b) above during the preceding calendar year; (iii) summarize in reasonable detail Sage's communications and meetings involving the FDA related to Captisol as used in the Licensed Product during the preceding calendar year; (iv) detail Sage's anticipated preclinical and clinical use of Captisol in the Licensed Product for the then-current calendar year; (v) provide CyDex with Sage's non-binding, reasonable, estimated rolling projection for sales of the Licensed Product, in terms of volume quantities and Net Sales values, for the then-current

and the next two succeeding calendar years; and (vi) set forth such other information regarding Captisol as mutually agreed upon by the parties.

5.3 **Audit**. Upon reasonable prior notice, such Section 5.1 records shall be available during regular business hours for examination and audit at the expense of CyDex, and not more often than once each calendar year, by an independent certified public accountant selected by CyDex and reasonably acceptable to Sage, for the sole purpose of verifying the accuracy of the financial reports furnished by Sage pursuant to this Agreement. Any amounts shown to be owed but unpaid shall be paid within 30 days from the accountant's report from the original due date, plus interest accrued thereon (from the applicable original due date) at the rate set forth in Section 4.4 above. Any amounts shown to have been overpaid shall be refunded within 30 days CyDex shall bear the full cost of such audit unless such audit discloses failure by Sage to pay any applicable milestone payment due or an underpayment by Sage of more than 5% of the amount due or any other material inaccuracies in a Sage report, in which case Sage shall bear the full cost of such audit, plus (as in all eases of underpayment) the underpayment amount and interest at the rate set forth in Section 4.4 above. All information learned in the course of any audit or inspection under this Section 5.3 shall be deemed to be Confidential Information of Sage, subject to the terms and provisions of Section 8 below, except to the extent necessary for CyDex to enforce its rights under this Agreement.

6. DEVELOPMENT AND COMMERCIALIZATION BY SAGE.

6.1 **Diligence.** Sage shall (i) use at least Commercially Reasonable Efforts, and shall further require its Affiliates and Sublicensees to use at least Commercially Reasonable Efforts, to develop the Licensed Product, to seek Regulatory Approval of the Licensed Product in all countries and regions where it is commercially reasonable to so seek, and to commercialize the Licensed Product in each respective country and region following Regulatory Approval of the Licensed Product in such respective country/region, and (ii) comply with the requirements set forth in Exhibit D hereto. If Sage is unable to comply with the requirements set forth in Exhibit D hereto due to unanticipated events or changed circumstances that are beyond the reasonable control of Sage, including, for example, delays caused by changes to the development plan that are required in the exercise of sound scientific or commercial judgment due to new information regarding the development of product candidates or changes to the applicable regulatory requirements, then the Parties shall meet and make reasonable extensions to the deadlines provided on Exhibit D. For clarity, Sage may meet the requirements of this Section 6.1 through its activities with respect to the Licensed Product in just one of the Fields. In the event that Sage fails to meet the requirements of this Section 6.1, CyDex shall have the right to terminate this Agreement pursuant to Section 13.2 hereof.

6.2 **Costs and Expenses.** Other than those specified in this Agreement, Sage shall be solely responsible for all costs and expenses related to its development and commercialization of the Licensed Product and its development of the Probe Study Product, including without limitation, all Sage's costs and expenses associated with all preclinical activities and clinical trials, and all regulatory filings and proceedings relating to the Licensed Product or the Probe Study Product.

6.3 **In Vivo Studies.** If Sage wishes to conduct any in vivo study ([…***…], each a "Study") […***…], then Sage shall notify CyDex of any such Study and of the protocol therefor in writing at least […***…] days before commencing such Study, and the following provisions shall apply:

(a) **Dosing**. Sage shall not exceed the dosing matrix levels of Captisol indicated by Exhibit E hereto without the written consent of CyDex.

(b) **Review of Protocol.** […***…]. Sage shall give due consideration and reasonably incorporate any input that CyDex provides regarding such protocol to the extent it pertains solely to the use and administration of Captisol. The contents of each such protocol shall be deemed to be Confidential Information of Sage, subject to the terms and provisions of Section 8 below.

(c) **Compliance with Laws.** Sage represents and warrants that each Study will be performed in accordance with all applicable laws, regulations and requirements. Sage will provide or cause to be provided all appropriate warnings to participants enrolled in each Study and obtain or cause to be obtained appropriate documentation of informed consent from all participants in each such Study.

(d) **Adverse Events.** Sage agrees to immediately inform CyDex if any adverse effects are observed and ascribed to Captisol in any Study in accordance with Section 7.3 hereof if applicable and in a reasonable and prompt manner if Section 7.3 hereof is not applicable. To accurately track adverse events and preserve the validity of each Study, […***…].

(e) **Reporting and Study Data.** Sage agrees to provide CyDex with copies of the final and full reports of all Studies conducted under this Section 6.3, promptly upon completion thereof, and Sage hereby grants to CyDex a non-exclusive, royalty-free license (with the right to sublicense) to use and disclose such data as required by applicable law to […***…].

(f) **Review of Regulatory Filings and Publications.** At least 14 days before a submission of any proposed written publication material or regulatory submission (which shall be subject to the restrictions of Section 8 hereof). Sage shall provide to

CyDex for CyDex's review and comment a copy of any proposed written publication, material or regulatory submission reporting results of a Study where such publication material refers to […***…]. Sage shall give due consideration and reasonably incorporate any input that CyDex provides regarding […***…].

6.4 **Right of Reference.** Sage shall have the right to reference the […***…] in connection with obtaining Regulatory Approval for the Licensed Product.

6.5 **Access to Sage's Data.** […***…], its Sublicensees or Affiliates as required by applicable laws relating to adverse event reporting and/or in connection with development and commercialization of Captisol or for fulfilling its obligations under this Agreement, all at no cost to CyDex. […***…].

7. REGULATORY MATTERS.

7.1 **Captisol Information Submitted for Regulatory Review.** Except as otherwise set forth herein. Sage shall be solely responsible for all communications with regulatory agencies in connection with the Licensed Product or with respect to Sage's activities in connection with the Probe Study Product. Sage shall provide CyDex with copies of the portions of all regulatory submissions containing Captisol data alone (and not in conjunction with any product formulation) 60 days before submission and shall allow CyDex to review and comment upon said submissions. The contents of each such submission shall be deemed to be Confidential Information of Sage, subject to the terms and provisions of Section 8 below. Sage shall promptly inform CyDex of meetings with the FDA (or other regulatory agencies in the Territory) regarding the Licensed Product. If Sage submits written responses to the FDA that include data on Captisol alone, CyDex shall be permitted to review such written materials before submission. If CyDex reasonably objects to the contents of such written responses relating to Captisol, the parties agree to cooperate in working toward a reasonable and mutually agreeable response, provided that Sage shall be entitled to in good faith and with full regard for CyDex's interests and concerns make the final determination as to the contents of any such materials.

7.2 **Material Safety.** CyDex shall provide Sage, in writing, from time to time, with (a) relevant material information currently known to it regarding handling precautions, toxicity and hazards with respect to Captisol, and (b) the then-current material safety data sheet for Captisol. CyDex warrants that all such information shall to CyDex's knowledge be complete and accurate. Notwithstanding the foregoing or anything in this Agreement to the contrary, with respect to any information that is provided in accordance with this Agreement by CyDex, Sage is solely responsible for (i) use of such documentation, including without limitation, use in any regulatory submission to the FDA or any other regulatory agency, (ii) document control and retention, and (iii) determining the suitability of any such documentation for use in any regulatory submission.

7.3 **Adverse Event Reporting.** Sage shall adhere, and shall require that its Affiliates, Sublicensees, co-marketers and distributors adhere, to all requirements of applicable law and regulations that relate to the reporting and investigation of any adverse event, including without limitation an unfavorable an unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease, whether or not considered Captisol. Probe Study Product-related or Licensed Product-related, which occurs or worsens following administration of Captisol, Probe Study Product or Licensed Product. Sage shall provide CyDex with copies of all reports of any such adverse event which is serious (any such adverse event involving Captisol, the Probe Study Product or the Licensed Product that results in death, is life-threatening, requires or prolongs inpatient hospitalization, results in disability, congenital anomaly or is medically important (*i.e.*, may require other medical or surgical intervention to prevent other serious criteria from occurring)) which Sage has reason to believe are associated with Captisol within 10 business days following (i) Sage's submission of any such report to any regulatory agency, or (ii) receipt from Sage's Sublicensee, co-marketer or distributor of any such report to any regulatory agency. Sage shall also advise CyDex regarding any proposed labeling or registration dossier changes affecting Captisol. Reports from Sage shall be delivered to the attention of Chief Scientific Officer, CyDex, with a copy to General Counsel, Ligand, at the address set forth in Section 14.7. The parties shall mutually cooperate with regard to investigation of any such serious adverse event, whether experienced by Sage, CyDex or any other Affiliate, Sublicensee, co-marketer or distributor of CyDex or Sage.

7.4 **Product Recalls.** If any Captisol should be alleged or proven not to meet the Specifications, Sage shall notify CyDex immediately, and both parties shall cooperate fully regarding the investigation and disposition of any such matter. In the event of a dispute arises between the parties as to whether or not Captisol purchased by Sage meets the Specifications, such dispute shall be immediately resolved by submitting it to an independent quality control laboratory mutually agreed upon by the parties. The findings of such independent laboratory shall be binding upon the parties. The cost of the independent quality control laboratory shall be borne by the party whose results are shown by such laboratory to have been incorrect. If (i) Sage and CyDex agree in writing that it is appropriate to recall any Licensed Product, or (ii) the FDA requires the recall of any Licensed Product, and in either case, to the extent that such recall is due to issues relating to Captisol, then CyDex agrees, upon substantiation thereof, to bear a proportionate share (based on the extent to which the recall was caused by issues relating to Captisol) of the reasonable direct costs associated with said recall, including a proportionate share of the actual cost of conducting the recall in accordance with the recall guidelines of the applicable governmental authority, including without limitation, a proportionate share of the cost of the Licensed Product subject to the recall. Sage shall in all events be responsible for conducting any such recalls with respect to the Licensed Product and shall

maintain records of all sales of Licensed Product and customers sufficient to adequately administer any such recall, for a period of five years after termination of this Agreement.

8. CONFIDENTIALITY.

8.1 **Definition.** Sage and CyDex each recognizes that, during the Term or the term of the Old Agreement, it may be (or was) necessary for a party (the **"Disclosing Party"**) to provide Confidential Information (as defined herein) to the other party (the **"Receiving Party"**) that is highly valuable, the disclosure of which would be highly prejudicial to such party. The disclosure and use of Confidential Information will be governed by the provisions of this Section 8. Neither Sage nor CyDex shall use the other's Confidential Information except as expressly permitted in this Agreement. For purposes of this Agreement, **"Confidential Information"** means all information disclosed by the Disclosing Party to the Receiving Party, whether under this Agreement or the Old Agreement, and which is obviously Confidential Information, or which is designated in writing by the Disclosing Party as "Confidential" (or equivalent), or which when disclosed orally is declared to be confidential by the Disclosing Party and confirmed in a writing delivered to the Receiving Party within 30 days of such disclosure, including but not limited to product specifications, data, know-how, formulations, product concepts, sample materials, business and technical information, financial data, batch records, trade secrets, processes, techniques, algorithms, programs, designs, drawings, and any other information related to a party's present or future products, sales, suppliers, customers, employees, investors or business. Without limiting the generality of the foregoing, CyDex's Confidential Information includes all materials provided as part of the Captisol Data Package, and Sage's Confidential Information includes Sage Patents and Sage Know-How.

8.2 **Obligation**. CyDex and Sage agree that they will disclose the other's Confidential Information to its (or its respective parent's) own officers, employees, consultants and agents only if and to the extent necessary to carry out their respective responsibilities under this Agreement or in accordance with the exercise of their rights under this Agreement, and such disclosure shall be limited to the maximum extent possible consistent with such responsibilities and rights. Neither party shall disclose Confidential Information of the other to any Third Party without the other's prior written consent, and any such disclosure to a Third Party shall be pursuant to the terms of a non-disclosure agreement no less restrictive than this Section 8. The party which disclosed Confidential Information of the other to any Third Party shall be responsible and liable for any disclosure or use by such Third Party (or its discloses) which would have violated this Agreement if committed by the party itself. Neither party shall use Confidential Information of the other except as expressly allowed by and for the purposes of this Agreement. Each party shall take such action to preserve the confidentiality of each other's Confidential Information as it would customarily take to preserve the confidentiality of its own Confidential Information {but in no event less than a reasonable standard of care). Unless otherwise specified in this Agreement and subject to terms and conditions in this Agreement, if so requested by the other party a party shall promptly return all relevant records and materials in its possession or control containing or embodying the other party's Confidential Information (including all copies and extracts of documents); *provided, however*, that each party may retain one archival copy (and such electronic copies that exist as part of the party's computer systems, network storage systems and electronic backup systems) of such records and materials solely to be able to monitor its obligations that survive under this Agreement,

8.3 **Exceptions.** The use and non-disclosure obligations set forth in this Section 8 shall not apply to any Confidential Information, or portion thereof, that the Receiving Party can demonstrate by appropriate documentation:

(i) at the rime of disclosure is in the public domain;

(ii) after disclosure, becomes part of the public domain, by publication or otherwise, through no fault of the Receiving Party or its disclosees;

(iii) is independently developed by Receiving Party personnel with no reference or access to the Confidential Information; or

(iv) is made available to the Receiving Party by an independent third party without obligation of confidentiality, provided, however, that to the Receiving Party's knowledge, such information was not obtained by said third party, directly or indirectly, from the Disclosing Party hereunder.

In addition, he Receiving Party may disclose information that is required to be disclosed by law, by a valid order of a court or by order or regulation of a governmental agency including but not limited to, regulations of the Securities and Exchange Commission, or in the course of litigation; *provided* that in all cases the Receiving Party shall give the other party prompt notice of the pending disclosure and make a reasonable effort to obtain, or to assist the Disclosing Party in obtaining, a protective order or confidential- treatment order preventing or limiting (to the greatest possible extent and for the longest possible period) the disclosure and/or requiring that the Confidential Information so disclosed be used only for the purposes for which the law or regulation required, or for which the order was issued.

8.4 **Injunction.** Each party agrees that should it breach or threaten to breach any provisions of this Section 8, the Disclosing Party will suffer irreparable damages and its remedy at law will be inadequate. Upon any breach or threatened breach by the Receiving Party of this Section 8, the Disclosing Party shall be entitled to seek temporary, preliminary and/or permanent injunctive relief in

addition to any other remedy which it may have, without need to post any bond or security, in addition to any and all other legal and equitable rights and remedies available to the Disclosing Party.

8.5 **Third Party Information.** The parties acknowledge that the defined term "Confidential Information" shall include not only a disclosing party's own Confidential information but also Confidential Information of a Third Party which is in the possession of a disclosing party.

Sage acknowledges that CyDex's Confidential Information includes information developed by Pfizer that is confidential to both CyDex and Pfizer. In so far as Confidential Information of Pfizer is disclosed, Pfizer is a third-party beneficiary of this Section 8 of this Agreement and may enforce it or seek remedies pursuant to it in accordance with its terms.

Sage agrees not to disclose to CyDex any Confidential Information of a Third Party which is in the possession of Sage, unless CyDex has given an express prior written consent (which specifies the owner of such Confidential Information) to receive such particular Confidential Information. If CyDex refuses to provide such consent, then any obligation of Sage to provide such information to CyDex under this Agreement shall be deemed waived by CyDex.

8.6 **Public Announcements.** The parties will mutually agree on a press release to be issued upon execution of this Agreement or reasonably soon thereafter. Neither party shall make any subsequent public announcement concerning this Agreement or the terms hereof not previously made public without the prior written approval of the other party with regard to the form, content, and precise timing of such announcement, except as may be required to be made by either party in order to comply with applicable law, regulations, court orders, or tax, securities filings, financing arrangements, acquisitions, or sublicenses. Such consent shall not be unreasonably withheld or delayed by such other party. Before any such public announcement, the party wishing to make the announcement will submit a draft of the proposed announcement to the other party in sufficient time to enable such other party to consider and comment thereon.

9. REPRESENTATIONS AND WARRANTIES.

9.1 **Mutual Representations and Warranties.** Each party represents and warrants to the other (as of the Effective Date) as follows:

(i) it is a corporation duly organized and validly existing under the laws of the state or country of its incorporation;

(ii) it has the power and right to enter into this Agreement and to perform its obligations hereunder;

(iii) this Agreement has been duly authorized, executed and delivered by such party and constitutes a legal, valid and binding obligation of such party enforceable against such party in accordance with its terms except as enforceability may be limited by applicable bankruptcy, insolvency, reorganization, receivership, moratorium, fraudulent transfer, or other similar laws affecting the rights and remedies of creditors generally and by general principles of equity;

(iv) the execution, delivery and performance of this Agreement by such party do not conflict with any agreement, instrument or understanding, oral or written, to which such party is a party or by which such party may be bound, nor violate any law or regulation of any court, governmental body or administrative or other agency having authority over such party;

(v) all consents, approvals and authorizations from all governmental authorities or other third parties required to be obtained by such party in connection with the execution and delivery of this Agreement have been obtained:

(vi) no person or entity has or will have, as a result of the transactions contemplated by this Agreement, any right, interest or valid claim against or upon such party for any commission, fee or other compensation as a finder or broker because of any act by such party or its agents; and

(vii) it has not entered into any agreement with any third party that is in conflict with the rights granted to the other party pursuant to this Agreement.

9.2 **CyDex Representation.** CyDex owns all right, title and interest in and to, or in-licenses with the right to sublicense, the Captisol Patents listed on Exhibit A attached hereto.

9.3 **Disclaimer.** THE WARRANTIES SET FORTH IN THIS SECTION 9 AND IN THE SUPPLY AGREEMENT ARE PROVIDED IN LIEU OF, AND EACH PARTY HEREBY DISCLAIMS, ALL OTHER WARRANTIES, EXPRESS AND IMPLIED, RELATING TO THE SUBJECT MATTER OF THIS AGREEMENT, CAPTISOL, THE LICENSED PATENTS OR THE CAPTISOL DATA PACKAGE, INCLUDING BUT NOT LIMITED TO THE IMPLIED WARRANTIES OF

MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE, TITLE AND NON-INFRINGEMENT OF THIRD PARTY RIGHTS.

10. INDEMNIFICATION.

10.1 **By CyDex**. CyDex shall defend, indemnify and hold Sage and its Affiliates and Sublicensees, and each of their respective directors, officers, agents and employees, harmless from and against any and all losses, judgments, damages, liabilities, settlements, penalties, fines, costs and expenses (including the reasonable costs and expenses of attorneys and other professionals) (collectively "**Losses**") incurred by Sage as a result of any claim, demand, action or other proceeding (each, a "**Claim**") by a Third Party, to the extent such Losses arise out of: (a) the manufacture, use, handling, promotion, marketing, distribution, importation, sale or offering for sale of Captisol by CyDex and its Affiliates (including without limitation, the sale of Captisol by CyDex to Sage under the Supply Agreement); (b) infringement of any person's intellectual property rights in Captisol *per se*; (c) CyDex's breach of this Agreement, including without limitation any of its representations and warranties set forth in Section 9.1, and (d) CyDex's negligence or misconduct.

10.2 **By Sage**. Sage shall defend, indemnify and hold CyDex and its Affiliates, and each of their respective directors, officers, agents and employees, harmless from and against any and all Losses incurred by CyDex as a result of any Claim by a Third Party, to the extent such Losses arise out of: (a) the manufacture, use, handling, promotion, marketing, distribution, importation, sale or offering for sale of the Licensed Product by Sage, its Affiliates and Sublicensees, or the manufacture, use, handling, distribution or importation of the Probe Study Product by Sage, its Affiliates and Sublicensees; (b) any acts or omissions by Sage in connection with pre-clinical studies and clinical studies of actual or potential Licensed Products or Probe Study Products; (c) infringement of any person's intellectual property rights in connection with the subject matter of this Agreement (other than intellectual property rights in Captisol *per se*); (d) Sage's breach of this Agreement, including without limitation any of its representations and warranties set forth in Section 9.1 and (e) Sage's negligence or misconduct.

10.3 **Expenses**. As the parties intend complete indemnification, all costs and expenses of enforcing any provision of this Section 10 shall also be reimbursed by the indemnifying Party.

