Sage Therapeutics, Inc.
Form 10-K
March 06, 2015
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2014

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 Offices)	**(Zip Code)**

(617) 299-8380

(Registrant s Telephone Number, Including Area Code)

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

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.0001 par value	**NASDAQ Global Market**

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ¨ No x

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 x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

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

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer x (Do not check if a smaller reporting company)	Smaller reporting company ¨

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

The aggregate market value of the registrant s voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold on March 2, 2015 was $43.89. The registrant has provided this information as of March 1, 2015 because its common stock was not publicly traded as of the last business day of its most recently completed second fiscal quarter.

As of March 1, 2015, there were 25,808,688 shares of common stock, $0.0001 par value per share, outstanding.

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Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important 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 the forward-looking statements.

The words anticipate, believe, estimate, expect, intend, may, plan, predict, project, target, poten should, continue, and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

- the accuracy of our estimates regarding expenses, future revenues and capital requirements;
- our plans to develop and commercialize our product candidates, initially as treatments for status epilepticus, refractory status epilepticus, super-refractory status epilepticus, essential tremor and severe postpartum depression;
- our ability to complete our ongoing clinical trials and to advance our product candidates into additional clinical trials, including pivotal clinical trials, and successfully complete such clinical trials;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party contract manufacturers and contract research organizations;
- our ability to obtain and maintain intellectual property protection for our proprietary assets;
- the size of the potential markets for our product candidates and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates for any indication once approved;
- our ability to obtain additional financing when needed;
- the success of competing products that are or become available for the indications that we are pursuing;

the loss of key scientific or management personnel; and

other risks and uncertainties, including those listed under Part I, Item 1A. Risk Factors.

These forward-looking statements are only predictions and we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, so you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in Part I, Item 1A. Risk Factors, that could cause actual future results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to the Annual Report on Form 10-K with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by applicable law.

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PART I

All brand names or trademarks appearing in this report are the property of their respective holders. Unless the context requires otherwise, references in this report to Sage the Company, we, us, and our refer to Sage Therapeutics, Inc.

Item 1. Business

We are a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat life-threatening, rare central nervous system, or CNS, disorders, where there are inadequate or no approved existing therapies. We are targeting CNS indications where patient populations are easily identified, acute treatment is typically initiated in the hospital setting, clinical endpoints are well-defined, and development pathways are feasible. This focus allows us to make highly informed decisions when advancing our product candidates through the development process. Our initial product candidates are aimed at treating different stages of status epilepticus, or SE, a life-threatening condition in which the brain is in a state of persistent seizure, as well as other seizure and non-seizure disorders.

The lead product candidate in our SE program, SAGE-547, is an intravenous, or IV, agent in Phase 1/2 clinical development as an adjunctive therapy, a therapy combined with current therapeutic approaches, for the treatment of super-refractory SE, or SRSE. The current standard of care for SRSE is empiric, and there are no therapies at present that have been specifically approved for this indication. We thus believe there is a significant medical need for SAGE-547.

SE is diagnosed when a patient has a seizure lasting longer than five minutes, and is associated with substantial morbidity and mortality. We estimate that in the United States each year there are up to 150,000 cases of SE, of which 30,000 SE patients die. We estimate that there are 35,000 patients with SE in the United States that are hospitalized in the intensive care unit, or ICU, each year. An SE patient is first treated with benzodiazepines, or BDZs, and if no response, then treated with other, second-line, anti-seizure drugs. If the seizure persists after second-line therapy, the patient is diagnosed as having refractory SE, or RSE, admitted to the ICU and placed into a medically induced coma. Currently, there are no therapies that have been specifically approved for refractory SE, or RSE; however, physicians typically use anesthetic agents to induce the coma and stop the seizure immediately. After a period of 24 hours, an attempt is made to wean the patient from, the anesthetic agents to evaluate whether or not the seizure condition has resolved. Unfortunately, not all patients respond to weaning attempts, in which case the patient must be maintained in the medically induced coma. At this point, the patient is diagnosed as having SRSE.

Prior to the start of our Phase 1/2 clinical trial of SAGE-547, we began to collect data in emergency use of SAGE-547 that we believe supports the safety and activity of SAGE-547 for treatment of SRSE. As of January 9,

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2015, ten patients, six males and four females with a mean age of 17, were treated with SAGE-547 by independent centers under emergency-use Investigational New Drug Applications, or INDs. Of note, each individual case of SRSE arose from a presumed different underlying etiology, the patients were of varying ages, and all patients had been placed in a long-duration medically induced coma. In each case, SAGE-547 was administered with a target steady state exposure similar to that planned for our ongoing Phase 1/2 clinical trial. Seven of these patients treated with SAGE-547 achieved resolution of SRSE either during the course of or soon after SAGE-547 treatment, one patient was not evaluable for efficacy of SAGE-547. The overall response rate was 78%, similar to the observed response rate in the Phase 1/2 clinical trial.

In October 2013, we filed an IND for SAGE-547 for the treatment of SRSE with the U.S. Food and Drug Administration, or FDA, and we received notification allowing us to proceed with our Phase 1/2 clinical trial of SAGE-547 in November 2013. We commenced our Phase 1/2 clinical trial to study safety, tolerability and efficacy of SAGE-547 in adult patients with SRSE in January 2014. This clinical trial is designed as an open-label trial in at least ten patients diagnosed with SRSE. As of January 31, 2015, there were 17 active study sites in the United States. In October 2014, the FDA approved a protocol amendment for our Phase 1/2 trial that enables us to treat pediatric patients as young as two years old, to increase the dose of SAGE-547 being administered to patients and to increase the duration of treatment to up to two weeks. We are continuing to enroll patients as an expansion cohort in this trial, which will proceed in parallel with our regulatory initiatives.

On January 9, 2015, we reported results from our Phase 1/2 clinical trial. Consistent with topline data announced in November 2014, the primary endpoint, safety and tolerability, was achieved in all patients. Of the 20 patients enrolled in the ongoing Phase 1/2 clinical trial, 17 patients were evaluable for efficacy. 71% of evaluable patients met the key efficacy endpoint of being successfully weaned off their anesthetic agents while SAGE-547 was being administered. In addition, 71% of evaluable patients were successfully weaned off SAGE-547 without recurrence of SRSE. As a group, patients who responded to SAGE-547 generally demonstrated rapid improvement over the first five days following treatment. Patients who responded also continued to improve over the 30-day follow-up period as assessed by several measures. SAGE-547 was generally well tolerated and no drug-related serious adverse events, as determined by the Safety Review Committee, were reported in treated patients. The mean exposure level of SAGE-547 was approximately 200 nM.

In addition, we continue to use SAGE-547 to establish proof of principle in clinical trials for additional indications. In October 2014, we began patient enrollment in an exploratory Phase 2a clinical trial of SAGE-547 in patients with essential tremor, a debilitating neurological disorder that causes involuntary, rhythmic shaking with no known cause. This trial is designed to evaluate the safety, tolerability, pharmacokinetics and activity of SAGE-547 in patients with essential tremor. In January 2015, we initiated a Phase 2a clinical trial of SAGE-547 in women with severe postpartum depression, or severe PPD, a distinct and readily identified form of major depressive disorder estimated to affect 15% to 20% of women following childbirth. This trial is designed to evaluate the safety, tolerability, pharmacokinetics and efficacy of SAGE-547 for the treatment of severe PPD. We plan to use the data from these exploratory studies to help guide the design of a second-generation molecule for the chronic treatment of these diseases.

In April 2014, the FDA granted us orphan drug designation for SAGE-547 as a treatment for SE. In July 2014, the FDA granted us fast track designation for the SAGE-547 development program.

SAGE-689 and SAGE-217 are two additional product candidates in our pipeline, which are currently in IND-enabling toxicology and safety pharmacology testing. SAGE-689 is being developed as an adjunctive second-line therapy for the treatment of SE. We are currently conducting IND-enabling studies of SAGE-689, with a plan to file an IND in late 2015 and to begin a Phase 1 clinical trial thereafter. SAGE-217 is being developed as an oral monotherapy for

orphan epilepsies, such as Dravet and Rett syndromes. The chemical characteristics of SAGE-217 potentially allow formulation as both an IV and oral, or PO, medication. In addition, we believe related molecules from our portfolio may be useful in the treatment of a variety of neurological and

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psychiatric disorders, including, for example, Fragile X syndrome, anxiety and tremor. We are currently conducting IND-enabling studies of SAGE-217 with a plan to file an IND by late 2015 and to begin a Phase 1 clinical trial thereafter.

Our current near-term product candidates are allosteric modulators of both synaptic and extrasynaptic, or existing outside of the synapse, $GABA_A$ receptors, a characteristic important in distinguishing our approach from current therapies. While altering the level of synaptic $GABA_A$ receptor activity can be beneficial in stopping seizures, this approach has limitations for the treatment of SE. As SE progresses in many patients, select synaptic $GABA_A$ receptors are down-regulated, or removed from the neuronal synaptic surface. As a result, drugs that target down-regulated receptors, such as benzodiazepines, or BDZs, often are not effective in stopping SE. In contrast, our product candidates work at both the synaptic and extrasynaptic $GABA_A$ receptors. Non-clinical studies suggest that these extrasynaptic $GABA_A$ receptors remain fully active during SE, offering the potential for drugs that impact GABA via the extrasynaptic $GABA_A$ receptor to alter GABA activity and abate seizure. We believe that by creating compounds that target both these receptors, we may be successful in treating seizures that do not respond to BDZ therapy.

Now and in the foreseeable future, our product development pipeline will be focused on allosteric modulation of two important receptor systems in the brain $GABA_A$ and NMDA. These receptor systems regulate inhibitory and excitatory neurotransmission, respectively. 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, epilepsy, and movement disorders among others. Thus these receptor systems are widely regarded as validated drug targets for a variety of CNS disorders, with decades of research and multiple approved drugs targeting these receptor systems. Drugs approved to modulate these receptor systems have had safety and efficacy limitations related to their poor pharmaceutical properties and adverse side effects. We believe that we will have the opportunity to develop molecules from our internal portfolio to more effectively address many of these disorders in the future.

Our ability to identify and develop such novel CNS therapies is enabled by our proprietary chemistry platform that is centered on a scaffold of chemically modified endogenous neuroactive steroid compounds. We believe our know-how around the chemistry and activity of allosteric modulators allows us to efficiently design molecules with different characteristics by enabling us to control important properties such as half-life, brain penetration and the types of receptors with which our drugs interact. Therefore, we believe our product candidates will have the potential to bind with targets in the brain with more precision, increased safety and tolerability, and fewer off-target side effects than either current CNS therapies or previous therapies, which have often failed in development.

SAGE was founded in 2010, based on leading research in the areas of brain function and neuroactive steroids, to explore novel approaches to CNS therapeutics. Since our inception, we have continued to expand our know-how of CNS therapeutics through our research and development programs and to pursue intellectual property protection for our proprietary chemistry platform. In addition, we have assembled a world-class management team that together has been a part of the successful discovery, development and commercialization of more than 20 marketed CNS therapies.

Our Strategy

Our goal is to become a leading biopharmaceutical company focused on development and commercialization of novel proprietary therapies for the treatment of life-threatening, rare CNS disorders.

Key elements of our strategy are to:

Rapidly advance SAGE-547 as a treatment for SRSE. We are developing SAGE-547 as an adjunctive therapy for the treatment of SRSE. Following the completion of our ongoing Phase 1/2 clinical trial of SAGE-547, we intend to complete the additional clinical trials required for approval of

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SAGE-547 as rapidly as possible. We believe we may be able to expeditiously complete these clinical trials due to the fact that the endpoints of such clinical trials will be measured shortly after initiation of therapy and the relatively small number of patients required to be enrolled in such clinical trials. We will also provide mechanisms for access to SAGE-547 for emergency use to patients who experience SRSE but do not meet the inclusion criteria of our ongoing trial, so that they can receive the potential benefit from this product candidate.

Utilize SAGE-547 in exploratory trials to help guide the development of second generation molecules for the applicable indications. We are using SAGE-547 to establish proof of principle in clinical trials for additional indications. The first two indications are essential tremor and severe PPD. The trials are designed to evaluate safety, tolerability, pharmacokinetics, and efficacy. We will use the data from the exploratory studies to help guide the design of second generation molecules for the chronic treatment of these diseases.