10.4 **Procedure.**

(a) The person intending to claim indemnification under this Section 10 (an **"Indemnified Party"**) shall promptly notify the other party (the **"Indemnifying Party"**) of any Claim in respect of which the Indemnified Party intends to claim such indemnification, and a reasonable explanation of the basis for the Claim and the amount of alleged Losses to the extent of the facts then known by the Indemnified Party. (Notwithstanding the foregoing, no delay or deficiency on the part of the Indemnified Party in so notifying the Indemnifying Party will relieve the Indemnifying Party of any liability or obligation under this Agreement except to the extent the Indemnifying Party has suffered actual prejudice directly caused by the delay or other deficiency.) The Indemnifying Party shall assume the defense thereof whether or not such Claim is rightfully brought; *provided, however*, that if the Indemnifying Party assumes the defense, the Indemnified Party shall have the right to employ counsel separate from counsel employed by the Indemnifying Party in any such action and to participate in the defense thereof, but the fees and expenses of such counsel employed by the Indemnified Party shall be at the sole cost and expense of the Indemnified Party unless the Indemnifying Party consents to the retention of such counsel or unless the named parties to any action or proceeding include both the Indemnifying Party and the Indemnified Party and a representation of both the Indemnifying Party and the Indemnified Party by the same counsel would be inappropriate due to the actual or potential differing interests between them. And *provided further* that, if the Indemnifying Party shall fail to assume the defense of and reasonably defend such Claim, the Indemnified Party shall have the right to retain or assume control of such defense and the Indemnifying Party shall pay (as incurred and on demand) the fees and expenses of counsel retained by the Indemnified Party.

(b) The Indemnifying Party shall not be liable for the indemnification of any Claim settled (or resolved by consent to the entry of judgment) without the written consent of the Indemnifying Party. Also, if the Indemnifying Party shall control the defense of any such Claim, the Indemnifying Party shall have the right to settle such Claim; *provided*, that the Indemnifying Party shall obtain the prior written consent (which shall not be unreasonably withheld or delayed) of the Indemnified Party before entering into any settlement of (or resolving by consent to the entry of judgment upon) such Claim unless (i) there is no finding or admission of any violation of law or any violation of the lights of any Person by an Indemnified Party, no requirement that the Indemnified Party admit fault or culpability, and no adverse effect on any other claims that may be made by or against the Indemnified Party and (ii) the sole relief provided is monetary damages that are paid in full by the Indemnifying Party and such settlement does not require the Indemnified Party to take (or refrain from taking) any action.

(c) Regardless of who controls the defense, the other party hereto shall reasonably cooperate m the defense as may be requested. Without limitation, the Indemnified Party, and its directors, officers, advisers, agents and employees, shall cooperate fully with the Indemnifying Party and its legal representatives in the investigations of any Claim.

11. LIMITATION OF LIABILITY.

EXCEPT FOR DAMAGES FOR WHICH A PARTY IS RESPONSIBLE PURSUANT TO ITS INDEMNIFICATION OBLIGATIONS SET FORTH IN SECTION 10 ABOVE, EACH PARTY SPECIFICALLY DISCLAIMS ALL LIABILITY FOR AND SHALL IN NO EVENT BE LIABLE FOR ANY INCIDENTAL, SPECIAL, INDIRECT OR CONSEQUENTIAL DAMAGES, EXPENSES, LOST PROFITS, LOST SAVINGS, INTERRUPTIONS OF BUSINESS OR OTHER DAMAGES OF ANY KIND OR CHARACTER WHATSOEVER ARISING OUT OF OR RELATED TO THIS AGREEMENT OR RESULTING FROM THE MANUFACTURE, HANDLING, MARKETING, SALE, DISTRIBUTION OR USE OF LICENSED PRODUCT OR USE (PURSUANT TO OR IN CONNECTION WITH THE RIGHTS GRANTED UNDER THIS AGREEMENT) OF THE LICENSED PATENTS AND CAPTISOL DATA PACKAGE, REGARDLESS OF THE FORM OF ACTION, WHETHER IN CONTRACT, TORT, STRICT LIABILITY OR OTHERWISE, EVEN IF SUCH PARTY WAS ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. EXCEPT WITH RESPECT TO THE INDEMNIFICATION SPECIFICALLY PROVIDED IN Section 10 ABOVE, IN NO EVENT SHALL EITHER PARTY'S TOTAL AGGREGATE LIABILITY FOR ALL CLAIMS ARISING OUT OF OR RELATED TO THIS AGREEMENT OR RESULTING FROM THE MANUFACTURE, HANDLING, MARKETING, SALE, DISTRIBUTION OR USE OF LICENSED PRODUCT OR PROBE STUDY PRODUCT OR USE OF THE LICENSED PATENTS AND CAPTISOL DATA PACKAGE PURSUANT TO OR IN CONNECTION WITH THE RIGHTS GRANTED UNDER THIS AGREEMENT EXCEED THE GREATER OF (I) $250,000 AND (II) THE TOTAL AMOUNTS ACTUALLY PAID UNDER THIS AGREEMENT BY SAGE TO CYDEX AS OF THE DATE SUCH CLAIM ARISES, PROVIDED, THAT THE FOREGOING LIMITATIONS SHALL NOT LIMIT CYDEX'S RIGHT TO TAKE ACTION TO ENFORCE THIS COMMERCIAL LICENSE AGREEMENT TO COLLECT AMOUNTS THAT ARE PROPERLY DUE AND OWING UNDER ARTICLE 4 HEREOF, NO ACTION, REGARDLESS OF FORM, ARISING OUT OF OR RELATED TO THIS AGREEMENT MAY BE BROUGHT BY EITHER PARTY MORE THAN TWO YEARS AFTER SUCH PARTY HAS KNOWLEDGE OF THE LEGAL AND FACTUAL BASIS EOR SUCH CAUSE OF ACTION OR AFTER EXPIRATION OF THE APPLICABLE STATUTORY LIMITATIONS PERIOD, WHICHEVER IS SOONER. FOR AVOIDANCE OF DOUBT, THE PARTIES' RESPECTIVE RIGHTS AND OBLIGATIONS WITH RESPECT TO ANY LIABILITY THAT MAY ACCRUE UNDER THE LICENSE AGREEMENT, ANY COMMERCIAL LICENSE AGREEMENT (OTHER THAN THIS AGREEMENT) OR ANY SUPPLY AGREEMENT OR IN CONNECTION WITH ACTIVITIES CONDUCTED PURSUANT TO OR CONTEMPLATED BY ANY SUCH AGREEMENTS SHALL BE DETERMINED PURSUANT TO THE TERMS OF THOSE AGREEMENTS AND NOT BY THE TERMS AND CONDITIONS SET FORTH IN THIS AGREEMENT.

12. MANAGEMENT OF LICENSED PATENTS.

12.1 **Prosecution and Maintenance**.

(a) **CyDex Patents.** CyDex shall maintain, at its sole cost and expense and using reasonable discretion, the Captisol Patents. CyDex shall have the sole right to control the prosecution and maintenance of patent applications and the selection of countries where patent applications arc tiled related to the Captisol Patents. CyDex agrees that, during the Term, it will use Commercially Reasonable Efforts to prosecute, obtain and maintain the Captisol Patents in the United States, China, Japan and the European Union. In the event that CyDex decides not to prosecute and maintain the Captisol Patents in a country or countries which is not a major market, CyDex shall provide not less than 30 days prior written notice of such decision, and Sage shall have the option to take over the prosecution and maintenance in such country or countries.

(b) **Licensed Product Patents.** Sage shall have the right to maintain, at its sole cost and expense and using reasonable discretion, the Licensed Product Patents. Sage shall have the sole right to control the prosecution and maintenance of patent applications and the selection of countries where patent applications are filed related to the Licensed Product Patents, provided that CyDex shall be provided with the right and opportunity to give comments and recommendations as to the overall strategy regarding the filing, prosecution and maintenance of the Licensed Product Patents. In the event that Sage decides not to prosecute and maintain the Licensed Product Patents in a country or countries, Sage shall provide not less than 30 days prior written notice of such decision, and CyDex shall have the option to take over the prosecution and maintenance in such country or countries.

(c) **Sage Patents and Sage Know-How.** Sage shall be the sole and exclusive owner of Sage Patents and Sage Know-How. Sage, at its own cost and expense, shall be solely responsible for prosecuting and maintaining Sage Patents.

12.2 **Infringement of Captisol Patents by Third Parties**.

(a) If Sage becomes aware that a third party may be infringing a Captisol Patent, it will promptly notify CyDex in writing, providing all information available to Sage regarding the potential infringement. CyDex shall take whatever, if any, action it deems appropriate, in its sole discretion, against the alleged infringer. If CyDex elects to take action, Sage shall, at CyDex's request and expense, cooperate and shall cause its employees and advisers to cooperate with CyDex in taking any such action, including but not

limited to, cooperating with the prosecution of any infringement suit by CyDex related to a Captisol Patent. Sage shall not take any such action against the alleged infringer related to a Captisol Patent without the written consent of CyDex.

(b) If Sage becomes aware that a third party may be infringing a Licensed Product Patent, it will promptly notify CyDex in writing, providing all information available to Sage regarding the potential infringement. Sage shall take whatever, if any, action it deems appropriate, in its sole discretion, against the alleged infringer if such infringement affects any of Sage's rights with respect to a Licensed Product. If Sage elects to take action, CyDex shall, at Sage's request and expense, cooperate and shall cause its employees and advisers to cooperate with Sage in taking any such action, including but not limited to, cooperating with the prosecution of any infringement suit by Sage related to a Licensed Product Patent. CyDex shall not take any such action against the alleged infringer related to a Licensed Product Patent without the written consent of Sage.

13. TERM AND TERMINATION.

13.1 **Term**. The term of this Agreement (the "**Term**") shall commence on the Effective Date and shall continue in effect unless and until terminated as set forth herein. Upon the expiration or termination of the Term, this Agreement, and the rights, licenses and obligations granted hereunder, shall terminate, subject only to Section 13.5.

13.2 **Termination for Breach**.

(a) **Notice.** If either party believes that the other is in material breach of this Agreement, then the party holding such belief (the **"Non-breaching Party"**) may deliver notice of such breach to the other party (the **"Notified Party"**). The Notified Party shall have […***…] days to cure such breach to the extent involving non-payment of amounts due hereunder, and […***…] days to either cure such breach for all other material breaches, or, if cure of such breach other than non-payment cannot reasonably be effected within such […***…] day period, to deliver to the Non-breaching Party a plan reasonably calculated to cure such breach within a timeframe that is reasonably prompt in light of the circumstances then prevailing but in no event in excess of an additional […***…] day period. Following delivery of such a plan, the Notified Party shall diligently carry out the plan and cure the breach and the cues period shall be extended by the time period provided in such plan but in no event to exceed […***…] days from the date of any initial breach notice delivered under this Section 13.2.

(b) **Failure to Cure.** If the Notified Party fails to cure a material breach of this Agreement as provided for in Section 13.2, then the Non-breaching Party may terminate this Agreement upon written notice to the Notified Party.

13.3 **Sage Right to Terminate**. Sage shall have the right to terminate this Agreement, without cause, on 180 days' prior written notice to CyDex.

13.4 **Termination of the Supply Agreement.** For clarity, this Agreement shall terminate if the Supply Agreement is terminated.

13.5 Survival. Notwithstanding any other provisions of this Agreement, any liability or obligation of either party to the other for acts or omissions before the termination of this Agreement shall survive the termination of this Agreement. And, such termination shall not relieve either party from obligations that are expressly indicated to survive termination of this Agreement, nor shall any termination of this Agreement relieve Sage of its obligation to pay CyDex royalties for all Licensed Product sold by Sage, its Affiliates or Sublicensees before the effective date of such termination. Sections 2.2 (Grant of License from Sage to CyDex), 4.1 (Payments and Royalties for Licenses) (to the extent owed but unpaid as of the date of termination of this Agreement), 4.2 (Currency), 4.3 (Taxes), 4.4 (Late Payments), 5 (Records; Reports; Audits), 6.5 (Access to Sage's Data), 7.3 (Adverse Event Reporting), 7.4 (Product Recalls), 8 (Confidentiality), 9.3 (Disclaimer), 10 (Indemnification), 11 (Limitation of Liability), 13.5 (Survival), and 14 (General Provisions) shall survive termination of this Agreement.

14. GENERAL PROVISIONS.

14.1 **Non-Solicitation**. During the Evaluation Period (as defined in the License Agreement) and for a period of one year thereafter, neither party shall solicit any employee of the other party to terminate his or her employment with such other party or to breach any other obligation to such other party. This section is not meant to encompass general solicitations such as may be found in newspaper advertisements and the like.

14.2 **Relationship of Parties**. Each of the parties hereto is an independent contractor and nothing in this Agreement is intended or shall be deemed to constitute a partnership, agency, employer-employee or joint venture relationship between the parties. No party shall have the right to, and each party agrees not to purport to, incur any debts or make any commitments or contracts for the other,

14.3 **Compliance with Law**. Each of the parties shall comply with all applicable international, federal, state and local laws, rules and regulations, including, but not limited to, import/export restrictions, laws, rules and regulations governing product quality and safety and patent, copyright and trade secret protection.

14.4 **Arbitration.**

(a) **Procedure**. Except as otherwise expressly set forth in this Agreement, any and all disputes or controversies arising out of or relating to this Agreement shall be exclusively and finally resolved by binding arbitration in accordance with the commercial arbitration rules of the American Arbitration Association then in effect, in Boston, Massachusetts. The arbitration shall be conducted by an arbitrator reasonably knowledgeable about the pharmaceutical industry and acceptable to CyDex and Sage. If CyDex and Sage cannot agree on a single arbitrator within 30 days after a demand for arbitration has been made, CyDex shall appoint an arbitrator, Sage shall appoint an arbitrator, the two arbitrators shall appoint a third arbitrator, and the three arbitrators shall hear and decide the issue in controversy. If either party fails to appoint an arbitrator within 45 days after service of the demand for arbitration, then the arbitrator appointed by the other party shall arbitrate any controversy in accordance with this Section 14.4(a). Except as to the selection of arbitrators, the arbitration proceedings shall be conducted promptly and in accordance with the rules of the American Arbitration Association then in effect. The expenses of any arbitration, including the reasonable attorney fees of the prevailing party, shall be borne by the party deemed to be at fault or on a pro-rata basis should the arbitration conclude in a finding of mutual fault.

(b) **Confidentiality of Proceedings.** All arbitration proceedings hereunder shall be confidential and the arbitrator(s) shall issue appropriate protective orders to safeguard each party's Confidential Information. Except as required by law, no party shall make (or instruct the arbitrator(s) to make) any public announcement with respect to the proceedings or decision of the arbitrators) without prior written consent of the other party.

(c) **Interim Equitable Relief.** Notwithstanding Section 14.4(a), but subject to the limitations set forth in Article 11, each party shall not be precluded from seeking equitable relief (including but not limited to interim injunctive relief) in any court having jurisdiction to protect its interests.

(d) **Binding Effect.** The provisions of this Section 14.4 shall survive any termination of this Agreement, and shall be severable and binding on the parties hereto, notwithstanding that any other provision of this Agreement may be held or declared to be invalid, illegal or unenforceable.

14.5 **Costs and Expenses**. Except as otherwise expressly provided in this Agreement, each party shall bear all costs and expenses associated with the performance of such party's obligations under this Agreement.

14.6 **Force Majeure**. Neither party shall be liable for failure to perform, or delay in the performance of, its obligations under this Agreement (other than payment obligations) when such failure or delay is caused by an event of force majeure. For purposes of this Agreement, an event of force majeure means any event or circumstance beyond the reasonable control of the affected party, including but not limited to, war, insurrection, riot, fire, flood or other unusual weather condition, explosion, act of God, peril of the sea, strike, lockout or other industrial disturbance, sabotage, accident, embargo, breakage of machinery or apparatus, injunction, act of governmental authority, compliance with governmental order or national defense requirements, or inability to obtain fuel, power, raw materials, labor or transportation facilities. If, due to any event offeree majeure, either party shall be unable to fulfill its obligations under this Agreement (other than payment obligations), the affected party shall immediately notify the other party of such inability and of the period during which such inability is expected to continue and the time for performance shall be extended for a number of days equal to the duration of the force majeure.

14.7 **Notices**. Any notice, request, or communication under this Agreement shall be effective only if it is in writing and personally delivered; sent by certified mail, postage pre-paid; facsimile with receipt confirmed; or by nationally recognized overnight courier with signature required, addressed to the parties at the addresses stated below or such other persons and/or addresses as shall be furnished in writing by any party in accordance with this Section 14.7. Unless otherwise provided, all notices shall be sent:

If to CyDex, to:

CyDex Pharmaceuticals, Inc.
11119 North Torrey Pines Road, Suite 200
La Jolla, CA 92037
Attention: President
Fax: (858) 550-7272

With a copy to:
General Counsel
Ligand Pharmaceuticals Incorporated
11085 North Torrey Pines Road, Suite 200
La Jolla, CA 92037
Fax: (858)550-7272

If to Sage, to:

Sage Therapeutics, Inc.
29 Newbury Street, Suite 301
Boston, MA 02116
Attention: President
Fax: (617) 859-2891

If sent by facsimile transmission, the date of transmission shall be deemed to be the date on which such notice, request or communication was given. If sent by overnight courier, the next business day after the date of deposit with such courier shall be deemed to be the date on which such notice, request or communication was given. If sent by certified mail, the third business day after the date of mailing shall be deemed the date on which such notice, request or communication was given.

14.8 **Use of Name; Publicity**. No party shall use the name, trademark, trade name or logo of the other party, its Affiliates or their respective employee(s) in any publicity, promotion, news release or public disclosure relating to this Agreement or its subject matter, without the prior express written permission of the other party, except as may be required by law or the rules of NASDAQ. The parties agree that a party may disclose this Agreement's existence and terms, and material developments or material information generated under this Agreement, in (i) securities filings with the Securities and Exchange Commission (or equivalent foreign agency) to the extent required by law, or (ii) under conditions of confidentiality/nonuse in connection with investment and similar corporate transactions. Notwithstanding the above, once a public announcement has been made, either party shall be free to disclose to third parties any information contained in said public announcement. In the event of a required public announcement, the party making such announcement shall provide the other party with a copy of the proposed text before such announcement sufficiently in advance of the scheduled release of such announcement to afford such other party a reasonable opportunity to review and comment upon the proposed text and the timing of such disclosure.

14.9 **Governing Law**. This Agreement shall be governed by and construed in accordance with the internal laws of the State of California (without giving effect to any conflicts of law principles that require the application of the law of a different state).

14.10 **Entire Agreement; Amendment**. The Commercial License Agreement and all Exhibits attached hereto contain the entire agreement of the parties relating to the subject matter hereof and thereof and supersede any and all prior or contemporaneous agreements, written or oral, between CyDex (and/or any of its Affiliates) and Sage (and/or any of its Affiliates) relating to the subject matter hereof and thereof, including, without limitation, the Old Agreement; provided, that (a) any confidentiality/nonuse provisions of any prior agreement (other than the Old Agreement) are not superseded and will remain in effect in addition to the confidentiality/nonuse provisions hereof, (b) the provisions stated to survive termination of the Old Agreement, as set forth in Section 13.5 therein, shall survive, other than Sections 6.3, 8 and 13.3, which are hereby terminated, and Section 4 therein shall survive only with respect to amounts owed but unpaid as of the Effective Date), and (c) the Supply Agreement is not superseded and will remain in effect. This Agreement cannot be amended except by way of an express writing signed by both parties.

14.11 **Binding Effect**. This Agreement shall be binding upon, and the rights and obligations hereof shall apply to, CyDex and Sage and any successor(s) and permitted assigns. The name of a party appearing herein shall be deemed to include the names of such party's successors and permitted assigns to the extent necessary to carry out the intent of this Agreement.

14.12 **Waiver**. The rights of either party under this Agreement may be exercised from time to time, singularly or in combination, and the exercise of one or more such rights shall not be deemed to be a waiver of any one or more of the others. No waiver of any breach of a term, provision or condition of this Agreement shall be deemed to have been made by either party unless such waiver is addressed in writing and signed by an authorized representative of that party. The failure of either party to insist upon the strict performance of any of the terms, provisions or conditions of this Agreement, or to exercise any option contained in this Agreement, shall not be construed as a waiver or relinquishment for the future of any such term, provision, condition or option or the waiver or relinquishment of any other term, provision, condition or option.

14.13 **Severability**. If any provision of this Agreement is determined by a final and binding court or arbitration judgment to be invalid, illegal or unenforceable to any extent, such provision shall not be not affected or impaired up to the limits of such invalidity, illegality or unenforceability; the validity, legality and enforceability of the remaining provisions of this Agreement shall not be affected or impaired in any way; and the parties agree to negotiate in good faith to replace such invalid, illegal and unenforceable provision (or portion of provision) with a valid, legal and enforceable provision that achieves, to the greatest lawful extent under this Agreement, the economic, business and other purposes of such invalid, illegal or unenforceable provision (or portion of provision). This Agreement shall not be invalidated by any future determination that any or all of the Licensed Patents have expired or been invalidated.

14.14 **Assignment**, Sage may not assign its rights or delegate its obligations under this Agreement, in whole or in part, by operation of law or otherwise, to any third party without the prior written consent of CyDex, which consent shall not be unreasonably withheld. Notwithstanding the foregoing, Sage may assign its rights and delegate its obligations under this Agreement to an Affiliate or to a third party successor, whether by way of merger, sale of all or substantially all of its assets, sale

of stock or otherwise, without CyDex's prior written consent. As a condition to any permitted assignment hereunder, the assignor must guarantee the performance of any assignee to the terms and obligations of this Agreement. Any assignment by Sage not in accordance with this Section 14.14 shall be void. CyDex has the right to assign its rights or delegate its obligations under this Agreement, in whole or in part, by operation of law or otherwise, to any third party, without any requirement for consent of Sage provided that CyDex also assigns all of its right, title and interest in all assets, including without limitation, intellectual property rights, pertaining to its Captisol business to the same third party contemporaneous with the assignment of this Agreement.

14.15 **Third Party Beneficiaries**. Except for the rights of Indemnified Parties pursuant to Section 10 hereof, and subject to Section 8.5 hereof, the terms and provisions of this Agreement are intended solely for the benefit of each party hereto and their respective successors or permitted assigns and it is not the intention of the parties to confer third-party beneficiary rights upon any other person, including without limitation Sublicensees. The enforcement of any obligation of CyDex under this Agreement shall only be pursued by Sage or such Indemnified Party, and not Sublicensees.

14.16 **Remedies Cumulative**. Except as provided in Section 11, any enumeration of a party's rights and remedies in this Agreement is not intended to be exclusive, and a party's rights and remedies are intended to be cumulative to the extent permitted by law and include any rights and remedies authorized in law or in equity.

14.17 **Headings**. The descriptive headings of this Agreement are for convenience only, and shall be of no force or effect in construing or interpreting any of the provisions of this Agreement.

14.18 **Interpretation**. The language used in this Agreement is die language chosen by the parties to express their mutual intent, and no provision of this Agreement will be interpreted for or against any party because that party or its attorney drafted the provision.

14.19 **Counterparts**. This Agreement may be executed in counterparts, each of which shall constitute an original document, but both of which shall constitute one and the same instrument.

[Remainder of this page left blank intentionally]

IN WITNESS WHEREOF, the parties have executed this Commercial License Agreement as of the Effective Date.

CYDEX PHARMACEUTICALS, INC.

By: /s/ Charles Berkman

Name: Charles Berkman

Title: VP and Secretary

SAGE THERAPEUTICS, INC.

By: /s/ Kimi Iguchi

Name: Kimi Iguchi

Title: CFO

August 21, 2013

AMENDMENT TO COMMERCIAL LICENSE AGREEMENT

THIS AMENDMENT TO COMMERCIAL LICENSE AGREEMENT (this "**Amendment**") is made this 30th day of April, 2014 (the "**Amendment Effective Date**") between:

CYDEX PHARMACEUTICALS, INC., a Delaware corporation ("**CyDex**"); and

SAGE THERAPEUTICS INC., a Delaware corporation ("**Sage**").

RECITALS

WHEREAS, CyDex and Sage entered into a Commercial License Agreement (the "**Agreement**") as of August 21, 2013;

WHEREAS, CyDex and Sage wish to amend the Agreement in accordance with Section 14.10 thereof, including by deleting the payment of $[…***…] upon the first submission of an IND, or an amendment to an IND, for a Probe Study (as defined in the Agreement prior to the Amendment Effective Date) and, instead, requiring such amount, along with an additional $[…***…], to be paid in consideration of CyDex entering into this Amendment, as set forth below;

NOW, **THEREFORE**, in consideration of the following mutual promises and other good and valuable consideration, the receipt and sufficiency of which are acknowledged, the parties, intending to be legally bound, agree as follows:

1. DEFINITIONS.

1.1 DEFINITIONS. All terms used, but not defined, in this Amendment shall have the meaning set forth in the Agreement.

1.2 AMENDED DEFINITIONS. The following definitions are hereby amended to read as follows:

"**Field**" means the treatment, diagnosis or prevention of any disease or symptom in humans or animals, including the Epilepticus Field, the TBI Field and each Additional Subfield.

"**Pfizer**" means Pfizer Inc.

"Probe Study" means the conduct of a human study (excluding any Phase III Study or Pivotal Study) of a Licensed Product in and for an Additional Subfield in fewer than fifty (50) subjects.

1.3 ADDITIONAL DEFINITIONS. The following definitions are added to Section 1 of the Agreement:

"**Additional Subfield**" means each disease or symptom in humans or animals that is not a Primary Subfield; for clarity, an Expansion to a particular Additional Subfield is not a separate Additional Subfield.

"**Epilepticus Field**" means the field of therapeutic use against status epilepticus in humans.

"**Expansion**" means, with respect to a particular Additional Subfield for which a clinical study was conducted, an NDA was filed or Marketing Approval was obtained, an additional clinical study, or receipt of NDA or Marketing Approval, of the Licensed Product in such Additional Subfield for a different subpatient population, line of therapy or new use as a monotherapy or in combination with another treatment or drug, other than the population, line of therapy or use for which the prior clinical study(ies) were conducted, NDA was filed or Marketing Approval was received.

"**Phase II Study**" means the conduct of a human study, as described in 21 C.F.R. §312.21(b) and its foreign equivalents, of a Licensed Product, but excluding any Probe Study.

"**Phase III Study**" means the conduct of a human study, as described in 21 C.F.R. §312.21(c) and its foreign equivalents, of a Licensed Product.

"Pivotal Study" means a controlled pivotal clinical study of a Licensed Product that is prospectively designed to demonstrate statistically whether such Licensed Product is effective and safe for use in a particular indication in a manner sufficient to obtain Marketing Approval to market such product in the United States, China, Japan or Germany (via the European Union (including the European Medicines Authority) or otherwise).

"**Primary Subfield**" means each of the following: the Epilepticus Field or the TBI Field.

"**Subfield**" means each Primary Subfield, on a Primary Subfield-by-Primary Subfield basis, and each Additional Subfield, on an Additional Subfield-by-Additional Subfield basis.

"**TBI Field**" means the treatment of traumatic brain injury in humans.

1.4 Deleted Definitions. The definitions of "Probe Condition" and "Probe Study Product", and all references thereto, are hereby deleted from the Agreement.

2. Probe Study License. Section 2.1(b) of the Agreement is hereby amended to read:

(b) [Intentionally Omitted].

3. Negative Covenant. Section 2.1(e) of the Agreement is hereby amended to read:

(e) Negative Covenant. During the term of this Agreement, CyDex and its Affiliates shall not grant any rights to any Third Party that conflict with the exclusive rights granted herein to Sage or that conflict with or otherwise impair Sage's ability to conduct the activities described herein. Without limiting the generality of the foregoing, in the event that CyDex or any of its Affiliates become aware that a Third Party is conducting research, development or commercial activities using the Compound with Captisol, then CyDex shall take all reasonable measures to cease the supply of Captisol to such Third Party and to any other Third Party that is determined to be supplying Captisol to such Third Party.

4. Payments.

4.1 Section 4.1(a)(ii) of the Agreement is hereby amended to read:

(ii) CyDex acknowledges receipt of the payment of $300,000 on the Effective Date.

4.2 In consideration of CyDex entering into this Amendment, Sage agrees to pay to CyDex $200,000 on the Amendment Effective Date.

4.3 Section 4.1(b) of the Agreement is hereby amended to read:

(b) Milestone Payments.

(i) Epilepticus Field and TBI Field. Within […***…] days following the occurrence of each of the milestone events listed below with respect to the Licensed Product in either Primary Subfield, Sage shall provide written notice to CyDex of the achievement of such milestone event, and within […***…] days of the occurrence of each of the milestone events, pay to CyDex the applicable non-refundable milestone fee listed next to each such event in further consideration of the rights granted Sage hereunder. The milestone payments (each payable only one time per each of the Primary Subfields, regardless of the number of times achieved by the Licensed Product for such Primary Subfield; for the avoidance of doubt, if the same Licensed Product first achieves one or more given milestones for both the Epilepticus Field and the TBI Field, then the milestone payment for that event must be paid twice; and in no event shall the maximum payment under this Section 4.1(b)(i) exceed $[…***…]) are as follows. If any such milestone is achieved in the relevant Primary Subfield before all prior sequential milestones have been actually achieved in such Primary Subfield, then any and all prior sequential milestones which were not previously actually achieved shall be deemed to have thereby been achieved with respect to such Primary Subfield, and the milestone payments for such deemed-achieved milestones shall also be payable with respect to such Primary Subfield within such […***…] days.

	MILESTONE ACHIEVED IN THE RELEVANT PRIMARY SUBFIELD	**MILESTONE PAYMENT**
(i)	[…***…]	$ […***…]
(ii)	[…***…]	$ […***…]
(iii)	[…***…]	$ 750,000
(iv)	Upon receipt of the first Marketing Approval from the FDA for a Licensed Product	$ 3,000,000

(ii) Additional Subfields. Within […***…] days following the occurrence of each of the milestone events listed below with respect to the Licensed Product in an Additional Subfield, Sage shall provide written notice to CyDex of the achievement of such milestone event, and within […***…] days of the occurrence of each of the milestone events, pay to CyDex the applicable non-refundable milestone fee listed next to each such event in further consideration of the rights granted Sage hereunder. The milestone payments (each payable only one time per each of the first two (2) Additional Subfields, regardless of the number of times achieved by the Licensed Product for such Additional Subfield; for the avoidance of doubt, if the same Licensed Product first achieves one or more given milestones for two Additional Subfields, then the milestone payment for that event must be paid twice; and in no

event shall the maximum payment under this Section 4.1(b)(ii) exceed $[…***…]) are as follows. Subject to the preceding sentence, if any such milestone is achieved in the relevant Additional Subfield before all prior sequential milestones have been actually achieved in such Additional Subfield, then any and all prior sequential milestones which were not previously actually achieved with respect to such Additional Subfield shall be deemed to have thereby been achieved, and the milestone payments for such deemed-achieved milestones shall also be payable with respect to such Additional Subfield within such […***…] days.

	MILESTONE	MILESTONE PAYMENT
(i)	[…***…]	$ […***…]
(ii)	[…***…]	$ […***…]
(iii)	[…***…]	$ […***…]
(iv)	[…***…]	$ […***…]

4.4 Section 4.1(d) of the Agreement is hereby deleted in its entirety.

5. DILIGENCE. The penultimate sentence of Section 6.1 of the Agreement is hereby amended to read:

For clarity, Sage may meet the requirements of this **Section 6.1** through its activities with respect to the Licensed Product in just one of the Subfields.

6. REPRESENTATIONS AND WARRANTIES. CyDex represents and warrants to Sage (as of the Amendment Effective Date) as follows:

(i) Neither it nor any of its Affiliates has entered into any agreement with any third party (including any Pre-Existing Agreement) that is in conflict with the rights granted to Sage pursuant to this Agreement; and

(ii) Neither CyDex nor any of its Affiliates has granted any Affiliate of CyDex or any Third Party any rights to develop or commercialize any pharmaceutical composition comprising the Compound combined with or formulated using Captisol.

7. INDEMNIFICATION. Section 10.1(c) is hereby amended to read:

(c) CyDex's breach of this Agreement, including without limitation any of its representations and warranties set forth in **Sections 9.1** and **9.2** of the Agreement or in Section 6 of the Amendment,

8. INTERPRETATION. The following sentence is added to the end of Section 14.18 of the Agreement:

Except as the context otherwise requires, (a) the word "including" or correlatives thereof, means "including without limitation," and (b) the word "or" means "and/or."

9. ENTIRE AGREEMENT/AMENDMENTS. Except as amended by this Amendment, the Agreement shall remain in full force and effect. After the Amendment Effective Date, every reference in the Agreement to the "Agreement" shall mean the Agreement as amended by this Amendment.

10. Counterparts. This Amendment may be executed in counterparts, each of which shall constitute an original document, but both of which shall constitute one and the same instrument.

[Remainder of this page left blank intentionally]

IN WITNESS WHEREOF, the parties have executed this Amendment to Commercial License Agreement as of the Amendment Effective Date.

CYDEX PHARMACEUTICALS, INC.

By: /s/ Charles Berkman
Name: Charles Berkman
Title: VP and Secretary

SAGE THERAPEUTICS, INC.

By: /s/ Jeffrey Jonas
Name: Jeffrey Jonas
Title: CEO

EXHIBIT 10.5

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. […***…] denotes omissions.

Non-Exclusive License Agreement

between
The Regents of the University of California

and

Sage Therapeutics, Inc.
for
Allopregnanolone in the Treatment of Status Epilepticus and Post-Partum Depression

File No. […*…]**

Table of Contents

Non-Exclusive License Agreement
for
Allopregnanolone in the Treatment of Status Epilepticus
and Post-Partum Depression

(File No. **[…***…]**)

This non-exclusive license agreement ("Agreement") is effective this 23rd day of October 2013 ("Effective Date"), by and between The Regents of the University of California ("The Regents"), a California corporation, having its statewide administrative offices at 1111 Franklin Street, 12th Floor, Oakland, California 94607-5200, as represented by its Davis campus, having an address at UC Davis InnovationAccess, 1850 Research Park Drive, Suite 100, Davis, California 95618 and Sage Therapeutics, Inc. ("Licensee"), a Delaware corporation, having a principal place of business at 215 First Street, Cambridge, Massachusetts 02142. The Regents and Licensee will be referred to herein, on occasion, individually as "Party" or collectively as "Parties."

RECITALS

Whereas, the Material (defined below) was made at the University of California, Davis campus ("UC Davis") by Dr. Michael Rogawski ("Investigator");

Whereas, the development of the Material was sponsored in part by one or more agencies of the United States Government; accordingly, under Federal law, the Material is tangible research product owned by The Regents; also, any related invention rights are subject to the rights of the United States Government under 35 USC §§ 200-212 and implementing regulations; and The Regents is obligated to grant to the United States Government a non-exclusive, non-transferable, irrevocable, paid-up license to use the Material by or on behalf of the United States Government throughout the world;

Whereas, Licensee has requested from The Regents the Material as defined in Paragraph 1.1 below for the Research Use defined in Paragraph 1.6(ii) below, which Material was developed with the Department of Defense support under contract number W81XWH-09-1-0746 administered by the USA Med Research ACQ Activity;

Whereas, The Regents and Licensee have entered into a Letter Agreement (UC Agreement Control No. 2013-30-0469) effective March 12, 2013 ("Letter Agreement") for the purpose of granting Licensee an exclusive right to negotiate an exclusive license;

Whereas, The Regents and Licensee entered into an Investigational New Drug Application ("IND") Data Transfer Agreement (UC Agreement Control No. 2013-210514) effective April 1, 2013 ("IND Data Transfer Agreement") for the purpose of reference of data in Licensee's pre-IND interactions with the Food and Drug Administration ("FDA") in advance of a submission of Licensee's IND application for use of Allopregnanolone for the treatment of status epilepticus and pre-IND discussion pertaining to an IND application for such indication with the FDA;

Whereas, The Regents and Licensee entered into a Material Transfer Agreement (File No. 2013-816-M) effective July 9, 2013 ("MTA") for the purpose of The Regents to transfer a portion of the Material, Allopregnanolone (GMP grade chemical), to Licensee for developing a clinically relevant formulation for treatment of status epilepticus, such use limited to formulation/process development (prototype batch, material compatibility, filter study validation); engineering batch manufacture; and analytical support (re-release of API);

Whereas, The Regents and Licensee desire to have the Data (defined below) and Material (defined below) used by Licensee so that products resulting therefrom may be developed, commercialized and available for public use and benefit; and

Whereas, Licensee desires to acquire, and The Regents desires to grant, a license under Property Rights in accordance with the terms herein.

Now, therefore, the Parties agree as follows:

1. DEFINITIONS

1.1 "Material" means approximately […***…] kilograms of Allopregnanolone (GMP grade chemical), approximately […***…] grams of which was provided to Licensee prior to the Effective Date pursuant to the MTA.

1.2 “Modifications” mean substances created or made by or on behalf of the Licensee that either contain or incorporate the Material or were otherwise created through the use of the Material. For the purpose under this Agreement, pharmaceutical formulations of Material shall be considered Modifications. Notwithstanding the above, Licensee shall not chemically modify or alter the chemical structure of the Material.

1.3 “Data” means the confidential Investigational New Drug (IND) application package (IND Number 111,085) owned by The Regents and generated by the The Regents’ Investigator for the use of Allopregnanolone for Traumatic Brain Injury and any updates to such IND.

1.4 “Derived Product” means a product containing Allopregnanolone produced by or on behalf of Licensee for Sale or Sold as a drug for status epilepticus and/or post-partum depression.

1.5 “Property Rights” means all personal proprietary rights of The Regents covering the tangible personal property in the Data and Material.

1.6 “Licensed Field of Use” means the (a) use of Data for Reference Use as defined below and (b) use of Material or Modifications for Research Use as defined below.

(i) “Reference Use” means use of Data by the Licensee, and by affiliates, contractors, consultants, agents and/or vendors on behalf of Licensee, for the sole purpose of reference or incorporation to the extent that such reference or incorporation identifies, labels it as an excerpt from Data and acknowledges UC Davis as the source of the Data in Licensee’s IND application(s) with the FDA for use of Allopregnanolone for the treatment of status epilepticus and/or postpartum depression. […***…].

(ii) “Research Use” means use of Material or Modifications to develop a clinically relevant pharmaceutical formulation and use of such pharmaceutical formulation for FDA-approved human clinical trials for treatment of status epilepticus and/or post-partum depression. Research Use includes transfer of Material by Licensee to a third party who uses such Material to create a Modification on behalf of Licensee.

1.7 “Sale” means, for Derived Products, the act of selling, leasing or otherwise transferring, providing, or furnishing such product for any consideration. Correspondingly, “Sell” means to make or cause to be made a Sale, and “Sold” means to have made or caused to be made a Sale.

1.8 “Net Sales” means the gross invoice price charged by, and the value of any noncash consideration owed to, Licensee for Sales of Derived Products in the Licensed Territory, less the sum of the following actual and customary deductions where applicable: cash, trade or quantity discounts; sales, use, tariff, ^import/export duties or other excise taxes when included in gross sales, but not value-added taxes assessed or income taxes derived from such sales; transportation and related freight/shipping insurance charges; and allowances or credits to customers because of rejections or returns.

1.9 “Licensed Territory” means the United States of America and its territories and possessions, and any foreign countries where Property Rights exist.

1.10 “Research Use Results” means all technical information and data relating to the Licensed Field of Use.

2. GRANT; RESTRICTIONS

2.1 Subject to the limitations set forth in this Agreement, including without limitation the licenses granted to the United States Government referred to in the Recitals above and the rights reserved in Paragraphs 2.3 and 2.7 below, The Regents hereby grants to Licensee a non-exclusive license under Property Rights, in the Licensed Territory, to the extent such license rights may be lawfully granted, to (a) use Data for the Reference Use under the Licensed Field of Use in compliance with all applicable statutes and regulations, and (b) possess and use Material or Modifications solely for Research Use.

2.2 (a) The rights granted to Licensee under Paragraph 2.1 above are limited for the purposes stated in this Agreement. Any other use of Data, Material or Modifications is expressly prohibited.

(b) Licensee agrees to use Material or Modifications in compliance with all applicable statutes and regulations, including, but not limited to, those related to research involving the use of humans, animals or recombinant DNA. The Material or Modifications will not be used by Licensee for commercial purposes or any other use other than the Research Use (provided that the use of Materials or Modifications to develop a clinically relevant pharmaceutical formulation, use of such pharmaceutical formulation for FDA-approved human clinical trials, for the purposes of eventual commercial sale of such pharmaceutical formulation, shall not be considered a use for commercial purposes).

(c) Licensee shall not analyze the Material for chemical composition or physical structure or have or allow any component of the Material to be analyzed or make any use of any such analysis other than for quality testing purposes to meet FDA submission requirements. Licensee shall not make chemical modification or alter the chemical structure of the Material in any way except as pursuant to Paragraph 1.6.