Develop our next generation product candidates SAGE-689 and SAGE-217, in parallel to SAGE-547. We are developing a portfolio of proprietary molecules aimed at the treatment of the entire spectrum of SE. Our follow-on product candidates, SAGE-689 and SAGE-217, will utilize similar mechanistic pathways as SAGE-547 and are designed to have pharmaceutical properties that optimize their non-clinical profiles and potential clinical profiles for the treatment of RSE and orphan genetic epilepsies, such as Dravet and Rett syndromes.

Enhance the probability of success in treating SE by developing unique assets with differentiated features. Our initial product candidates are all positive allosteric modulators of the synaptic and extrasynaptic $GABA_A$ receptor. GABA is the major inhibitory neurotransmitter in the CNS and mediates downstream neurologic and bodily function via activation of $GABA_A$ receptors. However, while their mechanisms are similar, our newer compounds are differentiated from SAGE-547, in terms of their activity and pharmacokinetic profiles affording compounds with superior sedation properties or the opportunity to be dosed orally. Thus, while success with SAGE-547 would augur well for our earlier-stage compounds, the profiles of our new $GABA_A$ agents may allow better risk-benefit. All of our initial SE product candidates represent a class of selective agents that target both $GABA_A$ synaptic and extrasynaptic receptors that we believe, can overcome the tolerability and sedation limitations of existing $GABA_A$ targeted agents for the treatment of SE, including BDZs.

Grow our pipeline more broadly utilizing the strengths of our proprietary chemistry platform and scientific know-how, to lessen our long-term reliance on a single franchise and facilitate long-term growth. The potential of our $GABA_A$ platform goes beyond treatment of SE, our initial focus. We will have the potential to discover and develop $GABA_A$ receptor agents with differentiated selectivity for $GABA_A$ synaptic and extrasynaptic receptors, as well as having differing half-lives and routes of administration. These new molecules may have the potential to treat a wide range of psychiatric and neurological disorders, such as fragile X syndrome, anxiety, depression, sleep disorders, mania, tremor, tinnitus and post-traumatic stress disorder. Similarly, our NMDA platform will be explored to develop positive and negative allosteric modulators of NMDA receptors. These molecules may find use in the treatment of depression, Alzheimer s disease, attention deficit hyperactivity disorder and schizophrenia, as well as certain aspects of Huntington s disease and neuropathic pain. We believe our capacity to develop unique molecules creates important optionality for us; in the event any particular program should not meet its desired endpoint.

Focus our internal development activities on CNS indications where we can make well- informed, rapid go/no-go decisions. We believe our ability to design molecules that target CNS indications where patient populations are easily identified and, where well-defined objective endpoints and development pathways exist, allows us to make highly informed decisions when advancing our product candidates. For example, the information we learned with respect to SAGE-547 through our emergency-use cases in SRSE, provided us with a core understanding of the potential utility of this compound in our ongoing and planned clinical trials in the SRSE patient population.

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Build a commercial capability to bring our CNS therapeutics to physicians and patients for rare target indications. We are concentrating our internal efforts on CNS disorders where we believe the target commercial audience can be reached utilizing a highly specialized sales force similar to those of other rare-disease companies. As a result, we believe we can successfully launch and commercialize our initial product candidates on our own. In addition, SAGE-547, if approved, will reach the market in advance of our next product candidate, and therefore will allow physicians and hospitals sufficient time to use SAGE-547 and gain familiarity with its mechanism of action, which we believe has the potential to accelerate adoption of our follow-on products, SAGE-689 and SAGE-217.

Selectively partner our programs to enhance our value. We believe that we are differentiated in our ability to create or develop proprietary novel molecules that impact validated targets such as $GABA_A$ and NMDA receptors for a wide variety of CNS indications. As a result we have identified potential drug candidates that may have advantageous profiles compared to existing and development-stage therapies for large underserved CNS indications, such as depression and cognition. Given the large number of potential patients and physicians for these indications, we may enter into selective partnerships with companies who have clinical expertise and pre-existing commercial infrastructure in areas such as depression and cognition, in order to accelerate development or maximize our return on investment.

Understanding the Foundations of Our Approach

Neurotransmission

The CNS is composed of a vast and complex network of different structures and cell types, most of which serve directly or indirectly to provide a means for the nervous system to signal or communicate with other nerve cells in order to regulate and control all brain function. The cell type responsible for this signaling is called a neuron. Chemical or electrical signals can exert their effects on neurons by traveling across a physical gap located between two neurons, called a synapse. Presynaptic neurons transmit signals whereas postsynaptic neurons react to the signals. The human brain contains approximately 86 billion neurons, each having hundreds to tens of thousands of synapses to allow for this communication. This process is essential to all things, from organ function, to movement, to memory and all behavioral processes.

Neurotransmission is the process by which signaling molecules, called neurotransmitters, are released by a presynaptic neuron, travel over the synaptic space and bind to and interact with receptors on a postsynaptic neuron. Depending on the nature of the neurotransmitter and receptor, this interaction results in excitation, inhibition or modulation of the receiving neuron s behavior.

Synaptic receptors are primarily located inside the synaptic cleft, or the space where the neurons communicate, and have been historically considered to be the most important part of the neuron. However, recent understanding of neurotransmission and brain function has shown there are many extrasynaptic receptors that also respond to neurotransmitters to exert their effects. For example, it is becoming increasingly understood that extrasynaptic $GABA_A$ receptor-mediated neurotransmission is critical to generalized neurological function and has demonstrated influence over general physiological states such as sleep, hunger, anxiety and seizure among other things.

Allosteric modulation

We are focused on developing drugs based on selective allosteric modulation of key CNS synaptic and extrasynaptic receptors. Molecules that function directly on synaptic or extrasynaptic receptors at the site where the native, or natural, molecule binds to inhibit or activate them are known as orthosteric. Alternatively, allosteric modulators are a

class of small molecules very different from classical orthosteric drugs, as they interact at a site different from the native site and allow for fine-tuning of neuronal signals.

Orthosteric drugs aimed at these key synaptic receptors are inherently limited due to their targeted effects of complete activation or complete inhibition of the neuron, with little subtlety in how they exert their effect. As a

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result, neurons are unable to respond to normal stimuli and can become over-stimulated by a neurotransmitter or be unable to respond to normal neurotransmission, thus negatively impacting both the efficacy and safety profile of a potential CNS drug. We believe that nowhere in the body is it more important to maintain normal rhythms than in the brain, and accordingly we believe that allosteric modulation approaches are better suited for the treatment of seizure and other CNS diseases.

We utilize our proprietary chemistry capabilities to design and identify drugs that are allosteric modulators that bind to either or both synaptic and extrasynaptic receptors. As a result, our drugs under development are capable of varying degrees of desired activity rather than complete activation or inhibition of the receptor as typically observed with orthosteric drugs. We believe this greater selectivity and modulatory control at extrasynaptic $GABA_A$ receptors may allow us to develop CNS drugs that offer significant therapeutic and safety advantages over orthosteric drugs.

Allosteric modulation of extrasynaptic $GABA_A$ receptors to treat SE

Our initial focus is on the development of positive allosteric modulators of both synaptic and extrasynaptic sites of the $GABA_A$ receptor. BDZs are allosteric modulators that primarily act at a particular receptor, the synaptic $GABA_A$ receptor, with little or no activity at extrasynaptic $GABA_A$ receptors. BDZs have many positive drug-like attributes, including safety in overdose, reproducible dosing and predictable actions in humans. However, BDZs are inherently limited due to abuse potential, sedation, memory and performance impairment, and development of tolerance. We believe that our approach to $GABA_A$ receptor allosteric modulation has the potential to be superior to BDZs because our products target both synaptic and extrasynaptic receptors. Therefore we believe we can enhance the potential utility of modulating the $GABA_A$ receptor for new indications, and effectively avoid some of the limitations of BDZs.

SE patients are often considered to be resistant to the action, or pharmacology, of drugs that only target the synaptic $GABA_A$ receptors, such as BDZs, the first-line therapy for SE. Positively modulating, or up-regulating, $GABA_A$ receptors results in a beneficial effect in some patients with seizures. However, in persistent SE, synaptic $GABA_A$ receptors are down-regulated, or diminished in their activity.

Our initial product candidates are focused on allosteric modulation of both the synaptic and extrasynaptic $GABA_A$ receptors unlike BDZs that primarily interact only with synaptic $GABA_A$ receptors. The extrasynaptic $GABA_A$ receptor is structurally distinct, possesses unique pharmacology and is located in a different place than the synaptic $GABA_A$ receptor. In addition, the extrasynaptic $GABA_A$ receptor remains intact during prolonged periods of seizure with no down-regulation. Since our selective allosteric $GABA_A$ modulators target both the extrasynaptic and synaptic $GABA_A$ receptors, we believe they can treat seizures that are otherwise BDZ-resistant.

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Published non-clinical testing utilizing well-validated animal models of SE and sophisticated instruments for identifying the expression of both synaptic and extrasynaptic $GABA_A$ receptors on the surface of neurons support this hypothesis. These studies, performed in rats, demonstrate the reduced number and activity of synaptic $GABA_A$ receptors during SE, in contrast to the preserved number and activity of extrasynaptic $GABA_A$ receptors under the same conditions. These studies were done by measuring the amount of $GABA_A$ synaptic and $GABA_A$ extrasynaptic receptors that are present on the surface of the neurons. The analysis of protein present for each of the respective receptors in animals in the SE-state, versus normal animals, shows the difference in $GABA_A$ receptor expression.

We believe animal models of seizure also portray the advantages of our allosteric approach over therapy with BDZs. The figure below shows the results of a rodent study where the subject animals were placed into an SE-like condition of prolonged seizure resulting in continuous spontaneous seizures. SAGE-547 was then administered to certain animals while the others received a BDZ. The results demonstrate that BDZs are unable to adequately control the seizure condition that we believe is due to down-regulation of synaptic $GABA_A$ receptors. In contrast, SAGE-547, working at both synaptic and extrasynaptic $GABA_A$ receptors, appears to have treated the seizures in these animals and resolved their SE.

Allosteric modulation of NMDA receptors to address other CNS conditions

Orthosteric drug candidate approaches to modulating the NMDA receptor have also been fraught with difficulties. NMDA receptor antagonists have been explored for treating Alzheimer s disease and neuropathic pain and for inducing anesthesia. Drugs that antagonize NMDA receptors are limited by adverse effects, such as neurotoxicity, deteriorating mental status and psychotomimetic, or the onset of psychotic symptoms following the administration of the drug. NMDA receptor agonists have been tested in schizophrenia and many believe may have a role in enhancing cognition and mood. However, their ability to be used at effective doses in humans is limited by non-clinical findings indicating these agents may induce cell death through excess excitation of nerve cells.

We are evaluating in non-clinical testing a number of positive and negative allosteric modulators of the NMDA receptor that we believe can overcome the difficulties associated with orthosteric approaches. Like our $GABA_A$ allosteric modulators, our NMDA receptor allosteric modulators work at sites located in the synaptic and extrasynaptic spaces of the neuron and enhance, or modulate, the activity of the native molecule without directly activating the NMDA receptor. Initial non-clinical testing of our NMDA receptor allosteric modulators has indicated we can avoid the excitotoxicity and psychotomimesis seen with directly activating, orthosteric compounds. This in turn may allow us to discover and develop, alone or with partners, compounds to treat conditions such as depression, Alzheimer s disease, attention deficit hyperactivity disorder and schizophrenia, as well as certain aspects of Huntington s disease, and neuropathic pain. In addition, we are evaluating development of these molecules for rare and genetically defined populations where modulation of NMDA may have therapeutic benefit.

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Our proprietary chemistry platform

Our proprietary chemistry platform is centered on novel chemical scaffolds of endogenous or chemically modified synthetic neuroactive steroid compounds that are allosteric modulators of $GABA_A$ or NMDA receptors. We have leveraged this platform to assemble a chemistry portfolio of greater than 1,400 compounds. We believe our proprietary chemistry platform allows us to:

- optimize the properties of neuroactive steroid compounds to develop proprietary, new chemical entities, with the potential to be used as oral, IV or intramuscular therapies;
- control important properties such as half-life, brain penetration and the types of receptors our drugs act upon, thereby modulating either inhibition or excitation either acutely or chronically; and
- create drugs that exert control over the intensity of receptor activation or deactivation, with the potential to hit targets in the brain with more precision, increased safety and tolerability and fewer off-target side effects than current CNS therapies.

Our Product Pipeline

We are focusing our efforts on developing product candidates that are derived from active endogenous steroids with properties that selectively target synaptic and extrasynaptic $GABA_A$ or NMDA receptors. We believe that our proprietary approach to drug discovery and development enables us to create both IV and orally bioavailable selective allosteric modulators that can be applied to multiple CNS target indications. The lead product candidates, SAGE-547, SAGE-689 and SAGE-217, all allosteric modulators of the $GABA_A$ receptor, are being developed as treatments for SRSE, RSE and orphan genetic epilepsies, respectively. We intend to develop and commercialize these initial product candidates on our own, if approved. We are also developing additional potential product candidates from both our $GABA_A$ and NMDA receptor programs that will serve mood and cognitive disorders, such as Alzheimer s Disease and depression, which we may choose to selectively partner in select geographies or commercial settings.

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Status Epilepticus (SE) Development Program

Status epilepticus (SE)

Seizures are brief episodes of abnormal excessive or synchronous neuronal activity in the brain. The outward effect can vary from rapid uncoordinated movement of the trunk and extremities, known as tonic-clonic seizure, to a brief loss of awareness, known as an absence seizure. An electroencephalogram, or EEG, is a measurement of electrical activity within neurons of the brain. Each line of an EEG represents a different region of the brain and becomes aberrant during a state of seizure. In cases of recurring or frequent seizures, or with persistent and long seizures, uncontrolled neurotransmission results in remodeling or changes to brain synaptic function. These physiological and anatomical changes to the brain include changes to the receptor systems of neurons, and shape of the neuron thereby impacting its ability to function, resulting in disorganization of brain proteins and potentially neuronal death.

SE is a life-threatening seizure condition in which the brain is in a state of persistent seizure and there is uncontrolled neuronal excitation. The Neurocritical Care Society defines SE as one continuous unremitting seizure lasting longer than five minutes, or recurrent seizures without regaining consciousness between seizures for greater than five minutes. Common causes of SE in adults include preexisting epilepsy, cerebrovascular disease, metabolic and electrolyte disturbances, encephalopathies, head trauma and drug or substance intoxication. SE is more common in children, often as a result of high fever during the first year of life. It is the most common neurologic emergency in pediatric practice.

SE is associated with substantial morbidity and mortality. We estimate that in the United States each year, there are up to 150,000 cases of SE, of which 30,000 SE patients die. We estimate that 35,000 patients with SE in the United States are hospitalized in the ICU each year. This results in an overall inpatient cost of $3.8 billion to $7.0 billion per year in the United States.

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SE treatment paradigm

The numbers in the chart above represent the estimated number of U.S. patients affected by SE at various stages each year.

SE is a medical emergency and is treated with aggressive pharmacological approaches. When a patient first presents with SE, medical personnel, typically emergency medical technicians at the scene of the seizure or during emergency transport, will treat the patient with IV BDZs such as diazepam, lorazepam or midazolam. Approximately 65% of patients treated with IV BDZs will respond to such treatment, and the seizure will be abated. If the patient does not respond, he or she will be brought to an emergency room where anti-seizure drugs such as phenytoin or valproic acid, will be administered.

If a patient s SE continues after administration of BDZs and anti-seizure drugs, the patient is diagnosed as having RSE, which must be treated quickly to cease the seizure activity, maintain the patient s airway and prevent brain damage. RSE patients are immediately admitted to the ICU and placed in a medically induced coma to stop all seizure-related activity. Currently, there are no therapies that have been specifically approved for RSE. The primary drugs used to induce coma are continuously infused IV agents such as propofol, midazolam or pentobarbital.

The RSE patient is continually monitored through EEG to ensure burst suppression is achieved. Burst suppression is a pattern of brain waves seen on an EEG characterized by periods of activity alternating with periods of little or no activity in the brain, informing medical personnel of the effectiveness of the medically induced coma. The goal of burst suppression is to allow the brain and corresponding neuronal tissue to restore function and reset to normal pre-seizure levels. After a short period of burst suppression, typically 24 hours, physicians attempt to wean the patient from the medically induced coma to evaluate EEG activity to assess if the neuronal activity has returned to normal levels. If unsuccessful, the patient is placed back into the medically induced coma in order to protect underlying neurological activity and brain function. At this point, patients are considered to be in a state of SRSE.

Currently, there are no therapies that have been specifically approved for SRSE. Treatment approaches consist of diagnosis and treatment of underlying medical conditions, adding and changing anti-seizure drugs, and repeated attempts at weaning in conjunction with IV anesthetic agents. The majority of SRSE patients either die or have significant comorbidities, such as decreased blood pressure and cardiorespiratory collapse.

Our proprietary pipeline of product candidates are designed to treat varying stages of SE. Each product candidate has distinct pharmacologic and pharmacokinetic profiles that we believe will make them differentiated products with potential utility across the spectrum of SE.

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Our SE product candidates

SAGE-547

SAGE-547, a proprietary formulation of allopregnanolone, is a known metabolite of progesterone formed in the CNS in humans through the actions of two enzymes. SAGE-547 is being developed as an IV adjunctive therapy in conjunction with underlying anesthesia as a treatment for SRSE. SAGE-547 is currently in Phase 1/2 clinical trial for SE and in exploratory Phase 2a clinical trials for essential tremor and severe PPD. In April 2014, the FDA granted us orphan drug designation for SAGE-547 as a treatment for SE. In July 2014, the FDA granted us fast track designation for the SAGE-547 development program.

We believe SAGE-547 has an optimal profile for the treatment of SRSE. SAGE-547 has a wide therapeutic window that allows for allosteric modulation of the $GABA_A$ receptor both synaptically and extrasynaptically without inducing deep anesthesia. The pharmacological properties of SAGE-547, including a short half-life of one hour, allows for continuous IV administration. The ability to titrate SAGE-547 creates the opportunity to tailor therapy to a specific SRSE patient s needs as well as to efficiently administer and withdraw the compound.

Non-clinical results

We believe the clinical development program for SAGE-547 is supported by significant non-clinical data and strong scientific rationale. There are numerous reports that demonstrate the non-clinical efficacy of allopregnanolone as well as multiple studies that we have conducted showing the in vitro and in vivo pharmacologic efficacy of SAGE-547 in seizure models, thus providing a strong non-clinical rationale for SAGE-547 in certain forms of seizure, such as SRSE.

A comprehensive toxicology dose escalating study exploring the effects of SAGE-547 in two species (rat and dog) is currently underway, the first segment of which we submitted to the FDA in the second quarter of 2014, and is expected to be completed in the first quarter of 2015. We must complete these studies before we commence a pivotal clinical trial for SAGE-547.

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Emergency-use experience with SAGE-547

We have compiled evidence of activity with SAGE-547 in emergency-use settings that support the safety and potency of SAGE-547 for the treatment of SRSE. To date, a total of ten patients, six males and four females with a mean age of 17, were treated with SAGE-547 by independent centers under emergency-use INDs. Of note, each individual case of SRSE arose from a presumed different underlying etiology, the patients were of varying ages and all patients had been placed in a long-duration medically induced coma. In each case SAGE-547 was administered with a target steady state exposure similar to that planned for our ongoing Phase 1/2 clinical trial. Seven of these patients treated with SAGE-547 achieved resolution of SRSE either during the course of or soon after SAGE-547 treatment, one patient was not evaluable for efficacy of SAGE-547. The overall response rate was 78%.

* Estimated

We can provide no assurance that the positive results observed to date in emergency-use cases are attributable to SAGE-547; as such cases were not carried out in the controlled environment of a clinical trial. Further, we can provide no assurance that the administration of SAGE-547 to other patients in our clinical trials or otherwise will have positive results.

Clinical

In October 2013, we filed an IND for SAGE-547 for the treatment of SRSE with the FDA, and we received notification allowing us to proceed with our Phase 1/2 clinical trial of SAGE-547 in November 2013. We commenced our Phase 1/2 clinical trial to study safety, tolerability and efficacy of SAGE-547 in adult patients with SRSE in January 2014. This clinical trial is an open-label trial in at least ten patients diagnosed with SRSE. As of January 31, 2015, there were 17 active study sites in the United States. An SE patient who has failed therapy with first- and second-line agents and has failed IV general anesthesia, or GA, administered over 24 hours is eligible to be included in this trial. Patients will be excluded from participation in this trial if their SE is due to anoxic brain injury or they have end-organ damage of any major organ, such as the brain, the liver or the heart, which would make recovery from either SE or the underlying condition highly unlikely.

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The figure below demonstrates the design of the screening and treatment periods of this Phase 1/2 clinical trial. Following the treatment period, there is an acute two-day follow-up period and an extended three-week follow-up period.

The primary endpoints of this trial are to evaluate the safety and tolerability of SAGE-547 in SRSE patients. Safety and tolerability will be assessed by monitoring adverse events, EEG, physical examinations, neurological examinations, vital signs, clinical laboratory measures, electrocardiograms and concomitant medication usage. The secondary endpoint of this trial is to access the efficacy of SAGE-547 on SRSE, assessed by the need to place the patient back into a medically induced coma for seizure control during administration of SAGE-547, as well as the duration of the observed response. In order to allow full assessment of pharmacologic activity, this trial employs broad inclusion criteria, primarily excluding patients only if there is major damage to the brain, such as anoxic injury, devastating stroke or the presence of a large lesion. Other secondary objectives used to measure efficacy include scores on global and specific scales relating to cognition, agitation and depth of coma and survival.

On January 9, 2015, we reported results from our Phase 1/2 clinical trial. Consistent with topline data announced in November 2014, the primary endpoint, safety and tolerability, was achieved in all patients. Of the 20 patients enrolled in the ongoing Phase 1/2 clinical trial, 17 patients were evaluable for efficacy. 71% of evaluable patients met the key efficacy endpoint of being successfully weaned off their anesthetic agents while SAGE-547 was being administered. In addition, 71% of evaluable patients were successfully weaned off SAGE-547 without recurrence of SRSE. As a group, patients who responded to SAGE-547 generally demonstrated rapid improvement over the first five days following treatment. Patients who responded also continued to improve over the 30-day follow-up period as assessed by several measures. SAGE-547 was generally well tolerated and no drug-related serious adverse events, as determined by the Safety Review Committee, were reported in treated patients. The mean exposure level of SAGE-547 was approximately 200 nM.

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At baseline, all patients were measured by the Clinical Global Impression of Severity (CGI-S) scale, which tracks patient progress and treatment response over time, as well as the Glasgow Coma Scale, which helps gauge the severity of an acute brain injury. At baseline, 19 patients were classified as most extremely ill as measured by CGI-S, the remaining patient was described as severely ill. By day 30, the group of patients who responded to SAGE-547 had improved to mildly ill, which represents a three-step improvement in the severity of their illness. In contrast, the group of patients who did not respond to SAGE-547 did not improve beyond severely ill throughout the study period. As measured by the Glasgow Coma Scale, the group of patients who responded to SAGE-547 showed rapid improvement in the first five days following treatment and continued improvement throughout the complete study period.

The underlying etiology was explored in the 20 patients enrolled. SRSE was attributed to brain hemorrhage in four patients, infections in four patients, worsening of seizures in two patients, primary or metastatic brain tumors in two patients and to unknown causes in three patients. The other five cases of SRSE were caused by each of: stroke, sickle cell anemia, Lupus, posterior reversible encephalopathy syndrome and toxic ingestion.

Independent of treatment response, five patient deaths occurred within the study period, all driven by underlying conditions. Although 13 patients (65 percent) reported serious adverse events, none were considered drug-related.

The results obtained from the patients in this trial may not be representative of results obtained from future patients treated with SAGE-547 in this clinical trial. For a further description of this risk, see Risk Factors Risks Related to Product Development, Regulatory Approval and Commercialization Positive results from early 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. 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, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

In October 2014, the FDA approved a protocol amendment for our Phase 1/2 clinical trial that enables us to treat pediatric patients as young as two years old, to increase the dose of SAGE-547 being administered to patients and to increase the duration of treatment up to two weeks. We are continuing to enroll patients as an expansion cohort in this trial, and this enrollment will proceed in parallel with our regulatory initiatives.