2.3 The Regents reserves the right to do any one or more of the following:

(a) publish any technical data resulting from research performed by The Regents relating to the Data and Material;
(b) make and use the Data and Material and associated technology for educational and research purposes;
(c) practice Property Rights for educational and research purposes, including in order to make and use products;

(d) allow other educational and non-profit institutions to do any one or more of the activities of Subparagraphs 2.3 (a), (b), and (c) above, for educational and research purposes; and

(e) transfer or grant rights in the Data and Material as further described in Paragraph 2.7.

2.4 The Regents, through the Investigator, will endeavor to transfer to Licensee, the remaining amount (approximately […***…] grams) of the Material within fourteen (14) days from the date this Agreement is executed by The Regents and Licensee shall pay all the storage, handling, associated shipping costs and incidental expenses, which shall be included in (and not separate from) the Material Fee (defined below). Licensee acknowledges that The Regents, through the Investigator, has transferred a portion of Material to Licensee in accordance with the terms and conditions of the MTA. The Material will be delivered to:

[…***…]

2.5 The Regents is not obligated to provide any replacements or any additional amounts of Material.

2.6 Except as otherwise permitted under this Agreement, Licensee will not Sell, donate, abandon, or otherwise transfer Data to any third party and will not Sell, donate, abandon, or otherwise transfer ownership of Material to any third party. Licensee acknowledges that The Regents retains ownership of Data and that ownership of Data is not transferred to Licensee under this Agreement. However, ownership (title) of the Material will transfer to Licensee upon receipt by Licensee. For such Material that has title transferred to Licensee, such Material will otherwise remain as Material under this Agreement and all other terms of this Agreement will apply.

2.7 The Regents is free to transfer or grant rights in the Data to third parties for any purposes.

3. SUBLICENSES

3.1 This Agreement specifically excludes the right of Licensee to issue sublicenses.

4. MATERIAL FEE

4.1 Licensee will pay to The Regents a sum of […***…] Dollars ($[…***…]) for the costs of storage, packaging, transport and incidental expenses for the Material (“Material Fee”).

4.2 The Material Fee is due fifteen (15) days after receipt of an invoice therefor. The Material Fee is non-creditable, non-refundable and not an advance against royalties or other payments due under this Agreement.

5. ROYALTIES AND MILESTONES

5.1 Licensee will pay to The Regents earned royalties (“Earned Royalties”) at the rate of […***…] percent ([…***…]%) of the Net Sales in the Licensed Territory of each Derived Product for fifteen (15) years after first Sale of each such Derived Product.

5.2 Earned Royalties accruing to The Regents will be paid to The Regents semiannually within […***…] days after the end of each […***…] month period as follows: November 1 (for the […***…] month period commencing March 1 of that year), and May 1 (for the […***…] month period commencing September 1 of the prior calendar year).

5.3 All consideration due The Regents will be payable in United States dollars. When Derived Products are Sold for monies other than United States dollars, the Earned Royalties will first be determined in the foreign currency of the country in which the Sale

was made and then converted into equivalent United States dollars. The exchange rate will be that quoted in the *Wall Street Journal* on the last business day of the reporting period.

5.4 Payments due for Sales occurring in any country outside the United States will not be reduced by any taxes, fees, or other charges imposed by the government of such country on the remittance of royalty income. Licensee will also be responsible for all bank transfer charges.

5.5 Licensee will make all payments under this Agreement either by check or electronic transfer, payable to "The Regents of the University of California" and Licensee will forward such payments to The Regents at the address shown in Paragraph 20.1 below.

5.6 No Earned Royalties will be collected or paid hereunder on Sales of Derived Products to, or for use by, the United States Government. Licensee will reduce the amount charged for such Sales by an amount equal to the Earned Royalties otherwise due The Regents as provided herein.

5.7 (a) Within sixty (60) days after the […***…], whichever occurs first, Licensee will pay to The Regents a one-time, non-refundable and non-creditable milestone fee of seventy-five thousand dollars ($75,000).

(b) Within sixty (60) days after the […***…], whichever occurs second and for which a milestone fee was not paid under Paragraph 5.7(a), Licensee will pay to The Regents a onetime, non-refundable and non-creditable milestone fee of twenty-five thousand dollars ($25,000).

(c) For clarity, the milestone fees in clauses (a) and (b) above shall each be payable only once, […***…].

6. DILIGENCE

6.1 Licensee, upon execution of this Agreement, will use commercially reasonable efforts to proceed with the development, manufacture, and Sale of one or more Derived Products and will use commercially reasonable efforts to market such Derived Products in quantities sufficient to meet the market demand.

6.2 In addition to its obligations under Paragraph 6.1, Licensee specifically commits to obtain all necessary governmental approvals in each country where Derived Products are made, manufactured, used, Sold, imported, or offered for Sale.

6.3 If Licensee is unable to meet any of its diligence obligations set forth in Paragraphs 6.1 and 6.2, then The Regents will have the right and option to terminate this Agreement in accordance with Paragraph 10.1 below.

7. PROGRESS AND ROYALTY REPORTS

7.1 For the period beginning January 1, 2014, within sixty (60) days after each subsequent June 30 and December 31, Licensee will submit to The Regents a semi-annual progress report covering Licensee's Research Use Results and the test conditions used, activities related to the development and testing of all Derived Products, and the obtaining of necessary governmental approvals, if any, for marketing Derived Products in the United States. These progress reports will be made for all development activities. If Licensee fails to submit a timely progress report to The Regents, The Regents will be entitled to terminate this Agreement in accordance with Paragraph 10.1 below. If either Party terminates this Agreement before any Derived Products are Sold or before this Agreement's expiration, a final progress report covering the period prior to termination must be submitted within thirty (30) days of termination.

7.2 Each progress report will be a sufficiently detailed summary of activities of Licensee so that The Regents may evaluate and determine Licensee's progress in the development of Derived Product and Research Use, and in meeting its diligence obligations under Article 6, and will include (but not be limited to) the following: summary of work completed and in progress; current schedule of anticipated events and milestones; and anticipated market introduction dates.

7.3 In Licensee's progress report immediately subsequent to the first Sale by Licensee of Derived Products, Licensee will report the date of such first Sale.

7.4 After the first Sale of a Derived Product, Licensee will provide semi-annual royalty reports to The Regents on or before November 1 (for the six (6)-month period commencing March 1 of that year), and May 1 (for the six (6)-month period commencing September 1 of the prior calendar year). Each such royalty report will include at least the following:

(a) The number of Derived Products manufactured and the number of Derived Products Sold;
(b) Gross revenue from Sale of Derived Products;
(c) Net Sales pursuant to Paragraph 1.8;

(d) Itemized deductions pursuant to Paragraph 1.8;

(e) Listing of distributors Selling Derived Products; and

(f) Total Earned Royalties due to The Regents.

7.5 If no Sales of Derived Product have occurred during the reporting period, a statement to this effect is required in the royalty report for that period.

8. BOOKS AND RECORDS

8.1 Licensee will keep full, true, and accurate books of accounts containing all particulars that may be necessary for the purpose of showing the amount of Earned Royalties payable to The Regents and Licensee's compliance with other obligations under this Agreement. Said books of accounts will be kept at Licensee's principal place of business or the principal place of business of the appropriate division of Licensee to which this Agreement relates. Said books and the supporting data will be open at all reasonable times during normal business hours upon at least ten (10) business days' notice, for five (5) years following the end of the calendar year to which they pertain, to the inspection and audit by representatives of The Regents reasonably acceptable to Licensee for the purpose of verifying Licensee's royalty statement or compliance in other respects with this Agreement. Such representatives will be bound to hold all information in confidence except as necessary to communicate Licensee's noncompliance with this Agreement to The Regents. The Regents may conduct such an inspection and audit only once in any twelve (12)-month period, and may not conduct such an inspection and audit with respect to the same time period more than once.

8.2 The fees and expenses of The Regents' representatives performing such an examination will be borne by The Regents. However, if an error in underpaid royalties to The Regents of more than five percent (5%) of the total Earned Royalties due for any year is discovered, then the fees and expenses of these representatives will be borne by Licensee.

9. LIFE OF THE AGREEMENT

9.1 This Agreement shall be effective as of the Effective Date and unless terminated earlier pursuant to Article 6, Article 10, Article 11 or Article 25, this Agreement shall continue in effect until fifteen (15) years after the last-to-occur first Sale of a Derived Product (the effective period of the Agreement being referred to herein as the "Term"). Notwithstanding the foregoing, in no event will the Term extend beyond twenty-seven (27) years after the Effective Date. Upon expiration of this Agreement, the license set forth in Paragraph 2.1 shall become perpetual, irrevocable, royalty-free and fully paid-up, subject to Paragraph 9.2.

9.2 Any termination or expiration of this Agreement will not affect the rights and obligations set forth in the following Articles:

Article 1	Definitions
Article 8	Books and Records
Article 9	Life of the Agreement
Article 12	Disposition of Material, Modifications, and Derived Products on Hand upon Termination
Article 13	Use of Names and Trademarks
Article 14	Limited Warranties
Article 15	Indemnification
Article 19	Notices
Article 20	Payments
Article 22	Confidentiality
Article 27	Applicable Law; Venue; Attorneys' Fees
Article 28	Scope of Agreement

9.3 The termination or expiration of this Agreement will not relieve Licensee of its obligation to pay any monies owing at the time of such termination or expiration and will not relieve any obligations, of either Party to the other Party, established prior to termination or expiration.

10. TERMINATION BY THE REGENTS

10.1 If Licensee should violate or fail to perform any material term of this Agreement, then The Regents may give written notice of such default ("Notice of Default") to Licensee. If Licensee should fail to repair such default in accordance with Paragraph 10.3 and, if applicable, Paragraph 10.4, The Regents will have the right to terminate this Agreement and the license herein by providing a second written notice ("Notice of Termination") to Licensee. If a Notice of Termination is sent to Licensee, this Agreement will automatically terminate on the effective date of such notice. Such termination will not relieve Licensee of its obligation to pay any royalty or fees owing at the time of such termination and will not impair any accrued rights of The Regents. These notices will be subject to Article 19 (Notices).

10.2 Notwithstanding Paragraph 10.1 above, this Agreement will automatically terminate in the event of Licensee's insolvency or the filing of a petition for relief under the United States Bankruptcy Code (a) by Licensee as a debtor or (b) against Licensee as an alleged debtor, if such petition against Licensee has not been stayed or dismissed within sixty (60) days after filing.

10.3 After The Regents has given the Notice of Default, and if Licensee fails to repair such default within sixty (60) days after the effective date of such notice, if the Parties can mutually agree, no later than one hundred twenty (120) days after the effective date of the Notice of Default as to the measures Licensee is to take to adequately address the material term that has been breached by Licensee, then this Agreement will not terminate subject to Licensee's performance of such measures. If the Parties are unable to mutually agree on the measures Licensee is to take to address the material breach, then the Parties will submit the dispute to an unrelated third party arbitrator to determine the measures Licensee is to take to address the material breach, in accordance with Paragraph 10.4 ("Baseball Arbitration").

10.4 Any Baseball Arbitration shall be held in San Francisco, California, according to the then-current commercial arbitration rules of the American Arbitration Association ("AAA"), except to the extent such rules are inconsistent with this Paragraph 10.4. The Baseball Arbitration will be conducted by one (1) arbitrator who shall be reasonably acceptable to the Parties and who shall be appointed in accordance with AAA rules. If the Parties are unable to select an arbitrator, then the arbitrator shall be appointed in accordance with AAA rules. Any arbitrator chosen hereunder shall have educational training and industry experience sufficient to demonstrate a reasonable level of experience relevant to the nature of the matter in dispute. Within twenty (20) days after the selection of the arbitrator, each Party shall submit to the arbitrator and the other Party a proposal for the steps Licensee is to take to address the material breach, together with any relevant evidence in support thereof (the "Proposals"). Within fifteen (15) days after the delivery of the last Proposal to the arbitrator, each Party may submit a written rebuttal of the other Party's Proposal and may also amend and re-submit its original Proposal. The Parties and the arbitrator shall meet within fifteen (15) days after the Parties have submitted their Proposals, at which time each Party shall have one (1) hour to argue in support of its Proposal. The Parties shall not have the right to call any witnesses in support of their arguments, nor compel any production of documents or take any discovery from the other Party in preparation for the meeting. Within thirty (30) days after such meeting, the arbitrator shall select one of the Proposals so submitted by one of the Parties as the resolution of the dispute, but may not alter the terms of either Proposal and may not resolve the dispute in a manner other than by selection of one of the submitted Proposals. If a Party fails to submit a Proposal within the initial twenty (20) day time frame set forth above, the arbitrator shall select the Proposal of the other Party as the determination of the steps Licensee shall take to remedy the material breach. Any time period set forth in this Paragraph 10,4 may be extended by mutual agreement of the Parties. The content (but not the existence or outcome) of the proceedings shall be confidential. Each Party shall bear its own costs incurred in Baseball Arbitration, and Licensee shall pay the costs of the arbitrator. The Regents shall have the right to issue the Notice of Termination in respect of the applicable material breach following Baseball Arbitration only if Licensee fails to perform the measures to address such material breach as set forth in the Proposal selected by the arbitrator.

11. TERMINATION BY LICENSEE

11.1 Licensee will have the right at any time to terminate this Agreement by giving notice in writing to The Regents. Such notice of termination will be subject to Article 19 (Notices) and termination of this Agreement will be effective sixty (60) days after the effective date of such notice.

11.2 Any termination pursuant to Paragraph 11.1 will not relieve Licensee of any obligation or liability accrued hereunder prior to such termination or rescind anything done by Licensee or any payments made to The Regents hereunder prior to the time such termination becomes effective, and such termination will not affect in any manner any rights of The Regents arising under this Agreement prior to such termination.

12. DISPOSITION OF MATERIAL, MODIFICATIONS AND DERIVED PRODUCTS ON HAND UPON TERMINATION

12.1 Upon termination of this Agreement, for a period of one hundred and twenty (120) days after the date of termination, Licensee may complete and Sell any partially made Derived Products; provided that all such Sales will be subject to the terms of this

Agreement including, but not limited to, the payment of Earned Royalties and the rendering of royalty reports thereon. Licensee may not otherwise make, have made, use, Sell, have Sold, offer for Sale, or import Derived Products after the date of termination.

12.2 Upon termination of this Agreement for any reason, Licensee will destroy any Material or Modifications in its possession within fifteen (15) days following the effective date of termination. Licensee will provide The Regents within thirty (30) days following said termination date with written notice that the Material and Modifications have been destroyed.

13. USE OF NAMES AND TRADEMARKS

13.1 Nothing contained in this Agreement will be construed as conferring any right to use in advertising, publicity or other promotional activities any name, trademark, trade name, or other designation of either Party by the other (including any contraction, abbreviation, or simulation of any of the foregoing). Unless required by law or consented to in writing by The Regents, the use by Licensee of the name "The Regents of the University of California" or the name of any University of California campus in advertising, publicity or other promotional activities (other than as set forth in Paragraph 23.1) is expressly prohibited.

14. LIMITED WARRANTIES

14.1 The Regents warrants to Licensee that it has the lawful right to grant this license.

14.2 This license and the associated Property Rights and Material are provided WITHOUT WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR ANY OTHER WARRANTY, EXPRESS OR IMPLIED. THE REGENTS MAKES NO REPRESENTATION OR WARRANTY THAT THE PROPERTY RIGHTS, DATA, MATERIAL, MODIFICATIONS OR DERIVED PRODUCTS, WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK OR OTHER PROPRIETARY RIGHT.

14.3 (a) EXCEPT FOR LICENSEE'S OBLIGATIONS REGARDING CLAIMS OF THIRD PARTIES PURSUANT TO ARTICLE 15 (INDEMNIFICATION), IN NO EVENT WILL EITHER PARTY BE LIABLE FOR ANY INCIDENTAL, SPECIAL, OR CONSEQUENTIAL DAMAGES RESULTING FROM EXERCISE OF THIS LICENSE OR THE USE OF THE DATA, MATERIAL, MODIFICATIONS, PROPERTY RIGHTS, OR DERIVED PRODUCTS.

(b) EXCEPT FOR LICENSEE'S OBLIGATIONS REGARDING CLAIMS OF THIRD PARTIES PURSUANT TO ARTICLE 15 (INDEMNIFICATION) AND EXCEPT AS MAY RESULT FROM A BREACH OF ARTICLE 22 (CONFIDENTIALITY), NEITHER PARTY WILL BE LIABLE FOR ANY LOST PROFITS, COSTS OF PROCURING SUBSTITUTE GOODS OR SERVICES, LOST BUSINESS, ENHANCED DAMAGES FOR INTELLECTUAL PROPERTY INFRINGEMENT, OR FOR ANY INDIRECT, INCIDENTAL, CONSEQUENTIAL, PUNITIVE, OR OTHER SPECIAL DAMAGES SUFFERED BY THE OTHER PARTY OR ITS AFFILIATES ARISING OUT OF OR RELATED TO THIS AGREEMENT FOR ALL CAUSES OF ACTION OF ANY KIND (INCLUDING TORT, CONTRACT, NEGLIGENCE, STRICT LIABILITY AND BREACH OF WARRANTY) EVEN IF SUCH PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.

14.4 Nothing in this Agreement is or will be construed as:

(a) a warranty or representation by The Regents as to the validity, enforceability, or scope of any Property Rights;

(b) a warranty or representation that anything made, used, offered for Sale, imported, or Sold under any license granted in this Agreement is or will be free from infringement of patents of third parties;

(c) an obligation to bring or prosecute actions or suits against third parties for misappropriation of Data, Material, Modifications or Derived Products;

(d) conferring by implication, estoppel, or otherwise any express or implied license or rights under any patents, patent applications, data, copyrights or materials of The Regents, other than with respect to the Data or Material; or

(e) an obligation to furnish any know-how, technology, or technological information not provided in the Material.

15. INDEMNIFICATION

15.1 Licensee will indemnify, hold harmless, and defend The Regents and its officers, employees, and agents; sponsor(s) of the research that led to the Data and Material; and the creators and inventors of any Data and Material covered by Property Rights and their employers against any and all claims, suits, losses, damage, costs, fees, and expenses to the extent resulting from, or arising out of, any third party claim relating to the exercise of this license. This indemnification will include, but will not be limited to, any product liability. If The Regents, in its sole discretion, believes that there will be a conflict of interest with counsel chosen by Licensee, then The Regents may retain counsel of its choice to represent it, and Licensee will pay all expenses for such representation.

15.2 Licensee assumes all liability for damages that may arise from its use, storage or disposition of the Material or Modifications. The Regents shall not be liable to Licensee for any loss, claim or demand made by Licensee, or made against Licensee by any other party, due to or arising from the use, storage or disposition of the Material or Modifications by Licensee. Licensee shall be solely responsible for any use of the Material or Modifications at Licensee's facilities or otherwise by Licensee employees, agents, contractors, or other representatives. Licensee shall indemnify, defend, and hold The Regents and all The Regents' directors, officers, employees, agents, contractors and other representatives (collectively the "Indemnitees") harmless from any claim, litigation, liability, inspection, investigation, administrative proceeding, or other action initiated or threatened by a private party, a government agency, or any other person or entity (collectively "Claims") arising from receipt, storage, use, or disposition of Materials or Modifications by or on behalf of Licensee pursuant to this Agreement or otherwise, and regardless of the basis or cause of such Claim. Each Party shall promptly inform the other of any such Claim of which the Party becomes aware, and each shall communicate with the other's designated counsel regarding the management of such Claim. Licensee shall keep The Regents informed of, and consult with The Regents in connection with the selection of counsel to defend the any Claim and the progress of such litigation or settlement. Licensee shall not have any right to settle any Claim without the specific prior written approval from a designated legal representative of The Regents, Licensee acknowledges that any such settlement proposal submitted to The Regents for approval shall contain a full release of liability for The Regents.

15.3 Licensee, at its sole cost and expense, will insure its activities in connection with any work performed hereunder and will obtain, keep in force, and maintain the following insurance:

(a) Commercial Form General Liability Insurance (contractual liability included; Commercial Form General Liability Insurance will also include clinical trials insurance coverage when applicable, at the levels below) with limits as follows:

Each Occurrence	$[…***…]
Products/Completed Operations Aggregate	$[…***…]
Personal and Advertising Injury	$[…***…]
General Aggregate	$[…***…]

If the above insurance is written on a claims-made form, it will continue for three (3) years following termination or expiration of this Agreement. The insurance will have a retroactive date of placement prior to or coinciding with the Effective Date of this Agreement; and

(b) Worker's Compensation as legally required in the jurisdiction in which Licensee is doing business.