We have also initiated an expanded access program in parallel with our ongoing clinical trial for SRSE. The goal of this program is to ensure availability of our experimental medicines for SRSE for appropriate patients. Through our expanded access program, SAGE-547 will be provided free of charge to the institution and appropriate patients. We will consider granting expanded access to SAGE-547 for individual patient programs, including emergency-use programs, consistent with the policies established by the local regulatory authorities. Information obtained through this program will more fully inform our understanding of the overall benefit/risk profile of SAGE-547 and will help guide decision making for future clinical trials.

In addition, we continue to use SAGE-547 to establish proof of principle in clinical trials for additional indications. In October 2014, we began patient enrollment in an exploratory Phase 2a clinical trial of SAGE-547 in patients with essential tremor, a debilitating neurological disorder that causes involuntary, rhythmic shaking with no known cause. This trial is designed to evaluate the safety, tolerability, pharmacokinetics and activity of SAGE-547 in patients with essential tremor. In January 2015, we also initiated a Phase 2a clinical trial of SAGE-547 in women with severe PPD, a distinct and readily identified form of major depressive disorder estimated to affect 15% to 20% of women following childbirth. This trial is designed to evaluate the safety, tolerability, pharmacokinetics and efficacy of SAGE-547 for the treatment of severe PPD. We plan to use the data from these exploratory studies to help guide the design of a second-generation molecule for the chronic treatment of these diseases.

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SAGE-689

SAGE-689 is being developed as an adjunctive IV therapy for the treatment of SE patients whose seizures have not resolved after treatment with BDZs in a non-hospital setting. Patients with SE at this stage are transported by ambulance to the hospital and frequently receive treatment in the emergency room with anti-seizure drugs. If their seizure does not resolve rapidly the patient must be transferred to the ICU and immediately placed into a medically induced coma to minimize the risk of brain damage. SAGE-689 is currently in IND-enabling toxicology and safety pharmacology testing.

We are developing SAGE-689 so that it will have what we believe is the optimal profile as a second-line therapy for the treatment of SE prior to a patient being placed into a medically induced coma. These characteristics include a wide therapeutic window to allow for modulation of the $GABA_A$ receptor without inducing deep anesthesia, and a short half-life to permit rapid onset and loss of activity. The latter property will facilitate rapid discharge or transfer to the ICU without residual drug on board. SAGE-689 is being formulated for IV or intramuscular administration to optimize these characteristics in a clinical setting.

We plan on filing an IND for SAGE-689 by late 2015 and to begin a Phase 1 clinical trial thereafter. Our Phase 1 clinical development program for SAGE-689 will be designed to rapidly assess relevant product characteristics for this compound, such as quality of sedation, impact on EEG in normal patients and possibly in patients with epilepsy, pharmacokinetics and general safety. Our Phase 1 clinical trial will also inform us of SAGE-689 s ability to induce EEG-confirmed burst suppression.

Depending upon the results of our Phase 1 clinical trial, we anticipate that subsequent development of SAGE-689 will involve studies of its utility as an adjunctive therapy, comparing it in combination with best practice, versus practice alone.

Non-clinical results

The non-clinical evaluation for SAGE-689 encompasses standard toxicology and pharmacology. In addition, our focus has been on understanding the potential for SAGE-689 to be deployed as a short half-life agent in the treatment of SE in an emergency situation. Thus we have looked at non-clinical models that will assess its sedative profile, its cardiovascular safety, its effect on EEG and its ability to induce burst suppression as a proxy for anti-seizure activity.

The results from non-clinical animal models may not be replicated in clinical trials. Many drug candidates, including many targeting CNS disorders, with promising non-clinical profiles have failed to demonstrate similar safety, non-toxicity and efficacy in humans. To the extent possible, animal models attempt to replicate both the phenotype of the human disease and its underlying causality to assess the putative efficacy of a drug candidate. However, in many cases, the cause of the human disease is not fully elucidated, thereby decreasing the likelihood that the animal model will accurately predict the efficacy of a drug candidate in humans. The non-clinical results reported for SAGE-689 below should be read with these limitations in mind.

Efficacy

SAGE-689, a selective positive allosteric modulator at $GABA_A$ receptors, possesses anticonvulsant, anxiolytic and sedative properties in animal models. This activity provides a non-clinical rationale for potential efficacy of SAGE-689 in patients with various forms of seizure. In an SE model in rodents, a single IV bolus dose of SAGE-689 (5 mg/kg and 15 mg/kg) given up to 60 minutes following induction of SE produces complete cessation of seizure activity. In the same SE model, BDZs do not show effectiveness in seizure cessation. Furthermore, SAGE-689

effectively halts re-occurrence of seizure activity for up to three hours after treatment with the compound as measured by EEG. SAGE-689 produces dose-related protection from seizure activity in rodent model of SE.

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With respect to sedation, SAGE-689 is an effective, fast acting and rapidly reversible sedative/hypnotic agent when given acutely in both rats and dogs. Single IV bolus injections of SAGE-689 produce a spectrum of sedative effects, from light sedation at low doses to general anesthesia at higher doses. In emergency room settings, propofol is often used as a sedative for emergency situations and for seizure control. We thus compared SAGE-689 s safety and activity to propofol in several non-clinical animal experiments, and in general, SAGE-689 showed a more manageable profile for achieving varying levels of sedation. In particular, progressively deeper levels of sedation with SAGE-689 were achieved with more control and broader plasma exposures than with propofol, indicating that SAGE-689 in humans will allow, we believe, a more optimal level of controlled sedation than with propofol. Recovery from sedation after withdrawal of SAGE-689 was rapid, occurring within 15 minutes after cessation of a one hour continuous IV infusion in the rat. These recovery times are comparable with those observed after a one hour continuous infusion of propofol in animal studies.

Pharmacokinetics

SAGE-689 was found to have high systemic clearance and short half-life in both rodents and dogs. CNS penetration was observed in rats following both IV bolus and IV infusion doses, and brain to plasma ratios exceed one, showing ease of transport into the brain, which is necessary for efficacy in humans.

Non-clinical safety

Cardiovascular safety is an important attribute of any agent that is administered via IV infusion, whether used for sedation or other purposes. We compared SAGE-689 to propofol in these non-clinical studies. Safety studies were conducted in telemetered male beagle dogs administered SAGE-689. SAGE-689 exhibited less severe cardiovascular and respiratory effects than propofol across a wide range of exposures, with a therapeutic index for moderate sedation across a wide range of exposurpropofol. In addition, no apnea, or absence of breathing, was observed after IV administration of SAGE-689 in this study, and although a detailed analysis was not performed, there were no obvious, prevalent or reproducible abnormalities associated with the electrocardiogram during the administration of SAGE-689. Thus, non-clinical data suggest an acceptable cardiovascular safety profile for SAGE-689 that we believe in humans has the potential to have a better risk-benefit profile than propofol.

SAGE-217

SAGE-217 is being developed as an oral monotherapy for orphan genetic epilepsies, such as Dravet and Rett syndromes. The chemical characteristics of SAGE-217 potentially allow formulation as both an IV and PO medication. SAGE is first intending to develop this compound as an oral agent where we believe an expedited pathway is possible. SAGE-217 is currently in IND-enabling toxicology and safety pharmacology testing.

We are developing SAGE-217 so that it will have what we believe is an optimal profile as a monotherapy for epilepsy in many forms. SAGE-217 is expected to have the ability to induce deep anesthesia and produce EEG-confirmed burst suppression. The long half-life of SAGE-217 will allow potential once-daily dosing, and will also allow it to auto-taper on cessation as well as avoiding rapid fluctuations of blood levels when administered. The long half-life, ability to induce deep and prolonged anesthesia, oral availability, and potency at extrasynaptic $GABA_A$ receptors will distinguish it from other product candidates and other currently available therapies.

It is these target characteristics, we believe, that may make SAGE-217 useful as a treatment for orphan genetic seizure disorders, such as Rett syndrome and Dravet syndrome. In addition, potential anti-seizure activity may make SAGE-217 useful in general epilepsy and in forms of SE as an oral maintenance therapy after SE, RSE, or SRSE resolution is achieved, in order to prevent seizure recurrence.

We plan to file an IND for SAGE-217 by late 2015. In the Phase 1 development of SAGE-217, we intend to assess sedative qualities, safety profile, cardiovascular safety, impact on EEG and ability to induce burst suppression.

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Non-clinical results

The results from non-clinical animal models may not be replicated in clinical trials. Many drug candidates, including many targeting CNS disorders, with promising non-clinical profiles have failed to demonstrate similar safety, non-toxicity and efficacy in humans. To the extent possible, animal models attempt to replicate both the phenotype of the human disease and its underlying causality to assess the putative efficacy of a drug candidate. However, in many cases, the cause of the human disease is not fully elucidated, thereby decreasing the likelihood that an animal model will accurately predict the efficacy of a drug candidate in humans. The non-clinical results reported for SAGE-217 below should be read with these limitations in mind.

Efficacy

Similar to SAGE-689 and SAGE-547, SAGE-217 is pharmacologically active in various models of seizure. Efficacy studies in multiple non-clinical seizure models have shown good anti-seizure activity in pharmacoresistant models of SE. Through $GABA_A$ receptor modulation, SAGE-217 possesses potent anticonvulsant, anxiolytic and sedative activity when administered in vivo.

In an SE model in rodents, SAGE-217 produces complete cessation of seizures at 3 mg/kg and 5 mg/kg when dosed via IV infusion. Furthermore SAGE-217 effectively halts any seizure recurrence up to three hours after the treatment when measured by EEG. Additional studies in seizure models are ongoing to fully understand the utility of SAGE-217 for other seizure indications; however, we believe the ability to prevent seizure recurrence in these models may be an attribute unique to this molecule.

Pharmacokinetics

SAGE-217 was found to have low systemic clearance and long half-life in both rodents and dogs. CNS penetration was observed in rats following both oral and IV doses, and brain to plasma ratios exceed one, showing ease of transport into the brain, which is necessary for efficacy in humans. The pharmacokinetic profile of SAGE-217 suggests the compound will be amenable to once-a-day dosing in humans as an oral formulation, and will require only a very low infusion dose requirement when dosed via IV infusion.

Non-clinical safety

Safety studies on SAGE-217 are planned. Pharmacology studies completed suggest the molecule is well tolerated at efficacious doses demonstrating activity when administered either via IV infusion or orally.

Further Exploitation of $GABA_A$ and NMDA Receptors

We are exploring additional potential products in a variety of CNS disorders based on modulation of both the $GABA_A$ and NMDA receptors. In addition to our products focused on SE, other $GABA_A$ mediated CNS disorders upon which we believe our approach can have a material impact include Rett syndrome, Dravet syndrome, fragile X syndrome, anxiety, depression, sleep disorders, mania, tremor, tinnitus and post-traumatic stress disorder.

NMDA receptors also serve a critical role in CNS related activities; however current attempts at exploiting these receptors have been suboptimal due to limited efficacy and adverse events. We have produced a large pool of highly selective product candidates which are allosteric modulators of the NMDA receptor that we believe can be used for the treatment of cognitive dysfunction in diseases such as depression, Alzheimer s disease, attention deficit hyperactivity disorder and schizophrenia, as well as certain aspects of Huntington s disease, and neuropathic pain.

Our initial focus will remain on those indications where we can independently develop and commercialize our products, if approved. However, our broad potential pipeline lessens our reliance on the success of any one program. We believe our ability to design and develop novel molecules with distinct profiles and receptor subtype selectivity will provide us with an opportunity to create value by either in-house development or by partnering these assets with third parties who possess the development and commercialization capabilities to pursue these programs.

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Manufacturing and Supply

We do not own nor operate, and currently have no plans to establish, any manufacturing facilities. We currently resource all of our non-clinical and clinical compound supply through third party contract manufacturing organizations, or CMOs.

We currently have sufficient SAGE-547 drug product on hand for our Phase 1/2 clinical trial in SRSE, Phase 2a clinical trial in essential tremor and Phase 2a clinical trial in severe PPD and ongoing non-clinical studies. Additionally, we have SAGE-547 drug substance on hand to support Phase 3 clinical trials. We are working with our CMOs to modify the manufacturing process for SAGE-547 drug product to (i) increase the maximum shelf-life of this product candidate from one to two years to up to three years and (ii) eliminate the need for cold storage. We currently have sufficient SAGE-689 drug substance on hand for our ongoing non-clinical studies and have a scheduled manufacturing date for current good manufacturing practice, or cGMP, batches to support Phase 1 clinical trials. We currently have sufficient SAGE-217 drug substance on hand for our ongoing non-clinical studies and have begun manufacture of current good manufacturing practice, or cGMP, batches to support Phase 1 clinical trials.

We have established relationships with several key CMOs to enable both the non-clinical and clinical supply chains for SAGE-547, SAGE-689 and SAGE-217 active pharmaceutical ingredient, or API, as well as drug product under cGMP protocols. Key intermediates to support the large-scale production of these candidates are performed by other CMOs on a purchase order basis. We do not currently have arrangements in place for redundant supply of bulk drug substance. It is our intent to identify and qualify additional manufacturers to provide API and fill-and-finish services prior to submission of a new drug application to the FDA for all product candidates.

SAGE-547, SAGE-689 and SAGE-217 are low molecular weight compounds isolated as stable crystalline solids. We believe the syntheses of SAGE-547, SAGE-689 and SAGE-217 are reliable and reproducible from readily available starting materials, and the synthetic routes are amenable to large-scale and do not require unusual equipment or handling in the manufacturing process. The enantiomeric purity of SAGE-547, SAGE-689 and SAGE-217 is very high (>99.9%) as a result of the chirality being derived from the backbone of the natural product steroid-based raw materials. We expect to continue to identify and develop drug candidates that are amenable to cost-effective production at contract manufacturing facilities.

Research and Development

Research and Development expenses for the year ended December 31, 2014 were $24.1 million.

Sales and Marketing

Given our stage of development, we have not yet established a commercial organization or distribution capabilities, nor have we entered into any partnership or co-promotion arrangements with an established pharmaceutical company. We are concentrating our internal efforts on CNS disorders where we believe we can efficiently commercialize our product candidates on our own. For example, in the United States we believe that SE patients are easily identifiable in tertiary care centers where there are ICUs and staff trained in treating refractory or super-refractory SE patients. In a recent secondary analysis of Premier Network Hospitals 2012 billing data, we found approximately 70% of SRSE discharges, as determined by business rules we and our consultants established, occurred in 925 US hospitals of 300 beds or more. In addition, 56% of the SRSE discharges had a length of stay of 10 days or more thereby allowing hospitals to bill from approximately $170,000 to $550,000 in charges depending on the patient s length of stay and diagnosis-related group (DRG). As a result, we believe we can successfully launch and commercialize our initial product candidates on our own, using a small and highly specialized sales force similar to those of other rare-disease

companies. We also think there is a potential pharmacoeconomic argument should hospital length of stays become reduced due to earlier resolution of SRSE acknowledging SAGE-547 will have no effect on the underlying etiology.

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To develop the appropriate commercial infrastructure to launch our product candidates, we may establish alliances with one or more pharmaceutical company collaborators, depending on, among other things, the applicable indications, the related development costs and our available resources. We plan to selectively partner assets geared toward treating CNS disorders that impact large patient populations, such depression and cognition where there are no reliable and predictive animal models to guide drug development. In order to effectively and efficiently develop product candidates for these larger markets or more difficult indications, we intend to partner at an appropriate stage with companies who have clinical expertise and pre-existing commercial infrastructure in these areas.

Licenses

We have entered into several license agreements to support our various programs.

Washington University

In November 2013, we entered into a license agreement with Washington University, or WU. Under this agreement, and subject to certain rights of the U.S. government and rights retained by WU, WU granted to us an exclusive, worldwide license under certain patent rights to make, have made, sell, and offer for sale, use and import products covered by certain of its patent rights. WU s rights in a patent application disclosing and claiming SAGE-689 is included in this license agreement. Under this agreement, WU also granted us non-exclusive license under certain technical information and tangible research information to use such technical information and/or tangible research information to make, have made, sell, offer for sale, use and import products that embody or were made using a method or process covered in the technical information and/or tangible research information. The WU license also grants us a right to sublicense our licensed rights to third parties, provided each sublicensee enters into a written agreement with us with terms consistent with our agreement with WU. We must pay to WU a percentage of the revenue we receive from sublicensing our rights under this agreement, initially in the mid-teens and decreasing to the mid-single digits over time.

Pursuant to the WU license, we are required to use commercially reasonable efforts to continue active, diligent development of licensed products and to use commercially reasonable efforts to manufacture, promote and sell licensed products throughout the territory and in the field during the term of the agreement. We must deliver written reports to WU describing our progress no later than January 31 and July 31 of the first two calendar years of the agreement, and no later than January 31 of each calendar year thereafter.

We must pay to WU an annual maintenance fee until and including the year in which our first Phase 2 clinical trial is initiated, and we must make up to $0.7 million and $0.5 million in clinical development and regulatory milestones, respectively, to WU, for each licensed product, upon reaching certain milestones relating to the clinical development of our product candidates. The license agreement also requires us to make low single-digit royalty payments to WU in connection with the sales of licensed products.

The WU agreement will expire on a licensed product-by-licensed product basis upon the later of (i) the last day that at least one valid patent claim covering the licensed product exists, or (ii) the tenth anniversary of the day of the first commercial sale of the licensed product. We may terminate the WU Agreement early for convenience upon providing WU with 90 days written notice. WU may terminate this agreement early in the event of our failure to cure a material breach within the applicable cure period or our bankruptcy. In the event of early termination of this agreement before the expiration of the last to expire of the patent rights, we must immediately discontinue manufacture, sale and distribution of any licensed products.

CyDex Pharmaceuticals

In August 2013, we entered into a license agreement with CyDex Pharmaceuticals, Inc., or CyDex, a wholly owned subsidiary of Ligand Pharmaceuticals, Inc., which was amended in April 2014. Pursuant to the CyDex agreement, CyDex granted us an exclusive, non-transferable license under certain patent rights to research,

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develop, make, have made, import, use, offer for sale, and sell licensed products, which will consist of our compound, a certain neuroactive steroid known as allopregnanolone, formulated in CyDex s proprietary Captisol technology, in the licensed field. Captisol is an excipient that allows us to dissolve allopregnanlone, which has limited solubility in water, in an aqueous solution. Our field of use includes all fields for the treatment, prevention or diagnosis of any disease or symptom in humans or animals. We have also been granted a non-exclusive license to all toxicology/safety and other relevant scientific data owned, licensed or developed by CyDex and relating to Captisol for use in connection with licensed product in the licensed field. We have the right to grant sublicenses outright to third parties under the agreement, provided each sublicensee enters into a written agreement with us, and each sublicensee must abide by the restrictions of the CyDex license. Pursuant to the agreement, we granted CyDex a nonexclusive, royalty-free license to any Captisol improvements developed by us.

Pursuant to the CyDex license, we are required during the term of the agreement to use commercially reasonable efforts to continue active, diligent development of the licensed product, to seek regulatory approval of the licensed product and to commercialize the licensed product following regulatory approval. We must deliver periodic progress reports to CyDex.

We are obligated to make milestone payments of $0.8 million and $3.8 million, respectively, based on the achievement of clinical development and regulatory milestones for the development of SAGE-547, with the payments to be made once per field in the fields of SE and traumatic brain injury. For the development in two additional fields, we are obligated to make milestone payments, once per field, for the first two additional fields, on the achievement of clinical development and regulatory milestones of $1.3 million and $8.5 million, respectively. We must also pay low single-digit royalties to CyDex in connection with the sale of such licensed products. CyDex controls prosecution and enforcement of the licensed patent rights.

The CyDex license is perpetual until terminated. We may terminate the CyDex agreement for convenience upon providing 180 days prior written notice to CyDex. Either party has the right to terminate the agreement for failure to cure a material breach in the applicable cure period.

We have also entered into an amended supply agreement with CyDex pursuant to which we are required to purchase all of our supply of Captisol from CyDex and CyDex is required to supply us with Captisol, subject to certain limitations. Under this agreement, if we do not place an order for at least the quantity of Captisol we forecasted in the first quarter of any year, we will be required to pay 60% of the purchase price for the forecasted material not purchased to CyDex. CyDex has the right to raise prices for Captisol once per year based on an industry index maintained by the Bureau of Labor Statistics. The supply agreement also contains customary provisions regarding confidentiality, indemnification and non-solicitation, as well as customary representations and warranties. The supply agreement will terminate upon the termination of our license agreement with CyDex or upon breach by either party without cure after notice.

University of California

In October 2013, we entered into a license agreement with The Regents of the University of California, or the Regents, which was amended in May 2014. Pursuant to this agreement, and subject to certain rights of the U.S. government and rights retained by the Regents, the Regents granted us a non-exclusive, non-transferable license under all personal property rights of the Regents covering the tangible personal property in an IND application package owned by the Regents, or the Data, and a specified quantity of cGMP grade allopregnanolone, or the Material, to (i) use the Data for reference or incorporation in an IND for the use of the Material as a treatment of SE, essential tremor and/or severe PPD and (ii) use the Material or modifications of the Material to develop a pharmaceutical formulation for clinical trials for SE, essential tremor and/or postpartum depression. The rights licensed to us are not

sublicenseable.

Pursuant to this agreement, we are required to use commercially reasonable efforts to proceed with the development, manufacture and sale of one or more products containing allopregnanolone, a derived product

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under the agreement, for the treatment of SE, essential tremor and/or severe PPD. As of January 1, 2014, we must deliver written reports to the Regents describing our progress no later than 60 days subsequent to June 30 and December 31 of each fiscal year.

This agreement requires us to make up to $0.1 million in milestone payments in connection with the first derived product that meets the relevant milestones and we must also pay royalties of less than 1% to the Regents for each derived product for a period of 15 years following the first commercial sale of such derived product. This agreement 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. We may terminate this agreement early for convenience upon providing 60 days prior written notice to the Regents. The Regents may terminate this agreement early in the event of material default, including failure to provide timely progress reports, after the applicable cure period, or in the event of our bankruptcy. In the event of early termination of this agreement, we have the right to sell any partially made derived products for a period of 120 days from the date of termination, but may not otherwise make, have made, use, sell, have sold, offer for sale or import products containing allopregnanolone.

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture, and any other aspects of inventions that are commercially important to the development of our business. We 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.

We plan to continue to expand our intellectual property estate by filing patent applications directed to compositions, methods of treatment and patient selection created or identified from our ongoing development of our product candidates. Our success will depend 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, 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 and maintain our proprietary position. We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings or derivation proceedings declared by the United States Patent and Trademark Office, or U.S. PTO, to determine priority of invention.

Patents

Our patent portfolio includes patent applications in the early stages of prosecution and no patents have, as of yet, issued from our patent application estate. These patent applications fall into three categories: (1) SAGE-547; (2) $GABA_A$ receptor modulators; including genus and species claims to SAGE-689; and (3) NMDA receptor modulators.

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(1) We own three patent families generally related to SAGE-547. One of these patent families includes a patent application having claims to compositions containing allopregnanolone and a cyclodextrin. The compositions can be used for the treatment of CNS disorders such as traumatic brain injury and SE. The second patent family includes patent applications having claims directed to methods of treating seizure disorders, such as SE, by administering allopregnanolone using particular dosing regimens or multiple dosage phases. The third patent family includes methods of treating essential tremor and depression such as severe PPD. Any U.S. patents that may issue from these families of patent applications would have a statutory expiration date in January and August of 2033, and September 2035 respectively. The time period for electing to pursue foreign patent protection for the inventions disclosed in these patent applications by filing national stage patent applications in individual jurisdictions has not yet expired, and we will need to decide whether and where to pursue ex-U.S. protection before expiration of the applicable deadlines.