15.4 The coverage and limits referred to in Subparagraph 15.3(a) and 15.3(b) above will not in any way limit the liability of Licensee under this Article 15. Upon the execution of this Agreement, Licensee will furnish The Regents with certificates of insurance evidencing compliance with all requirements, and Licensee will promptly notify The Regents of any material modification of the insurance coverages. Such certificates will:

(a) provide for thirty (30) days' (ten (10) days for non-payment of premium) advance written notice to The Regents of any cancellation of insurance coverages;

(b) indicate that The Regents has been endorsed as an additional insured under the coverage described above in Paragraph 15.3; and

(c) include a provision that the coverage will be primary and will not participate with, nor will be excess over, any valid and collectable insurance or program of self-insurance maintained by The Regents.

15.5 The Regents will promptly notify Licensee in writing of any claim or suit brought against The Regents for which The Regents intends to invoke the provisions of this Article 15. Licensee will keep The Regents informed of its defense of any claims pursuant to this Article 15.

16. COMPLIANCE WITH LAWS/EXPORT CONTROLS

16.1 Licensee will comply with all applicable international, national, state, regional, and local laws and regulations in performing its obligations hereunder and in Licensee's use, manufacture, offer for Sale, Sale, or import of the Derived Products. Licensee will observe all applicable United States and foreign laws and regulations governing the transfer of Derived Products and related technical data to foreign countries, including, without limitation, the International Traffic in Arms Regulations (ITAR) and the Export Administration Regulations.

16.2 Licensee understands that The Regents is subject to United States laws and regulations (including the Arms Export Control Act, as amended, and the Export Administration Act of 1979), controlling the export of technical data, computer software, laboratory prototypes and other commodities, and The Regents' obligations to Licensee under this Agreement are contingent on and subject to compliance with such laws and regulations.

The transfer of certain technical data and/or commodities may require a license from the cognizant agency of the United States Government and/or written assurances by Licensee that Licensee will not export such technical data and/or commodities to certain foreign countries without prior approval of such agency. The Regents neither represents that such a license will not be required nor that, if required, it will be issued.

17. GOVERNMENT APPROVAL OR REGISTRATION

17.1 If this Agreement or any associated transaction is required by the law of any nation to be either approved or registered with any governmental agency, Licensee will assume all legal obligations to do so. Licensee will notify The Regents if it becomes aware that this Agreement is subject to a United States or foreign government reporting or approval requirement. Licensee will make all necessary filings and pay all costs including fees, penalties, and all other out-of-pocket costs associated with such reporting or approval process.

18. ASSIGNMENT

18.1 This Agreement is binding upon and will inure to the benefit of The Regents, its successors and assigns. This Agreement is personal to Licensee and assignable by Licensee only with the written consent of The Regents, provided that Licensee may, on written notice to The Regents, assign this Agreement, including, without limitation, all obligations owed to The Regents hereunder, to an acquiror of all or substantially all of Licensee's stock or assets to which this Agreement relates.

19. NOTICES

19.1 All notices under this Agreement will be deemed to have been fully given and effective when done in writing and delivered in person, or mailed by registered or certified U.S. mail, or deposited with a carrier service requiring signature by recipient, and addressed as follows;

To The Regents: UC Davis InnovationAccess
1850 Research Park Drive, Suite 100
Davis, CA 95618-6134
Attn.: Executive
Director, File No. […
***…]

To Licensee: Sage Therapeutics, Inc.
215 First Street
Cambridge, Massachusetts 02142
Attention: Chief Business Officer

Either Party may change its address upon written notice to the other Party.

20. PAYMENTS

20.1 Payments to The Regents that are not for the Material Fee will be made by check or bank wire transfer, to the following address:

Checks: The Regents of the University of California
Innovation Alliances and Services
1111 Franklin Street, 5th Floor
Oakland, CA 94607-5200
Attention: Chief Financial Officer
Referencing: […***…]

Bank wire (Licensee is responsible for all wire transfer fees):
[…***…]

Payments to The Regents for the Material Fee shall be made by check or bank wire transfer to the address below. Licensee is responsible for all wire transfer fees. Payments shall be made payable to "The Regents of the University of California".

[…***…]

In addition to the above, recipient shall return the chain of custody document signed by recipient to UC DAVIS at the above address within one (1) business day of receipt of shipment of the MATERIAL.

20.2 If monies owed to The Regents under this Agreement are not received by The Regents when due, Licensee will pay to The Regents interest charges at a rate of […***…] percent ([…***…]%) per annum. Such interest will be calculated from the date payment was due until actually received by The Regents. Such accrual of interest will be in addition to, and not in lieu of, enforcement of any other rights of The Regents related to such late payment. Acceptance of any late payment will not constitute a waiver under Article 21 (Waiver) of this Agreement.

21. WAIVER

21.1 The failure of either Party to assert a right hereunder or to insist upon compliance with any term or condition of this Agreement will not constitute a waiver of that right or excuse a similar subsequent failure to perform any such term or condition by the other Party. None of the terms and conditions of this Agreement can be waived except by the written consent of the Party waiving compliance.

22. CONFIDENTIALITY

22.1 Subject to Paragraphs 22.2 and 22.3 below, each Party will hold the other Party's business and technical information, and other proprietary information, including the negotiated terms of this Agreement ("Confidential Information"), in confidence and against disclosure to third parties with at least the same degree of care as it exercises to protect its own information and data of a similar nature. This obligation will expire ten (10) years after the termination or expiration of this Agreement.

22.2 Nothing contained herein will in any way restrict or impair the right of Licensee or The Regents to use, disclose or otherwise deal with any information or data which:

(a) at the time of disclosure to a receiving Party is available to the public or thereafter becomes available to the public by publication or otherwise through no act of the receiving Party;

(b) the receiving Party can show by written record was in its possession prior to the time of disclosure to it hereunder and was not acquired directly or indirectly from the disclosing Party;

(c) is independently made available to the receiving Party without restrictions by a third party;

(d) is independently developed by employees of the receiving Party who did not have access to the information disclosed by the disclosing Party; or

(e) is subject to disclosure under the California Public Records Act or other requirements of law.

22.3 The Regents will be free to release to its inventors, senior administrators employed by The Regents, and individual Regents, the terms and conditions of this Agreement upon their request. Licensee will be free to disclose the terms and conditions of this Agreement in connection with the filing of INDs and to *bona fide* potential or actual advisors, consultants, investors, acquirers, lenders, investment bankers or other potential financial partners in connection with Licensee's proposed financing or business combination activities. If any such release described in this Paragraph 22.3 is made, the applicable Party will inform the

recipient(s) of the confidentiality obligations set forth above and will request that they do not disclose such terms and conditions to others.

22.4 Licensee and The Regents agree to destroy or return to the disclosing Party Confidential Information received from the other in its possession within fifteen (15) days following the effective date of termination of this Agreement. However, each Party may retain one copy of Confidential Information of the other solely for archival purposes in non-working files for the sole purpose of verifying the ownership of the Confidential Information, provided such Confidential Information will be subject to the confidentiality provisions set forth in this Article 22. Licensee and The Regents agree to provide each other, within thirty (30) days following termination of this Agreement, with a written notice that Confidential Information has been returned or destroyed.

23. PUBLICATION OF RESEARCH USE RESULTS AND ACKNOWLEDGEMENT

23.1 Licensee may publish or present Research Use Results, provided Licensee provides The Regents with a copy of any proposed manuscript, abstract, poster session or presentation at least thirty (30) days prior to such publication or presentation. The Regents shall review such publication or presentation for Confidential Information or patentable material and may request a delay of the proposed publication or presentation for up to an additional thirty (30) days to allow for the removal of Confidential Information or the filing of patent application(s). Notwithstanding the foregoing, the Parties agree that no publication or presentation shall contain Confidential Information with respect to which it has confidentiality obligations pursuant to Article 22 (Confidentiality) of this Agreement without prior written consent of the Party whose Confidential Information is to be disclosed. Unless The Regents directs otherwise, any publication or presentation including press releases reporting the research carried out with the Material, Modifications or Data shall contain proper referencing in academic journal format or appropriate format, acknowledging UC Davis and The Regents as the source of the Material and/or Data.

23.2 Notwithstanding the above, if either Party determines that a clinical investigation utilizing the Material must or should be listed with the National Library of Medicine (ClinicalTrials.gov) or other databases to satisfy the requirements of the FDA Amendments Act of 2007 (“FDAAA”) or guidelines promulgated by the International Committee of Medical Journal Editors (“ICMJE”), the Parties shall meet and/or confer to create and upload one or more mutually agreeable listing(s).

24. DISCLOSURE, INVENTORSHIP, AND INTELLECTUAL PROPERTY RIGHTS

24.1 Licensee shall promptly notify The Regents of any potentially patentable discoveries or inventions made through the use of the Material, whether or not made within the specified limits of the approved Research Use. Licensee shall promptly supply The Regents with a copy of the invention disclosure.

24.2 Inventorship shall be determined according to United States patent law.

24.3 Collaborative efforts of The Regents and Licensee may create inventorship rights under United States patent law as well as under the law of any applicable jurisdiction in which a Party or both Parties may elect to file patent application(s). Each Party shall own its undivided interest in joint inventions. The Parties shall cooperate in discussing and securing patent rights to protect potentially patentable inventions.

25. FORCE MAJEURE

25.1 Except for Licensee’s obligation to make any payments to The Regents hereunder, and subject to Paragraph 25.2, below, the Parties will be excused from any performance required hereunder if such performance is rendered impossible or infeasible due to any catastrophe or other major event beyond their reasonable control, including, without limitation, war, riot, and insurrection; laws, proclamations, edicts, ordinances, or regulations; strikes, lockouts, or other serious labor disputes; and floods, fires, explosions, or other natural disasters. When such events have abated, the Parties’ respective obligations hereunder will resume.

25.2 Either Party to this Agreement will have the right to terminate this Agreement upon thirty (30) days’ prior written notice if either Party is unable to fulfill its obligations under this Agreement due to any of the causes specified in Paragraph 25.1 above for a period of one (1) year.

26. SEVERABILITY

26.1 The provisions of this Agreement are severable, and in the event that any provision of this Agreement is determined to be invalid or unenforceable under any controlling body of law, such invalidity or enforceability will not in any way affect the validity or enforceability of the remaining provisions hereof.

27. APPLICABLE LAW; VENUE; ATTORNEYS' FEES

27.1 THIS AGREEMENT WILL BE CONSTRUED, INTERPRETED, AND APPLIED IN ACCORDANCE WITH THE LAWS OF THE STATE OF CALIFORNIA, excluding any choice of law rules that would direct the application of the laws of another jurisdiction. Any legal action brought by the Parties relating to this Agreement will be conducted in San Francisco, California. The prevailing Party in any legal action under this Agreement will be entitled to recover its reasonable attorneys' fees in addition to its costs and necessary disbursements.

28. SCOPE OF AGREEMENT

28.1 This Agreement incorporates the entire agreement between the Parties with respect to the subject matter hereof and supersedes all previous communications, representations or understandings, whether oral or written, between the Parties relating to the subject matter hereof. The MTA specified in the Recitals above, effective July 9, 2013, is hereby superseded. For the avoidance of doubt, the IND Data Transfer Agreement has expired as of October 1, 2013; however, the surviving provisions of the IND Data Transfer Agreement will continue to exist.

28.2 This Agreement may be altered or modified only by written amendment duly executed by the Parties.

In witness whereof, the Parties have executed this Agreement in duplicate originals by their duly authorized officers or representatives.

SAGE THERAPEUTICS, INC.		**THE REGENTS OF THE UNIVERSITY OF CALIFORNIA**	
By:	/s/ Kiran Reddy	By:	/s/ David R. McGee
Name:	Kiran Reddy	Name:	David R. McGee
Title:	Chief Business Officer	Title:	Executive Director, UC Davis InnovationAccess
Date:	October 21, 2013	Date:	October 23, 2013

First Amendment to the Non-Exclusive License Agreement
between The Regents of the University of California and Sage Therapeutics, Inc.
for Allopregnanolone in the Treatment of Status Epilepticus
and Post-Partum Depression
UC Agreement Control No. 2014-01-0261
(File No. […***…]**)**

This first amendment to the Non-Exclusive License Agreement (UC Agreement Control No. 2014-01-0261; File No. […***…]) for "Allopregnanolone in the Treatment of Status Epilepticus and Post-Partum Depression" ("First Amendment") is effective on the 14th day of May, 2014 ("First Amendment Effective Date") between The Regents of the University of California ("The Regents"), a California corporation, having its statewide administrative offices at 1111 Franklin Street, 12th Floor, Oakland, California 94607- 5200, acting through UC Davis InnovationAccess, with an address at 1850 Research Park Drive, Suite 100, Davis, California 95618- 6153, and Sage Therapeutics, Inc. ("Licensee"), a Delaware corporation, having a principal place of business at 215 First Street, Cambridge, Massachusetts 02142. The Regents and Licensee will be referred to herein, on occasion, individually as "Party" or collectively as "Parties".

Recitals

Whereas, a Non-Exclusive License Agreement for "Allopregnanolone in the Treatment of Status Epilepticus and Post-Partum Depression" was entered into between The Regents and Licensee on October 23, 2013, having UC Agreement Control Number 2014-01-0261; File No. […***…] ("Agreement"); and

Whereas, the Parties desire to amend the Agreement by adding treatment of essential tremor to Derived Products, Licensed Field of Use and milestone fees provisions of the Agreement.

The Parties agree as follows:

1. The title of the Agreement is deleted in its entirety and replaced with the following:

Non-Exclusive License Agreement between The Regents of the University of California and Sage Therapeutics, Inc. for Allopregnanolone in the Treatment of Essential Tremor, Status Epilepticus, and Post-Partum Depression

2. Paragraph 1.4 of Article 1 (Definitions) of the Agreement is deleted in its entirety and replaced with the following:

1.4 "Derived Product" means a product containing Allopregnanolone produced by or on behalf of Licensee for Sale or Sold as a drug for essential tremor, status epilepticus, and/or post-partum depression.

3. Paragraph 1.6 of Article 1 (Definitions) of the Agreement is deleted in its entirety and replaced with the following:

1.6 "Licensed Field of Use" means the (a) use of Data for Reference Use as defined below and (b) use of Material or Modifications for Research Use as defined below.

(i) "Reference Use" means use of Data by the Licensee, and by affiliates, contractors, consultants, agents and/or vendors on behalf of Licensee, for the sole purpose of reference or incorporation to the extent that such reference or incorporation identifies, labels it as an excerpt from Data and acknowledges UC Davis as the source of the Data in Licensee's IND application(s) with the FDA for use of Allopregnanolone for the treatment of essential tremor, status epilepticus, and/or post-partum depression. […***…].

(ii) "Research Use" means use of Material or Modifications to develop a clinically relevant pharmaceutical formulation and use of such pharmaceutical formulation for FDA-approved human clinical trials for treatment of essential tremor, status epilepticus, and/or post-partum depression. Research Use includes transfer of Material by Licensee to a third party who uses such Material to create a Modification on behalf of Licensee.

4. Paragraph 5.7 of Article 5 (Royalties and Milestones) of the Agreement is deleted in its entirety and replaced with the following:

5.7 (a) Within […***…] days after the […***…], whichever occurs first, Licensee will pay to The Regents a one-time, non-refundable and non-creditable milestone fee of […***…] dollars ($[…***…]).

(b) Within […***…] days after the […***…], whichever occurs second and for which a milestone fee was not paid under Paragraph 5.7(a), Licensee will pay to The Regents a one-time, non-refundable and non-creditable milestone fee of […***…] dollars ($[…***…]).

(c) Within […***…] days after the […***…], whichever occurs third and for which a milestone fee was not paid under Paragraph 5.7(a) or Paragraph 5.7(b), Licensee will pay to The Regents a one-time, nonrefundable and non- creditable milestone fee of […***…] dollars ($[…***…]).

(d) For clarity, the milestone fees in clauses (a), (b), and (c) above shall each be payable only once, […***…].

This First Amendment does not in any way affect the unamended provisions of the Agreement.

In witness whereof, the Parties have executed this First Amendment in duplicate originals by their duly authorized officers or representatives.

SAGE THERAPEUTICS, INC.		**THE REGENTS OF THE UNIVERSITY OF CALIFORNIA**	
By:	/s/ Kimi Iguchi	By:	/s/ David R. McGee
Name:	Kimi Iguchi	Name:	David R. McGee
Title:	CFO	Title:	Executive Director, UC Davis InnovationAccess
Date:	5/12/14	Date:	5/14/14

EXHIBIT 10.6

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. […***…] denotes omissions.

EXCLUSIVE LICENSE AGREEMENT
PREAMBLE

This Agreement is made and entered into, effective as of November 11, 2013 ("**Effective Date**"), by and between: Washington University, a corporation established by special act of the Missouri General Assembly approved February 22, 1853 and acts amendatory thereto, having its principal offices at One Brookings Drive, St. Louis, Missouri 63130 (hereinafter referred to as "**WU**"); and SAGE Therapeutics, Inc., a corporation organized and existing under the laws of the State of Delaware having its principal offices at 215 First Street, 2nd Floor, Cambridge, MA 02142 (hereinafter referred to as "**Licensee**") and the following correspondence addresses;

Attn: Legal	Attn: Accounting	Attn: Technical
215 First Street, 2nd Floor	215 First Street, 2nd Floor	215 First Street, 2nd Floor
Cambridge, MA 02142	Cambridge, MA 02142	Cambridge, MA 02142
Email: jeff@sagcrx.com	Email: ap@sagerx.com	Email: Al@sagerx.com

License Issue Fee: Licensee shall pay a sum of fifty thousand dollars ($50,000), within fifteen (15) days after the Effective Date. Such License Issue Fee shall be non-refundable and shall not be credited against any other payments that may be due hereunder.

License Maintenance Fee: Licensee agrees to pay a sum of […***…] dollars ($[…***…]) by the first anniversary of the Effective Date and by each subsequent anniversary thereafter, until and including the year in which the first Phase II clinical study for a Licensed Product is initiated. All License Maintenance Fees shall be non-refundable and shall not be credited against any other payments that may be due hereunder.

Financial Milestone Payments: Licensee agrees to pay WU milestone payments in the amounts set forth below for milestones achieved by Licensee, its Affiliates or Sublicensees, within thirty (30) days after the date on which the applicable milestone event is met; provided, that each milestone payment shall be payable not more than once with respect to each Licensed Product.

Payment (U.S. Dollars)	Milestone Event for Each Licensed Product
a. $[…***…]	[…***…]
b. $[…***…]	[…***…]
c. $[…***…]	[…***…]
d. $[…***…]	[…***…]
e. $[…***…]	[…***…]

Non-Financial Diligence Milestones:

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

Each of the Non-Financial Diligence Milestones above needs to be achieved only once during the Term.

Milestone Extensions: Licensee may elect to extend each of the non-financial diligence milestones indicated above only once by an extension period of […***…] months by making a […***…] dollar ($[…***…]) payment (the "Milestone Extension Fee") for each such […***…] month extension provided that Licensee may exercise no more than three separate extensions (i.e., non-financial diligence milestone (e) above may not be extended beyond 14 years after the Effective Date as a result of Licensee's exercise of such extension right). If a specific milestone is extended, then the subsequent milestones are extended automatically by […***…] months

without requiring an additional payment. In addition, the non-financial diligence milestones indicated above shall each extend by a period of […***…] months to reflect any delay in the achievement of the applicable milestone attributable to External Factors.

Royalty Rate by Licensee or Sublicensee:

a. […***…]	[…***…] % of Net Sales for Licensed Products covered under Patent Rights, provided, however, that the Patent Royalty Rate shall be […***…]% of Net Sales for any Special Licensed Product, as set forth in Section 5.3.
b. […***…]	[…***…]% of Net Sales for Licensed Products covered under Technical Information and/or embodying Tangible Research Property, but not covered under Patent Rights, as set forth in Section 5.3.

Sublicensing Revenue: […***…]% of Sublicensing Revenue amounts actually received by Licensee from Sublicensees hereunder at any time during the first three years after the Effective Date, after which it will be […***…]% if received at any time during the next two years after the Effective Date, after which it will be […***…]% if received at any time during the next five years after the Effective Date, and […***…]% if received thereafter during the Term.

a. […***…]	[…***…]%
b. […***…]	[…***…]%
c. […***…]	[…***…]%
d. […***…]	[…***…]%

Equity: Licensee shall issue […***…] common shares (as per capitalization table, refer to Exhibit D) to WU within […***…] days after the Effective Date pursuant to an equity issuance agreement executed concurrently with this Agreement.

Licensee is solely responsible for all past, present and future patent expenses for Patent Rights incurred by WU during the Term, as set forth in Section 9.2. Licensee shall pay past patent expenses no later than […***…] days from the Effective Date of the Agreement.

Field: Therapeutic, diagnostic, prophylactic indications in humans and animals,

Territory: Worldwide, except as set forth in Section 1.32.

Term: 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 tenth anniversary of the day of the First Commercial Sale of such Licensed Product in such country.

RECITALS

A. WU possesses certain Patent Rights (as defined below), Technical Information (as defined below), and Tangible Research Property (as defined below).

B. Licensee has developed a plan to develop, manufacture, promote, import, sell and/or market products based on the Patent Rights, the Technical Information, and/or the Tangible Research Property, which plan is attached hereto as Exhibit A (the "**Development Plan**").

C. Licensee desires to obtain from WU certain licenses to the Tangible Research Property, Technical Information, and Patent Rights and WU desires to grant such licenses to Licensee.

TERMS AND CONDITIONS

NOW, THEREFORE, in consideration of the premises, covenants and agreements set forth herein and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties agree as follows:

1. Definitions.

As used in this Agreement, the following terms have the meaning ascribed to them below:

1.1 "**Agreement**" **is defined in the Preamble above.**

1.2 "**Affiliate**" means an entity that controls or is controlled by or is under common control with a party to this Agreement. For purposes of this definition, "**control**" means the direct or indirect ownership of more than 50% of the outstanding voting securities of a corporation, the direct or indirect ownership by a person or entity of more than 50% of the outstanding voting shares of another

entity, the right to receive more than 50% of the earnings of a person, corporation or other entity, or the right to control the business decisions of a person, corporation or other entity.

1.3 "**Calendar Half**" means each six-month period of a calendar year, or portion thereof, beginning on January 1 or July 1.

1.4 "**Claims**" is defined in Section 11.1 below.

1.5 "**Commercially Reasonable Efforts**" means, with respect to the efforts to be expended with respect to a specified objective, those reasonable, diligent, good faith efforts to accomplish such objective as a similarly situated biotechnology company would normally use to accomplish a similar objective.

1.6 "**Confidential Information**" is defined in Section 7.1 below.

1.7 "**Development Plan**" is defined in Recital C above.

1.8 "**Effective Date**" is defined in the Preamble above.

1.9 "**Election Notice**" is defined in Section 9.3 below.

1.10 "**External Factor**" means the occurrence of one or more of the following with respect to a Licensed Product; *provided* that such occurrence was not caused by any negligence, misconduct, violation of applicable laws, or failure to act by Licensee: (a) any change imposed by a regulatory agency which is new or unanticipated and requires Licensee's compliance; (b) the primary endpoint in any clinical study is not achieved; (c) adverse changes occur in applicable laws relating to the development or marketing of the Licensed Product; or (d) an event of force majeure occurs as set forth in Section 15.12.

1.11 "**Fees**" is defined in Section 11.1 below.

1.12 "**Field**" is defined in the Preamble above.

1.13 "**First Commercial Sale**" means the earliest date on which Licensee, its Affiliates or Sublicensees transfers a Licensed Product for compensation (including equivalent cash value for trades or other non-cash payments).

1.14 "**License Issue Fee**" is defined in the Preamble above.

1.15 "**Licensed Product**" means any product made, made for, used, sold, offered for sale, or imported by Licensee and/or any of its Affiliates and/or Sublicensees that : (a) in the absence of this Agreement would infringe at least one pending or issued Valid Claim (if such pending Valid Claim were issued in its then current form); (b) uses a process covered by a pending or an issued Valid Claim (if such pending Valid Claim were issued in its then current form); (c) embodies, or was made using a method or process that used, in whole or in part, or was otherwise derived from, Technical Information and/or Tangible Research Property that, when used by Licensee, its Affiliates and/or Sublicensees, was not publicly available for use by Third Parties; and/or (d) in the absence of this Agreement, would infringe at least one pending or issued Valid Claim (if such pending Valid Claim were issued in its then current form) of a Special Patent Right, regardless of whether Licensee is determined to have certain ownership rights in such Special Patent Right pursuant to Section 9.5. For the avoidance of doubt, for the purpose of this Section 1.15(d), the term "infringe" will assume that WU is the sole owner of such Special Patent Right, even if Licensee is determined to have certain ownership rights in such Special Patent Right pursuant to Section 9.5.

1.16 "**Licensee**" is defined in the Preamble above.

1.17 "**Licensee Indemnitee**" is defined in Section 11.1 below.

1.18 "**Losses**" is defined in Section 11.1 below.

1.19 "**Milestone Extension Fee**" is defined in the Preamble above.

1.20 "**Net Sales**" means the gross value, compensation, and payments, whether in cash or in kind, received by Licensee, its Affiliates or Sublicensees for Sales of Licensed Products, less all Permissible Deductions.

1.21 "**Patent Rights**" means, subject to Section 9.3 below, (a) the patents and patent applications listed in Exhibit B, (b) any other patents or patent applications owned by WU that are filed on invention disclosures which are made as of the Effective Date and listed in Exhibit B, and (c) all foreign counterparts, continuations, continuations-in-part (excluding any claim to new subject matter

therein not included in clause (a) or (b)), divisions, patents, extensions, reexaminations and reissues of any of the foregoing that trace their earliest priority filing date to any of the items set forth in clauses (a) or (b).

1.22 "**Permissible Deductions**" means, and shall be limited to, any (a) trade, quantity and cash discounts on Licensed Products actually provided to Third Parties in connection with arm's-length transactions, (b) credits, allowances or refunds, not to exceed the original invoice amount, for actual claims, damaged goods, rejections or returns of Licensed Products, (c) excise, sale, use, or custom duties, value added or other taxes, other than income taxes, paid by Licensee, its Affiliates or Sublicensees due to the Sale of Licensed Products, (d) government mandated rebates, including but not limited to Medicaid rebates paid by Licensee, its Affiliates or Sublicensees to Medicaid authorities, and (e) a lump sum deduction not to exceed one and a half percent (1.5%) of Net Sales in lieu of any other deductions from gross Sales receipts that are not accounted for in clauses (a) through (d) of this paragraph.

1.23 "**Sale**" means any transaction in which a Licensed Product is exchanged or transferred for any value, payment or compensation of any type or kind. A Sale of a Licensed Product will be deemed to have been made when such Licensed Product is paid for and the purchase price is collected by Licensee or its Affiliate or Sublicensee. Notwithstanding the foregoing, Sales of any kind shall not include and shall expressly exclude transfers by Licensee: (a) to a Sublicensee or Affiliate for distribution or their own internal testing of samples of any Licensed Product; *provided* that such testing is not conducted for or on behalf of any end user; and *further provided* that Licensee receives no payment for such Licensed Product in excess of the fully burdened (i.e., direct and indirect) costs of producing and transporting such materials; and (b) for its and its Affiliates' and Sublicensees' own non-commercial laboratory research and development purposes, manufacturing, marketing/promotional purposes, beta testing and/or clinical testing, provided that the foregoing is not performed for or on behalf of any end user and further provided that Licensee receives no payment for such Licensed Product in excess of the fully burdened (*i.e.*, direct and indirect) costs of producing and transporting such materials and/or providing such Licensed Product.

1.24 "**Special Licensed Product**" means a Licensed Product that (a) contains the molecule identified on Exhibit E and (b) is covered by one or more Valid Claim(s) of the Special Patent Rights in the country of Sale or country of manufacture. For clarity, any Licensed Product that does not contain the molecule identified on Exhibit E shall not be deemed a Special Licensed Product, even if such Licensed Product is covered by a Valid Claim of the Special Patent Rights in the country of Sale or country of manufacture.

1.25 "**Special Patent Rights**" means the Patent Right […***…] identified as such on Exhibit B, and all foreign counterparts, continuations, continuations-in-part (excluding any claim to new subject matter therein unless included in clauses (a) or (b) of Section 1.21), divisions, patents, extensions, reexaminations and reissues of such Patent Right that trace their earliest priority filing date to such Patent Right.

1.26 "**Sublicensee**" means a Third Party that has received a sublicense under the license rights granted to Licensee in Article 2 of this Agreement (the written agreement containing such sublicense, a "**Sublicense**"). This term includes any sublicensee of a Sublicensee as permitted pursuant to Section 2.9.1.

1.27 "**Sublicensing Revenue**" means all value, payment or compensation of any type or kind, other than earned royalties on Net Sales, received by Licensee from or through its Sublicensees to the extent such amounts are allocable to the licensing, cross-licensing or other authorized use of any license or right granted herein by WU and granted by Licensee to the applicable Sublicensee. Sublicensing Revenue shall include, without limitation, all fees, milestone payments, cash equivalents, equities, securities, equipment, property, rights or anything else of value received by Licensee as sublicensing consideration from or for the benefit of any Sublicensee, but shall exclude any amount received from any Sublicensee as (a) support of Licensee's or its Affiliates' research, development or clinical programs mandated under the Sublicense and directly relating to the Licensed Products as evidenced by detailed research and budget proposals provided to WU prior to Licensee's receipt of such funding, or (b) the portion of the purchase price for Licensee's and/or its Affiliates' debt or equity securities that reflects the then current market price of such securities or, if such securities are not publicly traded, the then current market value of such securities. For clarity, payment of milestone payments is in addition to the payment of Sublicensing Revenue and WU shall have the right to audit Licensee with respect to any such sublicensing transaction in accordance with Section 6.4. In the event that Licensee intends to enter into an agreement to sublicense the rights (regardless of whether WU's rights and Licensee's rights are licensed under the same or separate agreements) granted herein by WU along with other intellectual property that is not owned by WU, Licensee shall promptly deliver to WU a written report setting forth the proportion of any consideration payable to Licensee under such agreement that shall be allocable to the rights granted by WU under this Agreement. If WU disagrees with the apportionment made by Licensee in such report, WU shall so notify Licensee within […***…] days after receipt of Licensee's report and the parties shall meet to discuss and resolve such disagreement in good faith. If no amicable settlement is reached within […***…] days from the start of such discussions, the matter shall be finally settled by arbitration administered by the American Arbitration Association under its Commercial Arbitration Rules, the arbitration shall take place in St. Louis, Missouri, and the arbitral decision may be enforced in any court.

1.28 "**Tangible Research Property**" means, subject to Section 9.3 below, any and all tangible research tools and other tangible personal property that WU may provide to Licensee and that Licensee may accept. Licensee, its Affiliates and Sublicensees shall have no restrictions or obligations with respect to any item of Tangible Research Property from and after the date on which it became publicly available for use by Third Parties, provided that it did not become publicly available through Licensee's breach of its obligations under Sections 2.7 and 7 below.

1.29 "**Technical Information**" means, subject to Section 9.3 below, all ideas, trade secrets, research and development information, unpatented inventions, know-how, data, methods, procedures, processes and technical data and information (but excluding Tangible Research Property) owned by WU and disclosed in writing as per Section 7.1 to Licensee by WU, resulting from research performed by or under the direction of Dr. Douglas F. Covey relating to neuroactive steroids and/or steroids that modulate GABA(A) receptors, in each instance that contribute to the practice of the inventions in the Patent Rights. Technical Information excludes claims to inventions included in Patent Rights but, for clarity, may include other information disclosed but not claimed in patent applications. Licensee, its Affiliates and Sublicensees shall have no restrictions or obligations with respect to any item of Technical Information from and after the date on which it became publicly available for use by Third Parties, provided that it did not become publicly available through Licensee's breach of its obligations under Section 7 below.

1.30 "**Term**" is defined in the Preamble above.

1.31 "**Termination Fee**" is defined in Section 13.2 below.

1.32 "**Territory**" is worldwide, except that it shall exclude those countries to which export of technology or goods is prohibited at the applicable time by applicable U.S. export control laws or regulations.

1.33 "**Third Party**" means any person or entity other than WU, Licensee, or any of their respective Affiliates.

1.34 "**Valid Claim**" means a claim (a) of a pending patent application within the Patent Rights that has been pending for no longer than seven (7) years after its earliest priority date, or (b) of an issued and unexpired patent within the Patent Rights that has not been (i) held invalid or unenforceable by a court or other governmental agency of competent jurisdiction in a decision or order that is not subject to appeal, (ii) canceled, or (iii) abandoned in accordance with, or as permitted by, the terms of this Agreement or by
mutual written agreement of WU and Licensee.

1.35 "**WU**" is defined in the Preamble above.

1.36 "**WU Indemnitee**" is defined in Section 11.1 below.

2. License Grants and Restrictions.

2.1 Patent Rights. Subject to the terms and conditions of this Agreement, WU hereby grants to Licensee, and Licensee hereby accepts, a non-transferable (except pursuant to Section 15.6), exclusive (subject to Section 2.4 below) and royalty-bearing license under the Patent Rights, for the Term, to make, have made, sell, offer for sale, use, and import Licensed Products, solely in the Territory and in the Field. For the avoidance of doubt, Licensee acknowledges and agrees that no license is granted or implied under the Patent Rights outside the Field or the Territory.

2.2 Technical Information. Subject to the terms and conditions of this Agreement, WU hereby grants to Licensee, and Licensee hereby accepts, a non-transferable (except pursuant to Section 15.6), nonexclusive and royalty-bearing license for the Term to use the Technical Information solely for the purpose of making, having made, selling, offering for sale, using, and importing Licensed Products, solely in the Territory and in the Field. For the avoidance of doubt, Licensee acknowledges and agrees that no license is granted or implied under the Technical Information outside the Field or the Territory.

2.3 Tangible Research Property. Subject to the terms and conditions of this Agreement, WU hereby grants to Licensee, and Licensee hereby accepts, a non-transferable (except pursuant to Section 15.6), nonexclusive and royalty-bearing license, for the Term, to use the Tangible Research Property solely for the purpose of making, having made, selling, offering for sale, using, and importing Licensed Products, solely in the Territory and in the Field. For the avoidance of doubt, Licensee acknowledges and agrees that no license is granted or implied to use the Tangible Research Property for any other purpose.

2.4 Limitations on Patent Rights License. WU retains its right to use the Patent Rights to make, have made, use, and import Licensed Products in the Territory and in the Field for research and educational purposes including collaboration with other nonprofit entities, which shall expressly exclude any commercial purposes.

2.5 Clarifications. For the avoidance of doubt, the license "to have made" granted in Section 2.1 above means that the Licensee, its Affiliates and Sublicensees may contract with one or more Third Parties to make Licensed Products for Licensee, its Affiliates and Sublicensees for Sale or offer for Sale by Licensee, its Affiliates and Sublicensees within the scope of their sales operations or for research and development purposes. In any such event, Licensee, its Affiliates and Sublicensees shall require all such Third Parties to be bound to a written confidentiality agreement that contains non-use and nondisclosure obligations that are at least as restrictive as those that are contained in Article 7 below before any WU Confidential Information is disclosed to such Third Parties.

2.6 Government Rights. In accordance with Public Laws 96-517, 97-256 and 98-620, codified at 35 U.S.C. §§ 200-212, the United States government retains certain rights to inventions arising from federally supported research or development. Under these

laws and implementing regulations, the government may impose requirements on such inventions. Licensed Products embodying inventions subject to these laws and regulations sold in the United States must be substantially manufactured in the United States. The license rights granted in this Agreement arc expressly made subject to these laws and regulations as amended from time to time. Licensee shall be required to abide by all such laws and regulations.

2.7 Reservation of Rights and Restrictions. Nothing in this Agreement provides Licensee with any ownership rights of any kind in the Patent Rights, the Technical Information and/or any intellectual property rights in the Tangible Research Property. All ownership rights in the Patent Rights (other than any Special Patent Rights that may be jointly owned by Licensee), the Technical Information and intellectual property rights in the Tangible Research Property shall remain the sole and exclusive property of WU. The risk of loss of all Tangible Research Property shall pass to Licensee upon delivery. For the avoidance of doubt, Licensee's rights in any Tangible Research Property extend only to the specific Tangible Research Property delivered by WU to Licensee. Accordingly, Licensee shall have no right to any tangible research property retained by WU, including, without limitation, any original tangible research property that may be retained by WU and on which the Tangible Research Property delivered to Licensee may be based. No license or right is granted by WU, by implication or otherwise, to any patent other than the Patent Rights. Other than the licenses expressly granted in Sections 2.1, 2.2 and 2.3 above, all of WU's rights in and to the Patent Rights, the Tangible Research Property and any Technical Information are hereby reserved by WU. Licensee agrees not to practice or use the Patent Rights, the Tangible Research Property and/or the Technical Information or do any act in respect thereof outside the scope of the licenses expressly granted above, including, without limitation, providing any Tangible Research Property to any Third Party other than a Sublicensee. Licensee further agrees that it will not do any act or thing which would in any way contest WU's ownership in, or otherwise derogate from the ownership by WU, of any rights in the Patent Rights, the Tangible Research Property and/or Technical Information. In furtherance of the foregoing but without limiting the generality thereof, Licensee agrees not to register or attempt to register in the Territory or elsewhere any rights in the Patent Rights, the Tangible Research Property and/or Technical Information or to assist any Third Party to do so. Notwithstanding anything to the contrary in the foregoing, (a) Licensee shall have the right, subject to payment of royalties as set forth in Section 5.3(a)(ii), to prepare, file and prosecute any patent application and maintain any patent claiming inventions derived solely by or on behalf of Licensee from Technical Information and/or Tangible Research Property, and, as between Licensee and WU, Licensee shall be the sole owner of any such patent application or patent, and (b) the limitations on Licensee set forth in this Section 2.7, and Sections 8.2, 13.3(a), 13.5(a)-(d) and last sentence of Section 13.5 with respect to Patent Rights shall not apply to any Special Patent Right determined to be jointly owned by WU and Licensee.

2.8 Markings. Licensee shall ensure that appropriate markings, such as "Patent Pending" or the Patent Rights patent numbers or application serial numbers, appear, to the extent required by each country's patent laws, on all Licensed Products (or their packaging, as appropriate) sold by or on behalf of Licensee.

2.9 Sublicensing.

2.9.1 General. Subject to the further provisions of this Section 2.9, Licensee may grant sublicenses of the licenses granted to Licensee in Sections 2.1, 2.2 and 2.3 above to Affiliates, or to Third Parties by entering into a written agreement with any such Third Party. Each Sublicensee may grant a further sublicense under the sublicense granted by Licensee; provided, however, that no such further Sublicensee shall have the right to grant any further sublicense.

2.9.2 Requirements of each Sublicense Agreement. Licensee agrees that it will require all Sublicensees to comply with the terms and conditions set forth in this Agreement and applicable to Licensee. In furtherance of the foregoing but without limiting the generality thereof, each Sublicense shall, for the express benefit of WU, bind the Sublicensee to terms and conditions no less favorable to WU than those between WU and Licensee contained in this Agreement. To the extent that any term, condition, or limitation of any Sublicense is inconsistent with the terms, conditions and limitations contained in this Agreement, such term, condition, and/or limitation shall be null and void against WU, Without in any way narrowing or limiting the scope of the foregoing provisions of this Section 2.9.2, all Sublicenses shall contain the terms and conditions set forth in Exhibit C hereto. Within thirty (30) days after the effective date of any Sublicense, Licensee shall provide WU a complete copy of the Sublicense including, without limitation, any and all exhibits and/or attachments thereto; *provided*, that Licensee may redact any non-financial terms not reasonably relevant to obligations owed to WU hereunder provided that there is no dispute between the parties. If the Sublicense is written in a language other than English, the copy of the Sublicense shall be accompanied by a complete translation written in English. Upon delivery of such translation to WU, Licensee shall be deemed to represent and warrant to WU that such translation is a true and accurate translation of the Sublicense.

2.9.3 Survival of Sublicenses. At Licensee's written request, any Sublicense granted by Licensee under this Agreement will remain in effect in the event that this Agreement is terminated prior to expiration. Any such Sublicensee will automatically become a direct licensee of WU under the rights originally sublicensed to it by Licensee provided the Sublicensee did not cause the termination of this Agreement and the Sublicensee agrees to comply with the terms of this Agreement and to fulfill all the responsibilities of Licensee hereunder. Each such Sublicensee shall be an intended third party beneficiary of this Section 2.9.3. In the event that this Agreement is terminated, all amounts subsequently due to Licensee with respect to any such Sublicense granted under the licenses granted under this Agreement shall become paid directly to WU following the date of termination.

2.9.4 Primary Liability. Licensee will be primarily liable to WU for all of Licensee's obligations contained in this Agreement. Any act, error or omission of a Sublicensee that would be a breach of this Agreement if imputed to Licensee, will be deemed to be a breach of this Agreement by Licensee if Licensee has neither cured such breach nor terminated the applicable Sublicense within sixty (60) days after Licensee's receipt of such notice.