(2) We have exclusively licensed a portfolio of patent applications owned by WU, which are directed to certain GABA receptor modulating compounds and methods of using these compounds, for example in anesthesia or treatment of GABA-related disorders. This portfolio of patent applications includes seven families of patent applications. One of these seven families of patent applications is co-owned by us, and this co-owned family includes a pending U.S. patent application and a pending Patent Cooperation Treaty patent application. This co-owned application discloses and claims SAGE-689 and its use in anesthesia or treatment of GABA-related disorders. Any U.S. patents that may issue from the SAGE-689 patent family would have a statutory expiration date of December 2033. The time period for electing to pursue foreign patent protection for SAGE-689 by filing national stage patent applications in individual jurisdictions has not yet expired, and we will need to decide whether and where to pursue ex-U.S. protection before expiration of the applicable deadlines. In addition, U.S. 7,781,421, solely owned by WU, expires in September 2027. Any patents that may issue, if any, from the remaining five families solely owned by WU would have statutory expiration dates that range from 2032 to 2034.

(3) In addition to the patent applications licensed from WU, we own thirteen patent families, resulting from work done exclusively by us and our contract research organizations, directed to additional GABA receptor modulating compounds and methods of using these compounds, for example in anesthesia or treatment of GABA-related disorders. Any U.S. patents that may issue from these patent families would have a statutory expiration ranging from October 2032 to January 2036. Other than SAGE-547 and SAGE-689, we have pending within these patent families genus and species claims to the majority of the compounds in our $GABA_A$ receptor modulating compound collection, including SAGE-217. These patent families are in the early stages of patent prosecution and include families for which only provisional applications have been filed. The time period for electing to pursue foreign patent protection by filing national stage patent applications in individual jurisdictions has not yet expired for some of these patent families, and we will need to decide whether and where to pursue ex-U.S. protection before expiration of the applicable deadlines

(4) We also own six families of applications directed to modulators of NMDA receptors. Four of these patent families are directed to compounds that modulate NMDA receptors, which can be used to treat NMDA receptor-related disorders such as CNS related conditions. One of these patent families is directed to using a naturally occurring compound as a biomarker for a subject who would benefit from treatment with a modulator of NMDA receptors. One of these patent families is directed to using a modulator of NMDA receptors to treat a rare NMDA loss of function disorder. Any patents that may issue, if any, from these families of applications directed to modulators of NMDA receptors would have statutory expiration dates in September 2032 and January 2036.

Patent term

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority. The term of a U.S. patent can be lengthened by patent term adjustment, which

compensates the owner of the patent for administrative delays at the U.S. PTO. In some cases, the term of a U.S. patent is shortened by terminal disclaimer that reduces its term to that of an earlier-expiring patent.

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The term of a U.S. patent may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act, to account for at least some of the time the drug is under development and regulatory review after the patent is granted. With regard to a drug for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one U.S. patent that includes at least one claim covering the composition of matter of an FDA-approved drug, an FDA-approved method of treatment using the drug, and/or a method of manufacturing the FDA-approved drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug. Some foreign jurisdictions, including Europe and Japan, have analogous patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extension on patents covering those products, their methods of use, and/or methods of manufacture.

Trade secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. We typically 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. We protect trade secrets and know-how by establishing confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and partners. These agreements provide that all confidential information developed or made known during the course of an individual or entity s relationship with us must be kept confidential during and after the relationship. These agreements also provide that all inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriate of our proprietary information by third parties.

Competition

The biopharmaceuticals industry is highly competitive. There are many public and private biopharmaceutical companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our product candidates or address similar markets. It is probable that the number of companies seeking to develop products and therapies similar to our products will increase.

Currently, there are no therapies that have been specifically approved for treatment of RSE or SRSE. However, many products approved for other indications, for example, general anesthetics and anti-seizure drugs, are used off-label for various stages of SE therapy. Additionally, though not indicated, acupuncture, hypothermia, and electroconvulsive therapy are sometimes used prior to withdrawal of care for patients with SRSE.

In the field of neuroactive steroids focused on modulation of $GABA_A$ or NMDA receptors, our principal competitor is Marinus Pharmaceuticals, Inc., which we believe is developing a reformulated form of ganaxolone, a known $GABA_A$ positive allosteric modulator neuroactive steroid, for the potential treatment of drug-resistant partial complex seizures and fragile X syndrome. With the development of SAGE s GABA platform, we see this as a prime opportunity to progress the second generation of neuroactive steroids which are pharmacologically active with fewer and less severe off-target effects than first generation compounds. 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. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have

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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.

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug products. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. drug development

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA s refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- Completion of extensive non-clinical, sometimes referred to as non-clinical laboratory tests, non-clinical animal studies and formulation studies in accordance with applicable regulations, including the FDA s current Good Laboratory Practice, or GLP, regulations;

- Submission to the FDA of an IND application, which must become effective before human clinical trials may begin;

- Approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each trial may be initiated;

- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations, sometimes referred to as good clinical practices, or GCPs, to establish

the safety and efficacy of the proposed drug for each proposed indication;

Submission to the FDA of an NDA, for a new drug;

A determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;

Satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug s identity, strength, quality and purity;

Potential FDA audit of the non-clinical and/or clinical trial sites that generated the data in support of the NDA; and

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

The non-clinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. Non-clinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product.

The data required to support an NDA is generated in two distinct development stages: non-clinical and clinical. For new chemical entities, the non-clinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing. The conduct of the non-clinical tests must comply with federal regulations, including GLPs. The sponsor must submit the results of the non-clinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. Some non-clinical testing may continue even after the IND is submitted, but an IND must become effective before human clinical trials may begin. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials, including subjects will be exposed to unreasonable health risks, and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

The clinical stage of development involves the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor s control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA so long as the clinical trial is conducted in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki and/or the laws and regulations of the country or countries in which the clinical trial is performed, whichever provides the greater protection to the participants in the clinical trial.

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Clinical trials

Clinical trials are generally conducted in three sequential phases that may overlap, known as Phase 1, Phase 2 and Phase 3 clinical trials.

Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug.

Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy.

Phase 3 clinical trials generally involve large numbers of patients at multiple sites (from several hundred to several thousand subjects) and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

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

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, finding from other studies, or any finding from animal or in vitro testing that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB s requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, we must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

NDA and FDA review process

The results of non-clinical studies and of the clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the drug and proposed labeling, are submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP to assure and preserve the product s identity, strength, quality and purity. FDA approval of an NDA must be obtained before a drug may be offered for sale in the United States.

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In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA s fee schedule, effective through December 31, 2014, the user fee for an application requiring clinical data, such as an NDA, is $2.2 million. PDUFA also imposes an annual product fee for human drugs of $0.1 million and an annual establishment fee of $0.6 million on facilities used to manufacture prescription drugs. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has 10 months from the filing date in which to complete its initial review of a standard NDA and respond to the applicant, and six months from the filing date for a priority NDA. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product s identity, strength, quality and purity. Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. The review and evaluation of an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

After the FDA evaluates an NDA, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, non-clinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data

obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

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There is no assurance that the FDA will ultimately approve a drug product for marketing in the United States and we may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-marketing testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 testing which involves clinical trials designed to further assess a drug s safety and efficacy and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a risk evaluation and mitigation strategy, or REMS, to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication than that for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same product as defined by the FDA or if our product candidate is determined to be contained within the competitor s product for the same indication or disease. If a drug designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the European Union has similar, but not identical, benefits.

Expedited development and review programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug as a Fast Track product at

any time during the clinical development of the product. Unique to a Fast Track product, the FDA may review sections of the marketing application on a rolling basis before the complete NDA is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

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Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or offers a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. A product may also be eligible for accelerated approval. Drugs studied for their safety and efficacy in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it will require such post-marketing restrictions, as it deems necessary to assure safe use of the drug, such as:

distribution restricted to certain facilities or physicians with special training or experience; or

distribution conditioned on the performance of specified medical procedures.

The limitations imposed would be commensurate with the specific safety concerns presented by the drug. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Additionally, a drug may be eligible for designation as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more indications. The benefits of breakthrough therapy designation includes the same benefits as fast track designation, plus intensive guidance from FDA to ensure an efficient drug development program. Fast Track designation, priority review, accelerated approval and breakthrough designation do not change the standards for approval, but may expedite the development or approval process.

Pediatric trials

The Food and Drug Administration Safety and Innovation Act, or FDASIA, which was signed into law on July 9, 2012, amended the FDCA to require that a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from non-clinical studies, early phase clinical trials, and/or other clinical development programs.

Post-marketing requirements

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the product, providing the regulatory authorities with updated safety and efficacy information, product sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others,

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standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug s approved labeling (known as off-label use), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the Internet. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the applicant to develop additional data or conduct additional non-clinical studies and clinical trials. As with new NDAs, the review process is often significantly extended by FDA requests for additional information or clarification. Any distribution of prescription drug products and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or the PDMA, a part of the FDCA.

In the United States, once a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These manufacturers must comply with cGMP regulations that require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the product from the market.

Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product s approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA s policies may change, which could delay or prevent regulatory approval of our products under development.

Other regulatory matters

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the United States Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments. In the United States, sales, marketing and scientific/educational programs must also comply with state and federal fraud and abuse laws. These laws include the federal Anti-Kickback Statute, which makes it illegal

for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, or prescription of a particular drug, for which

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payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties, and exclusion from participation in federal healthcare programs. In addition, the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, among other things, amends the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes created by the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. Moreover, the ACA provides that 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.

Although we would not submit claims directly to payors, drug manufacturers can be held liable under the federal False Claims Act, which prohibits anyone from knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. The government may deem manufacturers to have caused the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $5,500 and $11,000 for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. If the government were to allege that we were, or convict us of, violating these false claims laws, we could be subject to a substantial fine and may suffer a decline in our stock price. In addition, private individuals have the ability to bring actions under the federal False Claims Act and certain states have enacted laws modeled after the federal False Claims Act.

Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management s attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

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U.S. patent term restoration and marketing exclusivity

Depending upon the timing, duration and specifics of the FDA approval of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product s approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Marketing exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. 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 an 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. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the non-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy. Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued Written Request for such a trial.

European Union drug development

In the European Union, our future products may also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of non-clinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the

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Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation is currently undergoing a revision process mainly aimed at harmonizing and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials, and increasing their transparency.

European Union drug review and approval

In the European Economic Area, or EEA, (which is comprised of the 27 Member States of the European Union (excluding Croatia) plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

European Union new chemical entity exclusivity

In the European Union, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator s data to

assess a generic application for eight years, after which generic marketing authorization can be submitted, and the innovator s data may be referenced, but not approved for two years. The overall ten-year

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period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

European Union orphan designation and exclusivity

In the European Union, the EMA s Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union Community and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the medicinal product.

In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following medicinal product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Rest of the world regulation

For other countries outside of the European Union and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with cGCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. In the United States no uniform policy of coverage and reimbursement for drug products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor by payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

Third-party payors are increasingly reducing reimbursements for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant

interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product

candidate or a decision by a third-party payor to not cover our product candidate could reduce physician usage of the product candidate and have a material adverse effect on our sales, results of operations and financial condition.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our product candidate, if any such product or the condition that it is intended to treat is the subject of a trial. It is also possible that comparative effectiveness research demonstrating benefits in a competitor s product could adversely affect the sales of our product candidate. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The ACA is expected to have a significant impact on the health care industry. The ACA is expected to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, the ACA is expected to expand and increase industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare Part D program. We cannot predict the full impact of the ACA on our business as many of the ACA reforms require the promulgation of detailed regulations implementing the statutory provisions that has not yet occurred. For example, the ACA imposed new reporting requirements on drug manufacturers for payments made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for knowing failures), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug manufacturers were required to begin collecting data on August 1, 2013 and were required to submit reports to CMS by March 31, 2014 (and by the 90th day of each subsequent calendar year). In addition, many states have adopted laws similar to the federal laws discussed above. Some of these state prohibitions apply to the referral of patients for healthcare services reimbursed by any insurer, not just federal healthcare programs such as Medicare and Medicaid. There has also been a recent trend of increased federal and state regulation of payments made to physicians. Certain states mandate implementation of compliance programs, impose restrictions on drug manufacturers marketing practices and/or

require the tracking and reporting of gifts, compensation and other remuneration to physicians. In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit

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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. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, started in April 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. The ATRA, among other things, also reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. We expect that additional federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, and in turn could significantly reduce the projected value of certain development projects and reduce our profitability.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

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Employees

As of January 31, 2015, we employed 31 full-time employees, including 20 in research and development and 11 in general and administrative and no part-time employees. 14 of our employees hold M.D. or Ph.D. degrees. We have never had a work stoppage, and none of our employees is represented by a labor organization or under any collective-bargaining arrangements. We consider our employee relations to be good.