3. Development Plan.

3.1 Development Plan. Licensee represents and warrants as of the Effective Date that (a) the Development Plan (refer Exhibit A) contains Licensee's good faith, bona fide plans for developing Licensed Products for commercialization, and (b) Licensee has or plans to obtain the knowledge, expertise, experience and resources to fully carry out such plans.

3.2 Progress Reports. Licensee will deliver to WU written reports on Licensee's progress against the Development Plan no later than January 31 and July 31 of the first two calendar years following the calendar year in which the Effective Date falls, and no later than January 31 of each calendar year thereafter. Each such report will summarize Licensee's progress against the Development Plan in reasonable detail including, without limitation, the progress achieved and any problems encountered in the development, prototyping, evaluation, testing, manufacture, Sale, and/or marketing of, as applicable, each Licensed Product. Upon reasonable request by WU from time-to-time, Licensee will meet with WU to consult with WU about Licensee's then-current progress against the Development Plan.

3.3 Changes to Development Plan. Licensee may not amend, change or otherwise modify 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 amendment or modification of the Development Plan, and Licensee shall give due consideration to all comments provided by WU.

4. Diligence.

4.1 Licensee agrees to, throughout the Term, use Commercially Reasonable Efforts, itself or through its Affiliates, Sublicensees or contractors, to develop Licensed Products, and to manufacture, promote and sell Licensed Products throughout the Territory and in the Field, which efforts may be satisfied with respect to development (but not commercialization) through achievement of the financial and non-financial milestones set forth in the Preamble after any applicable adjustment.

4.2 Should WU conclude in its reasonable judgment that Licensee fails to meet the diligence requirements set out in Section 4.1 above, WU may notify Licensee of its conclusions and the basis therefor. The parties shall then undertake to resolve WU's concerns through good faith negotiations for a period of 90 days. Should such negotiations fail to result in a plan reasonably acceptable to WU for achieving a level of diligence consistent with its obligations under Section 4.1 above, then WU may require Licensee to pay the Milestone Extension Fee set forth in the Preamble (if the alleged diligence failure relates to a milestone set forth in the Preamble) and, if Licensee fails to do so, or if the alleged diligence failure does not relate to a milestone set forth in the Preamble, WU may exercise its right to terminate this Agreement as provided in Article 13 below.

5. Fees, Payments and Royalties.

5.1 License Issue Fee. Licensee agrees to pay the License Issue Fee to WU as set forth in the Preamble.

5.2 License Maintenance Fee. Licensee agrees to pay the License Maintenance Fee to WU as set forth in the Preamble.

5.3 Royalties.

(a) Subject to Section 5.3(b) below, Licensee agrees to pay WU an earned royalty equal to (i) the […***…]% Patent Royalty Rate of Net Sales (including, for clarity, Net Sales by Sublicensees) of Licensed Products if there is a Valid Claim of the Patent Rights covering the Licensed Product in the country of Sale or country of manufacture; provided, however, that the earned royalty shall be equal to the […***…]% Patent Royalty Rate of Net Sales (including, for clarity, Net Sales by Sublicensees) of Special Licensed Product, or (ii) the […***…]% Non-Patent Royalty Rate of Net Sales (including, for clarity, Net Sales by Sublicensees) of Licensed Products if there is no Valid Claim of the Patent Rights covering the Licensed Product in the country of Sale or country of manufacture. Such earned royalties shall be paid by Licensee within […***…] days after the end of each Calendar Half in which the Sale of the Licensed Products to which such earned royalties occurs.

(b) If rights under any intellectual property owned by any Third Party are needed to practice, use, make, sell, offer to sell or import any Licensed Product, then royalties payable to WU with respect to such Licensed Product under Section 5.3(a)(1) may be reduced by Licensee dollar for dollar in an amount up to […***…] percent ([…***…]%) of any royalty payable by Licensee to any such Third Party for such right. However, in no event shall any such royalty be reduced below […***…]% (as a result of any such deductions) if the original royalty under Section 5.3(a)(i) is […***…]%, or below […***…]% if the original royalty under Section 5.3(a)(i) is […***…]%. The royalty reductions in this Section 5.3(b) shall only be applicable for Third Party licenses needed to

provide freedom to operate under the Patent Rights and do not apply to other licenses or permissions that Licensee may obtain to develop, produce or market a finished Licensed Product, including Third Party formulation technology.

5.4 Milestone Payments. Licensee agrees to pay WU milestone payments in the amounts set forth in the Preamble, within […***…] days after the date that the applicable milestone is achieved.

5.5 Clarifications. For the avoidance of doubt, no multiple royalty will be required to be paid on a single unit of Licensed Product or because a Licensed Product or its manufacture, use, Sale or importation is covered by more than one Valid Claim. However, WU will be entitled to the highest applicable royalty rate. No royalty shall be payable on Sales of any Licensed Product unless such Licensed Product is either covered by a Valid Claim in the country of Sale or country of manufacture, or embodies, or was made using a method or process included in, Technical Information and/or Tangible Research Property that, when used by Licensee or Sublicensee, as applicable, was not generally available for use by Third Parties. In order to ensure that WU obtains the full amount of royalty payments contemplated in this Agreement, if any Licensed Product is sold or transferred internally within Licensee, its Affiliates or any Sublicensee or other Third Party with whom Licensee or any of its Affiliates has any agreement or arrangement regarding consideration (including but not limited to an option to purchase stock, stock ownership, division of profits, or special rebates or allowances), the amount of the Sale shall be deemed to be the greater of (a) the price at which the Licensed Product is resold to the end user or (b) the fair market value of the Licensed Product.

5.6 Sublicensing Revenue Obligations. Licensee shall pay to WU the applicable percentage of Sublicensing Revenue identified in the Preamble above within […***…] days after the end of the Calendar Half in which Licensee receives the Sublicensing Revenue.

6. Place and Method of Payment; Reports and Records; Audit; Interest.

6.1 Method of Payment. All dollar ($) amounts referred to in this Agreement are expressed in United States dollars. All payments to WU shall be made in United States dollars by check or electronic transfer payable to "Washington University." Any Sales revenues for Licensed Products in currency other than United States dollars shall be converted to United States dollars at the conversion rate for the foreign currency as published in the Eastern edition of The Wall Street Journal as of the last business day in the United States of the applicable Calendar Half.

6.2 Place of Payment. Checks shall reference WU Contract Number […***…] and shall be sent to:

Accounting Department
Office of Technology Management
Washington University in St. Louis
660 South Euclid Avenue, CB 8013
St. Louis, MO 63110

All payments shall include the WU Contract Number to ensure accurate crediting to Licensee's account. Electronic transfers shall be made to a bank account designated in writing by WU.

6.3 Reports. Within forty-five (45) days after the end of each Calendar Half in which a Licensed Product is Sold, Licensee shall deliver to WU, a written report setting forth the calculation of all amounts due to Licensee under Sections 5.3 and 5.6 above for such Calendar Half. For Licensed Products, each such report shall show, at a minimum, (a) the number of Licensed Products Sold and amount of Sales by country during such Calendar Half, (b) the gross receipts for Sales of Licensed Products dining such Calendar Half including total amounts invoiced and received, (c) any Permissible Deductions giving totals by each type for such Calendar Half, (d) Net Sales of Licensed Products by country for such Calendar Half, and (e) royalties, fees and payments due to WU for such Calendar Half, giving totals for each category.

6.4 Books and Records. Licensee shall maintain complete and accurate books of account and records that would enable an independent auditor to verify the amounts paid as royalties, fees and payments under this Agreement. The books and records must be maintained for six (6) years following the Calendar Half after submission of the reports required by this Agreement. Upon reasonable notice by WU, Licensee must give WU (or auditors or inspectors appointed by and representing WU) access to all books and records relating to Sales of Licensed Products by Licensee to conduct, at WU's expense, an audit or review of those books and records. This access must be available at least once every twelve (12) months, during regular business hours, during the Term and for three (3) years following the termination or expiration of this Agreement. If any such audit or review determines that Licensee has underpaid royalties by 5% or more for any Calendar Half, Licensee shall (a) reimburse WU for the costs and expenses of the accountants and auditors in connection with the review and audit, and (b) immediately pay WU the amount of such underpayment along with interest on the past due amount as provided in Section 6.5 below.

6.5 Interest and Collection. Any amounts not paid by Licensee to WU when due shall accrue interest, from the date […***…] days after the balance is due, at an annual interest rate of […***…]% above the prime rate published in the Eastern edition of *The*

Wall Street Journal during the period of arrearage (or the maximum allowed by law, if less than the amount specified herein). In addition, Licensee will reimburse WU for all reasonable costs and expenses incurred (including reasonable attorneys' fees) in collecting any overdue amounts.

6.6 Foreign Taxes. Payments shall be paid to WU free and clear of all foreign taxes. If laws, rules or regulations require withholding of income taxes or other rates imposed upon payments set forth in this Agreement, Licensee shall make such withholding payments as required without subtracting such withholding payments from such payments to WU. Licensee shall submit appropriate proof of payment of the withholding rates to WU within a reasonable period of time. Licensee shall use efforts consistent with its
usual business practices to minimize the extent of any withholding taxes imposed under the provisions of the current or any future double taxation treaties or agreement between foreign countries, and the parties shall cooperate with each other with respect thereto, with the appropriate party under the circumstances providing the documentation required under such treaty or agreement to claim
benefits thereunder. Any refund, rebate or abatement of any tax in respect of which a withholding payment under this Section 6.6 has been made by Licensee shall be solely for the account of Licensee.

7. Confidentiality.

7.1 Definition of Confidential Information. The parties acknowledge that, prior to and during the Term, the parties may disclose to one another scientific, technical, trade secret, business, or other information which is treated by the disclosing party as confidential or proprietary, including but not limited to unpublished Patent Rights patent applications, Technical Information, Tangible Research Property, Development Plans, progress reports, and royalty reports (all such information is hereinafter referred to collectively as "Confidential Information"). Both parties agree that in order to ensure that each party understands which information is deemed to be confidential, all Confidential Information will be in written form and clearly marked as "Confidential," and if the Confidential Information is initially disclosed in oral or some other non-written form, it will be confirmed and summarized in writing and clearly marked as "Confidential" within thirty (30) days after disclosure. The receiving party shall hold the disclosing party's Confidential Information in confidence and shall treat such information in the same manner as it treats its own confidential information but not less than with a reasonable degree of care. In recognition that WU is a non-commercial, academic institution, Licensee agrees to limit to the extent possible the delivery of Licensee Confidential Information to WU. Each party retains the right to refuse to accept any Confidential Information from the other party which it does not consider to be essential to this Agreement or which it believes to be improperly designated, for any reason, but such refusal shall not eliminate the obligation of the individual making such a determination from treating such information as confidential hereunder where such information has been read by such individual. The Confidential Information provided to the receiving party will remain the property of the disclosing party, and will be disclosed only to those persons necessary for the performance of this Agreement.

7.2 Exclusions. Confidential Information does not include information that (a) was known to the receiving party prior to receipt from the disclosing party as evidenced by the receiving party's records; (b) is or becomes publicly available through no act by or on behalf of the receiving party; (c) is lawfully received by the receiving party from a Third Party without any restrictions, and/or (d) comprises identical subject matter to that which had been originally and independently developed by the receiving party personnel without knowledge or use of any Confidential Information as evidenced by the receiving party's records.

7.3 General Obligations. Subject to Section 2.5 above and to Sections 7.5 and 7.6 below, the receiving party agrees that during the Term and forever thereafter it will (a) refrain from disclosing any of the other party's Confidential Information to Third Parties, (b) disclose the other party's Confidential Information to only those employees of the receiving party necessary for the receiving party to use the Confidential Information in accordance with this Agreement and who are subject to restrictions on use and disclosure at least as restrictive as those set forth in this Agreement, (c) keep confidential the other party's Confidential Information, and (d) except for use in accordance with the rights and licenses which are expressly granted in this Agreement, refrain from using the other party's Confidential Information,

7.4 No License. By disclosing the Confidential Information to the other party, the disclosing party does not grant any express or implied rights to the other party under any patents, copyrights, trademarks, or trade secrets other than the licenses expressly granted herein. Each party reserves, without prejudice, the ability to protect its rights under any such patents, copyrights, trademarks, or trade secrets.

7.5 Judicial Procedures. The receiving party may, to the extent necessary, disclose the disclosing party's Confidential Information in accordance with a judicial or other governmental rule, regulation or order; *provided* that the receiving party either (a) gives the disclosing party reasonable notice prior to such disclosure to allow the disclosing party a reasonable opportunity to seek a protective order or equivalent, or (b) obtains written assurance from the applicable judicial or governmental entity that it will afford such Confidential Information the highest level of protection afforded under applicable law or regulation.

7.6 Permitted Disclosures. Licensee may, to the extent necessary, use and disclose the WU Confidential Information (a) to secure governmental approval to clinically test or market a Licensed Product, (b) if applicable, to secure patent protection for an invention within the Patent Rights or pursuant to Section 2.7, or (c) to actual or potential Sublicensees or contractors performing development and/or commercialization services with respect to Licensed Products, provided such potential Sublicensees or contractors

first agree in writing to be bound by terms that are at least as restrictive as the terms set forth in this Agreement. Licensee will, in any such event, take all reasonably available steps to maintain the confidentiality of the disclosed Confidential Information and to guard against any further disclosure.

8. Representations and Warranties.

8.1 Authority. Each of WU and Licensee represents and warrants to the other of them that (a) this Agreement has been duly executed and delivered and constitutes a valid and binding agreement enforceable against such party in accordance with its terms, (b) no authorization or approval from any Third Party is required in connection with such party's execution, delivery, or performance of this Agreement, and (c) the execution, delivery, and performance of this Agreement does not violate the laws of any jurisdiction or the terms or conditions of any other agreement to which it is a party or by which it is otherwise bound.

8.2 Compliance with Laws. Licensee represents and warrants that it will (a) use the Patent Rights, Tangible Research Property and Technical Information only to exploit the license rights granted in Sections 2.1, 2.2 and 2.3 in accordance with the provisions of this Agreement and with such laws, rules, regulations, government permissions and standards as may be applicable thereto in the Territory and in the Field, and (b) otherwise comply with all laws, rules, regulations, government permissions and standards as may be applicable to Licensee in the Territory with respect to the performance by Licensee of its obligations hereunder.

8.3 Reports. Licensee warrants that all reports provided by Licensee hereunder are true and correct and are certified true and correct by Licensee upon delivery to WU.

8.4 Additional Warranties of Licensee. Licensee represents and warrants that (a) it has obtained the insurance coverage required by Article 12 below, and (b) there is, to the best of its knowledge, no pending litigation and no threatened claims against it that could impair its ability or capacity to perform and fulfill its duties and obligations under this Agreement.

8.5 Additional Warranties of WU. WU represents and warrants that (a) it has in place an intellectual property policy that provides for its ownership (subject to any rights retained by the U.S. government by operation of law) of the Patent Rights, Technical Information and Tangible Research Property; (b) as of the Effective Date, it has received no notice of any Third Party claims challenging WU's ownership or control, and to the best of its knowledge, it is the sole owner, of the Patent Rights, Technical Information and Tangible Research Property, and has the authority to grant the licenses set forth herein; (c) it has obtained assignments from all WU inventors named in patent applications within the Patent Rights assigning to WU all their right, title and interest in and to the Patent Rights and to the best of WU's knowledge, no person or entity has infringed the Patent Rights or misappropriated the Technical Information and/or Tangible Research Property; and (d) it has not granted or conveyed to any other person or entity any right or option to the Patent Rights that would conflict with the rights granted to Licensee hereunder.

9. Application, Prosecution and Maintenance of Patent Rights.

9.1 Patent Applications.

9.1.1 Patent Rights. WU has the first right to control the preparation, filing, prosecution, issue and maintenance of Patent Rights patents and applications. Subject to compliance by Licensee of the terms and conditions of this Agreement (including, without limitation, Section 9.2 below), WU will (a) prosecute and maintain the applications and patents within the Patent Rights and (b) prepare, file and prosecute additional applications within the Patent Rights as Licensee may reasonably request, in WU's name and, if applicable, Licensee's name, at Licensee's sole cost and expense. WU will select qualified outside patent counsel and corresponding foreign associates reasonably acceptable to Licensee to prepare, file, prosecute and maintain U.S. patents/applications and foreign counterparts within the Patent Rights. WU will consult with Licensee regarding the prosecution of Patent Rights patent applications, including, without limitation, providing Licensee a reasonable opportunity to review and comment on proposed submissions to any patent office before the submission is filed, and giving due consideration to all comments provided by Licensee. WU will keep Licensee reasonably informed of the status of Patent Rights patents and applications by timely giving Licensee copies of significant communications relating to such Patent Rights that are received from any patent office or outside patent counsel of record or foreign associate. Should WU decide to abandon any Patent Rights patents and applications, WU shall notify Licensee of such intent at least thirty (30) days prior to any deadline at which such abandonment becomes irrevocable and Licensee may, at its own expense, prosecute and maintain said patent application. Should Licensee assume such prosecution and maintenance, WU agrees to reasonably cooperate with Licensee at Licensee's request to whatever extent is reasonably necessary, to procure patent protection for Patent Rights, including fully agreeing to execute any and all documents to provide Licensee the full benefit of the licenses granted herein.

9.2 Costs and Expenses. Subject to Section 9.3 below, Licensee agrees to reimburse WU for all reasonable costs and expenses incurred by WU in connection with the preparation, filing, prosecution, issue and/or maintenance of patents and applications within the Patent Rights both prior to the Effective Date and at any time thereafter during the Term. Licensee agrees to pay WU the amount of any such reimbursement within forty-five (45) days after receipt by Licensee of documentation for any such costs and expenses, which WU may provide to Licensee from time-to-time.

9.3 Failure to Reimburse. Licensee may elect not to reimburse WU for amounts due under Section 9.2 in respect to one or more Patent Rights patent and/or applications only by giving WU notice of such election at least ninety (90) days before the date on which the applicable cost or expense is to be incurred by WU (each an "**Election Notice**"). For purposes of this Section 9.3, a cost or expense shall be deemed to be incurred by WU on the earlier of (a) the date WU actually pays the cost or expense, or (b) the date WU becomes obligated to pay the cost or expense (which, for example, shall be the date WU engages a third party to perform the service which gives rise to a commitment to pay any such cost or expense). Any such Election Notice shall specify the Patent Rights patents and/or applications to which such Election Notice relates ("**Excluded Patent Rights**"). In the event any Election Notice is given by Licensee, (x) the term "**Patent Rights**" shall be modified to exclude such Excluded Patent Rights, (y) the term "**Technical Information**" shall be modified to exclude any research and development information, unpatented inventions, know-how, data, methods, and technical data and information that relate solely to the Excluded Patent Rights ("**Excluded Technical Information**"), and (z) the term "**Tangible Research Property**" shall be modified to exclude any and all tangible research tools and other tangible personal property that WU may have provided to Licensee that relate solely to the Excluded Patent Rights ("**Excluded Tangible Research Property**"**)**, in each instance as of the date the Election Notice is given. Accordingly, and for the avoidance of doubt, as of the date the Election Notice is given, the license to the Excluded Patent Rights, Excluded Technical Information and the Excluded Tangible Research Property granted to Licensee under Sections 2.1, 2.2 and 2.3 above shall terminate, and WU shall be free, without any further obligation to Licensee whatsoever, to abandon the applications or patents subject to the Election Notice, or to continue prosecution or maintenance, for WU's sole use and benefit, including a license to unrelated Third Parties, at WU's option and sole cost and expense. Licensee agrees to deliver to WU, along with any Election Notice, all Excluded Technical Information and Excluded Tangible Research Property to which such Election Notice relates. For the avoidance of doubt, WU will not refund any amounts paid under Section 9.2 to WU prior to WU's receipt of an Election Notice.

9.4 Community of Interest. The parties desire to avail themselves to the maximum extent possible of all applicable legal privileges. The parties intend that information regarding the preparation, filing, prosecution and maintenance of the applications and patents within the Patent Rights (**"Shared Information**") that would otherwise be subject to one or more legal privileges or protections is and shall be subject to those same privileges and protections despite the fact that it has been developed by or exchanged between or among them and/or their joint or independent counsel. The parties further intend that Shared Information is and shall be subject to the joint defense doctrine and common interest/community of interest doctrine. The parties acknowledge that the legal privileges and protections pertaining to Shared Information are held jointly by both parties, and that no individual party is authorized to waive any such privilege or protection. Further, this Agreement shall not affect the ethical, fiduciary or other obligations inherent in those attorney-client relationships other than to extend the cloak of confidentiality and privilege to the Shared Information as provided herein. Each party agrees that Shared Information obtained from the other party or developed jointly shall be used only for the preparation and prosecution of the Patent Rights and for no other purpose. Each party agrees to keep Shared Information confidential in accordance with Article 7.

9.5 Inventorship Determination. WU's and Licensee's legal counsel will determine whether Licensee is an inventor of the invention claimed in the Special Patent Right application. Such determination will commence upon the Effective Date and last no longer than thirty (30) days. Such inventorship determination shall have no bearing on the royalty rate to be paid with respect to the Special Licensed Product and the royalty rate will be […***…]% pursuant to Section 5.3(a)(i).

10. Infringement, Enforcement, and Defense.

10.1 Notice of Infringement. Throughout the Term, each of WU and Licensee agree to give the other prompt notice of (a) any known or suspected infringement of the Patent Rights or unauthorized use or disclosure of the Technical Information and/or Tangible Research Property in the Territory, and (b) any claim that a Licensed Product infringes the intellectual property rights of a Third Party.

10.2 Patent Rights.

10.2.1 Enforcement. Licensee, at its sole expense, will have the initial right to attempt to stop promptly any infringement of the Patent Rights in the Territory. Licensee may initiate and prosecute actions in its own name or, if required by law, in WU's name against Third Parties for infringement of the Patent Rights in the Territory through outside counsel of Licensee's choice who are reasonably acceptable to WU. Licensee shall consult with WU prior to and in conjunction with all significant issues, shall keep WU informed of all proceedings, and shall provide copies to WU of all pleadings, legal analyses, and other papers related to such actions. WU will provide reasonable assistance to Licensee, at Licensee's cost, in prosecuting, resolving and/or settling any such actions, including but not limited to joining as a party if necessary or desirable. If Licensee fails or declines to take any action under this Section 10.2.1 within a reasonable time after learning of the infringement of the Patent Rights, WU shall have the right (but not the obligation) to take appropriate actions including, without limitation, filing a lawsuit, at WU's cost. Licensee will provide reasonable assistance to WU, at WU's cost, in prosecuting, resolving and/or settling any such actions.

10.2.2 Restrictions on Settlement. Notwithstanding anything in this Agreement to the contrary, neither party may, without the advanced written consent of the other party, not to be unreasonably withheld, conditioned or delayed, settle, compromise, or otherwise enter into any form of settlement (or other similar agreement) regarding any claim of action brought under Section 10.2.1 above that either (a) admits liability on the part of the other party, (b) otherwise negatively affects the rights of the other party or

imposes any liability, restrictions or obligation upon the other party, (c) requires any financial payment by the other party, (d) concedes or otherwise portions the Territory, and/or (e) grants rights or concessions to a Third Party to the Patent Rights or any Licensed Products.

10.2.3 Proceeds. If Licensee obtains any value, payment or compensation of any type or kind as a result of any claim brought pursuant to Section 10.2.1 above, Licensee shall pay to WU a percentage of any such proceeds (after recouping reasonable and necessary attorney's fees and expenses incurred in connection with such claim) equal to the applicable Patent Royalty Rate.

10.3 Technical Information. WU shall have the exclusive right (but not the obligation) to institute legal action against any Third Party arising out of such Third Party's actual or threatened misappropriation of the Technical Information, and WU shall retain any and all proceeds from any such actions. Licensee shall have no right to make any demands or claims, bring suit, effect any settlements or take any other action with respect to any such misappropriation without the prior written consent of WU.

11. Indemnification.

11.1 Notwithstanding anything else in this Agreement, Licensee agrees to indemnify, reimburse and hold harmless WU, WU personnel, WU's Affiliates, and each of their respective trustees, faculty, staff, employees, students, directors, officers, agents, successors and assigns (altogether the "**WU Indemnitees**") from, for and against any and all judgments, settlements, losses, expenses, damages and/or liabilities (the "**Losses**") and any and all court costs, reasonable attorneys' fees, and expert witness fees and expenses ("**Fees**") that a WU Indemnitee may incur from any and all allegations, claims, suits, actions or proceedings brought by a Third Party (the "**Claims**") to the extent arising out of, relating to, or incidental to Licensee's breach of this Agreement or its use, commercialization, or other exploitation of Patent Rights, Technical Information or Tangible Research Property, whether by or through Licensee, Licensee's Affiliates, Sublicensees, or contractors, and including all Claims for infringement, injury to business, personal injury and product liability, but excluding Losses to the extent they are adjudicated by a Court of competent jurisdiction to be caused by the gross negligence or willful misconduct of a WU Indemnitee. WU agrees to indemnify, reimburse and hold harmless Licensee, Licensee personnel, Licensee's Affiliates, Sublicensees, and its and their staff, employees, directors, officers, agents, successors and assigns (together the "**Licensee Indemnitees**") from, for and against any and all Losses and Fees that a Licensee Indemnitee may incur from any and all Claims to the extent arising out of, relating to, or incidental to (a) WU's activities pursuant to this Agreement, including, without limitation, WU's use, storage or handling of Licensee property at WU, or (b) WU's breach of this Agreement or (c) use, commercialization, or other exploitation, of Technical Information or Tangible Research Property, whether by WU or any of its licensees, except Licensee, or (d) use of its retained rights in Patent Rights, whether by WU or any of its licensees, and including all Claims for infringement, injury to business, personal injury and product liability.

11.2 Obligations set forth in this Article 11 shall survive termination of this Agreement, shall continue even after assignment of rights and responsibilities, and shall not be limited by any provision of this Agreement outside this section. A party seeking indemnification under this Agreement shall: (a) give the indemnifying party prompt written notice of the Claim; (b) cooperate with the indemnifying party, at the indemnifying party's expense, in connection with the defense and settlement of the Claim; and (c) not settle or compromise the Claim without the written consent of the indemnifying party, which shall not be unreasonably withheld, conditioned or delayed. An indemnifying party may satisfy its duty to indemnify for Fees by accepting an irrevocable duty to defend the Claim on behalf of the WU Indemnitees or Licensee Indemnitees, as applicable, without a reservation of rights, at which time the indemnifying party shall be entitled to conduct and direct the defense of the applicable indemnitees against such Claim using attorneys of its own selection; for all other Claims, the applicable indemnitee shall be entitled to conduct and direct its own defense and that of other indemnitees using attorneys of its own selection with Fees subject to the indemnifying party's ongoing obligation to indemnify for Fees.

12. Insurance.

Throughout the Term and for a period of […***…] years thereafter, Licensee shall obtain and maintain comprehensive general liability insurance in the following minimum annual limits: $[…***…] per occurrence and $[…***…] in the aggregate; and

From the date at least one day prior to the first clinical study of a Licensed Product throughout the Term and for a period of […***…] years thereafter, Licensee shall obtain and maintain comprehensive product liability insurance in the following minimum annual limits: $[…***…] per occurrence and $[…***…] in the aggregate.

Each of the above insurance policies shall be with carrier(s) having at least A.M. Best ratings/class sizes of A/VII and shall name WU as an additional insured. Licensee will provide WU with a certificate of insurance within thirty (30) days after the Effective Date and annually thereafter. The certificates must provide that Licensee's insurer will notify WU in writing at least thirty (30) days prior to cancellation or material change in coverage. The specified minimum insurance coverage and limits do not constitute a limitation on Licensee's liability or obligation to indemnify or defend under this Agreement.

13. Term and Termination.

13.1 Term. The Term is defined in the Preamble and is subject to earlier termination as provided herein.

13.2 Termination By Licensee. Licensee may terminate this Agreement without cause by giving at least ninety (90) days' notice thereof to WU. Licensee shall pay WU all amounts due and owing to WU under this Agreement as of the date of termination, including the above mentioned ninety (90) day notice period, within ten (10) days after receipt of an invoice from WU for such amounts, as a termination fee ("**Termination Fee**").

13.3 Termination by WU. WU may terminate this Agreement by giving notice thereof to Licensee upon the occurrence of any one or more of the following events (in which event this Agreement shall terminate on the date such notice is given): (a) Licensee exercises any rights with respect to the Patent Rights, Tangible Research Property, and/or the Technical Information outside the scope of the licenses granted to Licensee in Article 2 above and does not cease such exercise within thirty (30) days after the day that WU gives Licensee notice demanding that such exercise cease, and/or (b) (i) a bankruptcy proceeding is filed by Licensee or a bankruptcy proceeding is filed against Licensee and is not dismissed within sixty (60) days, or (ii) Licensee suffers the appointment of a receiver, receiver and manager, or administrative receiver of the whole or any substantial portion of its assets or business, or (iii) a resolution is passed for its dissolution (other than for the purpose of amalgamation or reconstruction).

13.4 Breach and Failure to Cure. WU may terminate this Agreement by giving notice thereof to Licensee in the event Licensee commits a material breach of any provision of this Agreement and fails to cure such breach within sixty (60) days after the day that WU gives Licensee notice of such breach. Such termination shall be effective on the date such notice of termination is given. Licensee may terminate this Agreement by giving notice thereof to WU in the event WU commits a material breach of any provision of this Agreement and fails to cure such breach within sixty (60) days after the day that Licensee gives notice to WU of such breach, and such termination shall be effective on the date such notice of termination is given.

13.5 Duties Upon Expiration or Earlier Termination. For the avoidance of doubt, on the date of expiration or earlier termination of this Agreement, all license rights granted to Licensee under Article 2 above shall terminate; *provided, however*, that upon expiration of this Agreement, the licenses granted in Sections 2.2 and 2.3 shall survive and become irrevocable, perpetual, royalty-free and fully paid up. Licensee agrees to, promptly upon earlier termination (but not expiration) of this Agreement, deliver to WU all originals, copies, reproductions and summaries of all Tangible Research Property, Technical Information and WU's Confidential Information, and WU likewise agrees to deliver to Licensee all originals, copies, reproductions and summaries of all Licensee's Confidential Information promptly upon earlier termination of this Agreement, in each instance in the format in which it exists at the time of earlier termination of this Agreement, or in another mutually agreed format. Within ten (10) days after earlier termination (but not expiration) of this Agreement for any reason whatsoever, Licensee agrees to deliver a written report to WU of all Licensed Products in inventory. If this Agreement terminates before the expiration of the last-to-expire of the Patent Rights, then, upon the termination of this Agreement, Licensee agrees (a) to immediately discontinue the exportation of Licensed Products arising from the use of Patent Rights, Technical Information or Tangible Research Property that were made in the Territory, (b) to immediately discontinue the manufacture, Sale and distribution of the Licensed Products arising from the use of Patent Rights, Technical Information or Tangible Research Property in the Territory, (c) to immediately destroy all Licensed Products arising from the use of Patent Rights, Technical information or Tangible Research Property in inventory, and (d) not to manufacture, sell and/or distribute Licensed Products in the Territory until the expiration of the Term. Further, upon such termination, Licensee shall cease all use of the Patent Rights, Technical Information or Tangible Research Property.

13.6 Effect of Expiration or Earlier Termination. For the avoidance of doubt, the expiration or earlier termination of this Agreement shall not relieve Licensee of its obligation to account for and make payment to WU of any amount due hereunder that accrued during the Term, including, without limitation, any royalties and amounts under Sections 9.2 and 13.2 above.

14. Disclaimer and Limitation of Liability.

NOTWITHSTANDING ANYTHING HEREIN TO THE CONTRARY, EVERYTHING PROVIDED BY WU UNDER THIS AGREEMENT IS UNDERSTOOD TO BE EXPERIMENTAL IN NATURE, MAY HAVE HAZARDOUS PROPERTIES, AND, EXCEPT AS SET FORTH IN SECTION 8, IS PROVIDED WITHOUT ANY WARRANTY OF ANY KIND, EXPRESSED OR IMPLIED, INCLUDING WITHOUT LIMITATION, WARRANTIES OF MERCHANTABILITY OR FITNESS FOR ANY PARTICULAR PURPOSE, OR NON-INFRINGEMENT OF ANY THIRD-PARTY PATENT, TRADEMARK, COPYRIGHT OR ANY OTHER THIRD-PARTY RIGHT. WU MAKES NO WARRANTIES REGARDING THE QUALITY, ACCURACY, COMMERCIAL VIABILITY OR ANY OTHER ASPECT OF ITS PERFORMANCE PURSUANT TO THIS AGREEMENT OR REGARDING THE PERFORMANCE, VALIDITY, SAFETY, EFFICACY OR COMMERCIAL VIABILITY OF ANYTHING PROVIDED BY WU UNDER THIS AGREEMENT. LICENSEE DOES NOT WARRANT THAT ANY LICENSED PRODUCT WILL BE SUCCESSFULLY DEVELOPED, APPROVED OR COMMERCIALIZED OR THAT ANY SALE OR LEVEL OF SALES WILL BE ACHIEVED PROVIDED THAT THE FOREGOING DISCLAIMER SHALL NOT RELIEVE OR WAIVE LICENSEE'S DILIGENCE OBLIGATIONS UNDER THIS AGREEMENT. EXCEPT FOR THEIR RESPECTIVE INDEMNITY OBLIGATIONS, IN NO EVENT SHALL WU OR LICENSEE BE LIABLE FOR ANY INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES ARISING OUT OF OR IN ANY WAY CONNECTED WITH THIS AGREEMENT, WHETHER IN BREACH OF CONTRACT, TORT OR OTHERWISE, EVEN IF THE PARTY IS ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. EXCEPT FOR THEIR RESPECTIVE INDEMNITY OBLIGATIONS, EACH OF WU'S AND LICENSEE'S

AGGREGATE LIABILITY TO THE OTHER UNDER THIS AGREEMENT SHALL NOT EXCEED THE PAYMENTS MADE OR PAYMENTS DUE UNDER THIS AGREEMENT, RESPECTIVELY.

15. General Provisions.

15.1 Import/Export Controls. In performing their respective obligations under the Agreement, the parties will comply with United States export control and asset control laws, regulations, and orders, as they may be amended from time to time, applicable to the export or re-export of goods or services, including software, processes, or technical data. Such regulations include without limitation the Export Administration Regulations ("**EAR**"), International Traffic in Arms Regulations ("**ITAR**"), and regulations and orders administered by the Treasury Department's Office of Foreign Assets Control (collectively, "**Export Control Laws**"). WU is not transferring any information or material outside of the United States under this Agreement and is providing no representation regarding the export control status or classification of any information or materials provided hereunder.

15.2 Entire Agreement; Amendment. This Agreement embodies the entire understanding of the parties and supersedes all other past and present communications and agreements relating to the subject matter. No amendment or modification of this Agreement shall be valid unless made in writing and signed by authorized representatives of both parties.

15.3 Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the State of New York, other than its rules or procedures involving conflicts of laws.

15.4 Survival. Each provision of this Agreement that would by its nature or terms survive, shall survive any termination or expiration of this Agreement, regardless of the cause. Such provisions include, without limitation, Sections 1, 2.7(b), 2.9.3, 7, 8.2, 8.3, 9.4, 11, 12, 13.2, 13.5, 13.6, 14, 15.3, 15.4, 15.11, 15.13 and 15.14.

15.5 Notices. Notices delivered pursuant to this Agreement shall be to the following contacts or other addresses provided in accordance with this Section 15.5 and are effective on the next business day if sent by a nationally recognized commercial carrier's overnight delivery service, or when received if sent otherwise:

Office of Technology Management
Attention: Director
Washington University in St. Louis
660 South Euclid Avenue, CB 8013
St. Louis, MO 63110

SAGE Therapeutics,
Inc. Attention: CEO
215 First Street, 2nd Floor
Cambridge, MA 02142

15.6 Assignment. This Agreement is binding upon and inures to the benefit of the parties and their successors, but this Agreement may not be assigned by either party without the prior written consent of the other party; provided, however, that Licensee may assign this entire Agreement, without WU's consent, to an Affiliate or to a Third Party that acquires all or substantially all of Licensee's business or assets to which this Agreement relates through merger, sale, acquisition or otherwise; provided, further, that the successor agrees in writing to assume all the obligations and liabilities of Licensee to WU hereunder.

15.7 Construction. The recitals and Preamble to this Agreement are hereby incorporated as an integral part of this Agreement as if restated herein in full. Headings are included for convenience and reference only and are not incorporated as an integral part of this Agreement. This Agreement may be executed in any number of counterparts each of which shall be deemed an original and as executed shall constitute one agreement, binding on both parties, even though both parties do not sign the same counterpart.

15.8 Relationship of the Parties. Each party is an independent contractor and not a partner or agent of the other party. This Agreement will not be interpreted or construed as creating or evidencing any partnership or agency between the parties or as imposing any partnership or agency obligation or liability upon either party. Further, neither party is authorized to, and will not, enter into or incur any agreement, contract, commitment, obligation or liability in the name of or otherwise on behalf of the other party.

15.9 Severability. If any provision in this Agreement is held invalid, illegal, or unenforceable in any respect, such holding shall not affect any other provisions of this Agreement, and this Agreement shall be construed as if it had never contained the invalid, illegal, or unenforceable provisions.

15.10 Remedies. The failure of either party to insist upon or enforce strict performance by the other party of any provision of this Agreement, or to exercise any right or remedy under this Agreement will not be interpreted or construed as a waiver or

relinquishment of that party's right to assert or rely upon any such provision, right or remedy in that or any other instance; rather, the same will be and remain in full force and effect. All rights and remedies under this Agreement are cumulative of every other such right or remedy and may be exercised concurrently or separately from time-to-time.

15.11 Use of Names. Neither party may use the trademarks or name of the other party or its employees for any commercial, advertisement, or promotional purposes without the prior written consent of the other with WU acting through an authorized corporate officer. If either party is required by law, governmental regulation, or its own authorship or conflict of interest policies to disclose its relationship with the other party, including, but not limited to, in SEC filings, scientific publications or grant submissions, it shall provide the other party with a copy of the disclosure.

15.12 Force Majeure. Neither WU nor Licensee will be liable for failure of or delay in performing obligations set forth in this Agreement, and neither will be deemed in breach of its obligations, other than for payments, if such failure or delay is due to natural disasters or other causes reasonably beyond the control of a party and reasonable notice of the delay is provided to the other party.

15.13 WU Personnel. Licensee and WU agree that for all WU faculty or staff members who serve Licensee in the capacity of consultant, officer, employee, board member, advisor, or otherwise through a personal relationship with Licensee (a "**Consultant**") (a) such Consultant shall serve the Licensee in his or her individual capacity, as an independent contractor, and not as an agent, employee or representative of WU; (b) WU exercises no authority or control over such Consultant while acting in such capacity; (c) WU receives no benefit from such activity; (d) neither Licensee nor the Consultant may use WU resources in the course of such service and, as long as WU resources are not used, WU shall not own any result of Consultant's work; (e) WU makes no representations or warranties regarding such service and otherwise assumes no liability or obligation in connection with any such work or service undertaken by such Consultant; and (f) any breach, error, or omission by a Consultant acting in the capacity set forth in this paragraph shall not be imputed or otherwise attributed to WU, and shall not constitute a breach of this Agreement by WU.

15.14 Further Acts. Each party shall, at the reasonable request of the other, execute and deliver to the other such instruments and/or documents and shall take such actions as may be required to more effectively carry out the terms of this Agreement.

15.15 Impact on Tax-Exempt Status. WU advises (a) that it is exempt from federal income tax under Section 501(c) (3) of the Internal Revenue Code, (b) that maintenance of such exempt status is of critical importance to WU and to its members, and (c) that WU has entered into this Agreement with the expectation that there will be no adverse impact on its tax exempt status. As such, and if it becomes necessary, the parties agree to amend, modify or reform this Agreement as necessary (i) in order to ensure that there is no material adverse impact on WU's tax exempt status, and (ii) in a manner that preserves the economic terms of the Agreement as such are set forth in this Agreement.

[Signature page follows]

The signatures of the undersigned indicate that they have read, understand and agree with the terms of this Agreement and have the authority to execute this Agreement on behalf of their represented party and to bind their party to all the terms of this Agreement.

Signature: /s/ Evan Kharasch
Date: November 12, 2013
By: Evan Kharasch
Title: Vice Chancellor for Research

SAGE THERAPEUTICS, INC.

Signature: /s/ Jeff Jonas
Date: November 20, 2013
By: Jeff Jonas
Title: President and CEO

Read and Understood

/s/ Douglas Covey
Dr. Douglas Covey
WU Principal Investigator

Date: November 14, 2013

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 June 30, 2023 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 controls 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: August 7, 2023

/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 June 30, 2023 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 controls 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: August 7, 2023

/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 June 30, 2023, 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: August 7, 2023

/s/ Kimi Iguchi

Name: Kimi Iguchi
Title: Chief Financial Officer (Principal Financial and Accounting Officer)
Date: August 7, 2023