Facilities

We lease our office space, which consists of 13,300 square feet located in Cambridge, Massachusetts. Our lease expires on February 28, 2017. We expect to lease additional space prior to the expiration of our lease to meet the needs of the business.

Legal Proceedings

As of the date of this Annual Report on Form 10-K, we were not party to any legal matters or claims. In the future, we may become party to legal matters and claims arising in the ordinary course of business, the resolution of which we do not anticipate would have a material adverse impact on our financial position, results of operations or cash flows.

JOBS Act

On April 5, 2012, the Jumpstart Our Business Startups Act, or the JOBS Act, was signed into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an emerging growth company. As an emerging growth company, we are electing not to take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards and, as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Section 107 of the JOBS Act provides that our decision not to take advantage of the extended transition period is irrevocable.

In addition, we intend to rely on the other exemptions and reduced reporting requirements provided by the JOBS Act. Subject to certain conditions set forth in the JOBS Act, if as an emerging growth company we intend to rely on such exemptions, we are not required to, among other things, (i) provide an auditor s attestation report on our system of internal controls over financial reporting pursuant to Section 404, (ii) provide all of the compensation disclosure that may be required of non-emerging growth public companies under the Dodd-Frank Wall Street Reform and Consumer Protection Act, (iii) comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor s report providing additional information about the audit and the financial statements (auditor discussion and analysis), and (iv) disclose certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the Chief Executive Officer s compensation to median employee compensation. These exemptions will apply for a period of five years following the date of our IPO or until we no longer meet the requirements of being an emerging growth company, whichever is earlier.

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Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all other information in this Annual Report on Form 10-K, including our financial statements and related notes, before investing in our common stock. Any of the risk factors we describe below could adversely affect our business, financial condition or results of operations. The market price of our common stock could decline if one or more of these risks or uncertainties actually occur, causing you to lose all or part of the money you paid to buy our common stock. Additional risks that we currently do not know about or that we currently believe to be immaterial may also impair our business. Certain statements below are forward-looking statements. See Cautionary Note Regarding Forward-Looking Statements in this Annual Report on Form 10-K.

Risks Related to Product Development, Regulatory Approval and Commercialization

We depend heavily on the success of the product candidates within our status epilepticus, or SE, program, of which SAGE-547 is in Phase 1/2 clinical development and SAGE-689 and SAGE-217 are in non-clinical development. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, any of our product candidates.

We currently have no drug products for sale and may never be able to develop marketable drug products. Our business depends heavily on the successful non-clinical and clinical development, regulatory approval and commercialization of the product candidates in our lead program in SE, of which only one product candidate, SAGE-547, is in Phase 1/2 clinical development for the treatment of super-refractory SE, or SRSE, and our other product candidates, SAGE-689 and SAGE-217, are in non-clinical development. SAGE-547 will require substantial additional clinical development, testing and regulatory approval before we are permitted to commence its commercialization. The non-clinical studies and clinical trials of our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and, if approved, market any product candidate. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through non-clinical studies and clinical trials that the product candidate is safe and effective for use in each target indication. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our clinical trials. This process can take many years and may include post-marketing studies and surveillance, which will require the expenditure of substantial resources beyond the proceeds we have raised to date. Of the large number of drugs in development in the United States, only a small percentage will successfully complete the U.S. Food and Drug Administration, or FDA, regulatory approval process and will be commercialized. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development and non-clinical studies and clinical trials, we cannot assure you that any of our product candidates will be successfully developed or commercialized.

We are not permitted to market our product candidates in the United States until we receive approval of a New Drug Application, or an NDA, from the FDA, or in any foreign countries until we receive the requisite approval from such countries. We have initiated a Phase 1/2 clinical trial to study safety, tolerability and efficacy of SAGE-547 in patients with SRSE. If our Phase 1/2 clinical trial of SAGE-547 is successful, we expect that the FDA will require us to complete at least one pivotal trial in order to submit an NDA for SAGE-547 as a treatment for SRSE patients. However, the FDA may require that we conduct additional pivotal trials before we can submit an NDA for SAGE-547. We have had only limited feedback from the FDA on the design of our ongoing Phase 1/2 clinical trial of SAGE-547. Before beginning our pivotal trial for SAGE-547, the FDA needs to accept the results of our long-term toxicity studies in two animal species, the first segment of which we submitted to the FDA in the second quarter of 2014, as well as accept data from additional segments of our long-term toxicology studies, which are ongoing. The FDA may require that we conduct additional toxicity studies and may also require us to conduct additional

non-clinical studies before submitting an NDA for SAGE-547.

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Both SAGE-689 and SAGE-217 are in non-clinical development and have yet to begin the clinical development process. We plan to file Investigational New Drug Applications, or INDs, for both SAGE-689 and SAGE-217 late in 2015 and to begin a Phase 1 clinical trial for each of SAGE-689 and SAGE-217 thereafter.

Obtaining approval of an NDA is a complex, lengthy, expensive and uncertain process, and the FDA may delay, limit or deny approval of any of our product candidates for many reasons, including, among others:

- we may not be able to demonstrate that our product candidates are safe and effective in treating SE, refractory SE, or RSE, or SRSE, as applicable, to the satisfaction of the FDA;
- the results of our non-clinical studies and clinical trials may not meet the level of statistical or clinical significance required by the FDA for marketing approval;
- the FDA may disagree with the number, design, size, conduct or implementation of our non-clinical studies and clinical trials;
- the FDA may require that we conduct additional non-clinical studies and clinical trials;
- the FDA or the applicable foreign regulatory agency may not approve the formulation, labeling or specifications of any of our product candidates;
- the contract research organizations, or CROs, that we retain to conduct our non-clinical studies and clinical trials may take actions outside of our control that materially adversely impact our non-clinical studies and clinical trials;
- the FDA may find the data from non-clinical studies and clinical trials insufficient to demonstrate that our product candidates clinical and other benefits outweigh their safety risks;
- the FDA may disagree with our interpretation of data from our non-clinical studies and clinical trials;
- the FDA may not accept data generated at our non-clinical studies and clinical trial sites;
- if our NDA, if and when submitted, is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our 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;

the FDA may require development of a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval or post-approval;

the FDA or the applicable foreign regulatory agency may determine that the manufacturing processes or facilities of third-party contract manufacturers with which we contract do not conform to applicable requirements, including current Good Manufacturing Practices, or cGMPs; or

the FDA or applicable foreign regulatory agency may change its approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully market our product candidates. Any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

A Fast Track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

We have obtained Fast Track designation for SAGE-547, and we may do so for other product candidates as well. If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for the FDA

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Fast Track designation. The FDA has broad discretion whether or not to grant this designation, and even if we believe our product candidates are eligible for this designation, we cannot be sure that the review or approval will compare to conventional FDA procedures. The FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development programs.

The number of patients suffering from SE, RSE and SRSE is small or has not been established with precision. If the actual number of patients with SE, RSE and SRSE is smaller than we anticipate, we may encounter difficulties in enrolling patients in our clinical trials, thereby delaying or preventing development of our product candidates, and if any of our product candidates are approved, we believe our revenue and ability to achieve profitability would be materially adversely affected.

There is no precise method of establishing actual number of patients with SE, RSE or SRSE in any geography over any time period. Moreover, SE, RSE and SRSE are acute episode conditions. If we are not able to identify patients at the time of SE, RSE or SRSE onset, we will have difficulty completing our clinical trials. We estimate that the annual incidence of SE, RSE and SRSE in the United States is up to 150,000, 35,000 and 25,000 patients, respectively. If the actual number of patients with SE, RSE or SRSE is lower than we believe, we may experience difficulty in enrolling patients in our clinical trials, thereby delaying development of our product candidates. Further, if any of our product candidates are approved, the markets for our product candidates for these indications would be smaller than we anticipate which could limit our ability to achieve profitability.

Favorable results from the emergency-use cases of SAGE-547 do not ensure that clinical trials will be successful and the results in any future emergency-use cases may not be positive and could adversely impact our clinical development plans.

SAGE-547 has been administered to a small number of patients as part of emergency-use cases, which permitted the administration of SAGE-547 outside of clinical trials. No assurance can be given that positive results observed to date in these emergency-use cases are attributable to SAGE-547, as they were not carried out in the controlled environment of a clinical trial. Further, no assurance can be provided that administration of SAGE-547 to other patients in any future emergency-use cases or otherwise will have positive results. Emergency use is a term that is used to refer to the use of an investigational drug outside of a clinical trial to treat a patient with a serious or immediately life-threatening disease or condition and who has no comparable or satisfactory alternative treatment options. Regulators often allow emergency use on a case-by-case basis for an individual patient or for defined groups of patients with similar treatment needs. In the event there are negative results in future emergency-use cases, it could adversely affect or delay our clinical development of SAGE-547.

If serious adverse events or other undesirable side effects are identified during the use of SAGE-547 in emergency-use cases or in investigator sponsored trials of SAGE-547, it may adversely effect our development of SAGE-547 for SRSE.

In addition to use in emergency cases as described above, SAGE-547 is currently being tested in an investigator sponsored clinical trial for the treatment of traumatic brain injury, or TBI, by one of our collaborators and may be subjected to testing for other indications in additional investigator sponsored trials. Currently, we are also testing SAGE-547 in a proof of concept study in patients with essential tremor and a proof of concept study in patients with severe postpartum depression, or PPD. If serious adverse events or other undesirable side effects, or unexpected characteristics of SAGE-547 are observed in emergency-use cases or in investigator sponsored clinical trials of SAGE-547 or our exploratory clinical trials, it may adversely affect or delay our clinical development of SAGE-547, or we may need to abandon its development for SRSE entirely, and the occurrence of these events would have a material adverse effect on our business.

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Positive results from early 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. 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, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

Positive results from our non-clinical studies of our product candidates, and any positive results we may obtain from our early clinical trials of our product candidates, may not necessarily be predictive of the results from required later non-clinical studies and clinical trials. Similarly, even if we are able to complete our planned non-clinical studies or clinical trials of our product candidates according to our current development timeline, the positive results from our non-clinical studies and clinical trials of our product candidates may not be replicated in subsequent non-clinical studies or clinical trial results. For example, although 12 of the first 17 patients treated with SAGE-547 and evaluable for efficacy in our Phase 1/2 clinical trial met the key efficacy endpoint and none of the 20 patients enrolled in the study have yet experienced any severe adverse events related to SAGE-547, future patients enrolled and treated with SAGE-547 in this trial may not have the same outcome. Also, our later-stage clinical trials could differ in significant ways from our ongoing Phase 1/2 clinical trial of SAGE-547, which could cause the outcome of these later-stage trials to differ from our earlier stage clinical trials. For example, these differences may include changes to inclusion and exclusion criteria, efficacy endpoints and statistical design. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, non-clinical findings made while clinical trials were underway or safety or efficacy observations made in non-clinical studies and clinical trials, including previously unreported adverse events. 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. We have not completed any clinical trials for our product candidates yet, and if we fail to produce positive results in our planned non-clinical studies or clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected.

Failures or delays in the commencement or completion of our planned clinical trials of our product candidates could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.

We have commenced a Phase 1/2 clinical trial of SAGE-547 as a treatment for SRSE and proof of concept studies of SAGE-547 for patients with essential tremor and severe PPD. We will need to complete at least one additional trial prior to the submission of an NDA for SAGE-547 as a treatment for SRSE. Successful completion of our clinical trials is a prerequisite to submitting an NDA to the FDA and, consequently, the ultimate approval and commercial marketing of SAGE-547 for SRSE and our other product candidates. We do not know whether any of our clinical trials will begin or be completed on schedule, if at all, as the commencement and completion of clinical trials can be delayed or prevented for a number of reasons, including, among others:

- the FDA may deny permission to proceed with our planned clinical trials or any other clinical trials we may initiate, or may place a clinical trial on hold;

- delays in filing or receiving approvals of additional INDs that may be required;

negative results from our ongoing non-clinical studies;

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 a product candidate or other materials necessary to conduct clinical trials, for example delays in the manufacturing of sufficient supply of finished drug product;

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difficulties obtaining Institutional Review Board, or IRB, approval to conduct a clinical trial at a prospective site or sites;

challenges in recruiting and enrolling patients to participate in clinical trials, including the small size of the patient population, acute nature of SRSE, the proximity of patients to trial sites,

eligibility criteria for the clinical trial, the nature of the clinical trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications;

severe or unexpected drug-related side effects experienced by patients in a clinical trial;

delays in validating any endpoints utilized in a clinical trial;

the FDA may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;

reports from non-clinical or clinical testing of other CNS therapies that raise safety or efficacy concerns; and

difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to rigors of the clinical trials, lack of efficacy, side effects, personal issues or loss of interest.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRBs at the sites where the IRBs are overseeing a clinical trial, a data and safety monitoring board, or DSMB, 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 clinical hold;

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

changes in government regulations or administrative actions;

problems with clinical supply materials; and

lack of adequate funding to continue clinical trials.

Changes in regulatory requirements, FDA guidance or unanticipated events during our non-clinical studies and clinical trials of our product candidates may occur, which may result in changes to non-clinical studies and clinical trial protocols or additional non-clinical studies and clinical trial requirements, which could result in increased costs to us and could delay our development timeline.

Changes in regulatory requirements, FDA guidance or unanticipated events during our non-clinical studies and clinical trials may force us to amend non-clinical studies and clinical trial protocols or the FDA may impose additional non-clinical studies and clinical trial requirements. Amendments or changes to our 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. Similarly, amendments to our non-clinical studies may adversely impact the cost, timing, or successful completion of those non-clinical studies. If we experience delays completing, or if we terminate, any of our non-clinical studies or clinical trials, or if we are required to conduct additional non-clinical studies or clinical trials, the commercial prospects for our product candidates may be harmed and our ability to generate product revenue will be delayed.

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

have staffing difficulties;

fail to comply with contractual obligations;

experience regulatory compliance issues;

undergo changes in priorities or become financially distressed; or

form relationships with other entities, some of which may be our competitors.

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, regulatory and scientific requirements and standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with regulations and guidelines, including current Good Clinical Practices, or cGCPs, 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 and comparable foreign regulatory authorities for any products in clinical development. The FDA enforces cGCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. In addition, our clinical trials must be conducted with product candidates produced under cGMPs regulations and will require a large number of test patients. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties.

Although we design our clinical trials for our product candidates, CROs conduct all of the clinical trials. As a result, many important aspects of our drug development programs are outside of our direct control. In addition, the CROs may not perform all of their obligations under arrangements with us or in compliance with regulatory requirements, but we remain responsible and are subject to enforcement action that may include civil penalties up to and including criminal prosecution for any violations of FDA laws and regulations during the conduct of our clinical trials. If the CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development and commercialization of our product candidates may be delayed or our development program materially and irreversibly harmed. We cannot control the amount and timing of resources these CROs devote to our program or our clinical products. If we are unable to rely on clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of our clinical trials and this could significantly delay commercialization and require significantly greater expenditures.

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If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, we believe that our financial results and the commercial prospects for our product candidates in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

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

We do not currently have, nor do we plan to acquire, the infrastructure or capability to internally manufacture our clinical drug supply of our product candidates, or any future product candidates, for use in the conduct of our non-clinical studies and clinical trials, and we lack the internal resources and the capability to manufacture any product candidates on a clinical or commercial scale. For example, SAGE-547 used in the emergency-use cases was manufactured at an academic site, the active pharmaceutical ingredient for SAGE-547 for our Phase 1/2 clinical trial was manufactured at an academic site and SAGE-547 as formulated for our Phase 1/2 clinical trial was manufactured at a third-party contract manufacturer s site. The facilities used by our contract manufacturers to manufacture the active pharmaceutical ingredient and final drug product must 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 our NDA or relevant foreign regulatory submission to the applicable regulatory agency.

We do not control the manufacturing process of, and are completely dependent on, our contract manufacturers to comply with cGMPs for manufacture of both active drug substances and finished drug products. 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, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. 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 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 product candidates are noncompliant, we may need to find alternative manufacturing facilities, which would adversely impact our ability to develop, obtain regulatory approval for or market 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.

We do not have long-term supply agreements in place with our contract manufacturers and each batch of our product candidates is individually contracted under a quality and supply agreement. If we engage new contract manufacturers, such contractors must complete an inspection by the FDA and other applicable foreign regulatory agencies. We plan to continue to rely upon contract manufacturers and, potentially, collaboration partners to manufacture commercial quantities of our product candidates, if approved. Our current scale of manufacturing is adequate to support all of our needs for non-clinical studies and clinical trial supplies.

Even if we receive marketing approval for our product candidates in the United States, we may never receive regulatory approval to market our product candidates outside of the United States.

We have not yet selected any markets outside of the United States where we intend to seek regulatory approval to market our product candidates. In order to market any product outside of the United States, however,

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we 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 product candidate testing and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. 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 others. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair our ability to market our product candidates in such foreign markets. Any such impairment would reduce the size of our potential market, which could have a material adverse impact on our business, results of operations and prospects.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to generate any revenue.

We do not currently have an infrastructure for the sales, marketing and distribution of pharmaceutical products. In order to market our product candidates, if approved by the FDA or any other regulatory body, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition and prospects will be materially adversely affected.

Even if we receive marketing approval for our product candidates, our product candidates may not achieve broad market acceptance, which would limit the revenue that we generate from their sales.

The commercial success of our product candidates, if approved by the FDA or other applicable regulatory authorities, will depend upon the awareness and acceptance of our product candidates among the medical community, including physicians, patients and healthcare payors. Market acceptance of our product candidates, if approved, will depend on a number of factors, including, among others:

- the efficacy of our product candidates as demonstrated in clinical trials, and, if required by any applicable regulatory authority in connection with the approval for the applicable indications, to provide patients with incremental health benefits, as compared with other available CNS therapies;
- limitations or warnings contained in the labeling approved for our product candidates by the FDA or other applicable regulatory authorities;
- the clinical indications for which our product candidates are approved;
- availability of alternative treatments already approved or expected to be commercially launched in the near future;

the potential and perceived advantages of our product candidates over current treatment options or alternative treatments, including future alternative treatments;

the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;

the strength of marketing and distribution support and timing of market introduction of competitive products;

publicity concerning our products or competing products and treatments;

pricing and cost effectiveness;

the effectiveness of our sales and marketing strategies;

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our ability to increase awareness of our product candidates through marketing efforts;

our ability to obtain sufficient third-party coverage or reimbursement; or

the willingness of patients to pay out-of-pocket in the absence of third-party coverage.

If our product candidates are approved but do not achieve an adequate level of acceptance by patients, physicians and payors, we may not generate sufficient revenue from our product candidates to become or remain profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our product candidates, in addition to treating these target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community and third-party payors about the benefits of our product candidates may require significant resources and may never be successful.

Our product candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt non-clinical studies and clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities.

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

regulatory authorities may withdraw or limit their approval of such product candidates;

regulatory authorities may require the addition of labeling statements, such as a boxed warning or a contraindication;

we may be required to change the way such product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the product candidates;

we may be subject to regulatory investigations and government enforcement actions;

we may decide to remove such product candidates from the marketplace;

we could be sued and held liable for injury caused to individuals exposed to or taking our 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 product candidates and could substantially increase the costs of commercializing our product candidates and significantly impact our ability to successfully commercialize our product candidates and generate revenues.

Even if we receive marketing approval for our product candidates, we may still face future development and regulatory difficulties.

Even if we receive marketing approval for our product candidates, regulatory authorities may still impose significant restrictions on our product candidates, indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. Our product candidates will also be subject to ongoing FDA requirements governing the labeling, packaging, storage and promotion of the product and record keeping and

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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 related to the use of a drug. The FDA also has the authority to require, as part of an NDA or post-approval, the submission of a REMS. Any REMS required by the FDA may lead to increased costs to assure compliance with new 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.

Manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMPs and other regulations. If we or a regulatory agency discover problems with our product candidates, such as adverse events of unanticipated severity or frequency, or problems with the facility where our product candidates are manufactured, a regulatory agency may impose restrictions on our product candidates, the manufacturer or us, including requiring withdrawal of our product candidates from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our 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 could emerge adversely affecting our opportunity to generate revenue from the sale of our product candidates.

The biopharmaceuticals industry is highly competitive. There are many public and private biopharmaceutical companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our product candidates or address similar markets. It is probable that the number of companies seeking to develop products and therapies similar to our products will increase.

Currently, there are no therapies specifically approved for RSE or SRSE. However, many products approved for other indications, general anesthetics and anti-seizure drugs, are used off-label for various stages of SE therapy.

Additionally, though not indicated, acupuncture, hypothermia, and electroconvulsive therapy are sometimes used prior to withdrawal of care for patients with SRSE.

In the field of neuroactive steroids focused on modulation of $GABA_A$ or NMDA receptors, our principal competitor is Marinus Pharmaceuticals, Inc., which is developing a reformulated form of Ganaxolone, a known $GABA_A$ positive allosteric modulator neuroactive steroid, for potential treatment of drug-resistant partial complex seizures and fragile X syndrome.

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. Our commercial opportunity

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could be reduced or eliminated if our competitors develop and commercialize products that are 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.

We may seek to establish collaborations, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

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

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. The terms of any collaboration or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. 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 collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

In addition, any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and

other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

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We may not be successful in our efforts to identify or discover additional product candidates 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 primarily upon our ability to identify, develop and commercialize products based on our proprietary chemistry platform. Although some of our product candidates are in non-clinical and clinical development, our research programs may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

Because we have limited financial and management resources, we focus on a limited number of research programs and product candidates and are currently focused on our SE program. 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. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through future collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. 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.

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

Although we do not currently have any products on the market, once we begin commercializing our products, we may be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of our product candidates, if approved. Our future arrangements with third-party payors will expose us to 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 our product candidates, if we obtain marketing approval. 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, 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.

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.

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

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 Patient Protection and Affordable Care Act, 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 the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests.

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.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could be costly. It is possible that governmental authorities will conclude that our business practices 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 operations, including anticipated activities to be conducted by our sales team, 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. If any of the physicians or other providers or entities with whom we expect to do business is 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.

The FDA and other regulatory 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 agencies strictly regulate the promotional claims that may be made about prescription products, such as SAGE-547, SAGE-689, and SAGE-217, if approved. 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 product s approved labeling. For example, if we receive marketing approval for SAGE-547 as a treatment for SRSE, physicians may nevertheless prescribe SAGE-547 to their patients in a manner that is inconsistent with the approved label. If we are

found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

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Even if approved, reimbursement policies could limit our ability to sell our product candidates.

Market acceptance and sales of our product candidates will depend on reimbursement policies and may be affected by healthcare reform measures. Government authorities 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. We cannot be sure that reimbursement will be available for our product candidates and, if reimbursement is available, the level of such reimbursement. Reimbursement may impact the demand for, or the price of, our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates.

In some foreign countries, particularly in Canada and European countries, the pricing of prescription pharmaceuticals is subject to strict governmental control. In these countries, pricing negotiations with governmental authorities can take six months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates with other available therapies. If reimbursement for our product candidates is unavailable in any country in which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical trials, or if pricing is set at unsatisfactory levels, our operating results could be materially adversely affected.

Even though we have obtained orphan drug designation for SAGE-547 as a treatment for SE, there may be limits to the regulatory exclusivity afforded by such designation.

Even though we have obtained orphan drug designation for SAGE-547 for treatment of SE from the FDA, there are limitations to exclusivity afforded by such designation. In the United States, the company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for a period of seven years. This orphan drug exclusivity prevents the FDA from approving another application, including a full NDA to market the same drug for the same orphan indication, except in very limited circumstances, including when the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. For purposes of small molecule drugs, the FDA defines same drug as a drug that contains the same active moiety and is intended for the same use as the drug in question. To obtain orphan drug exclusivity for a drug that shares the same active moiety as an already approved drug, it must be demonstrated to the FDA that the drug is safer or more effective than the approved orphan designated drug, or that it makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition or if another drug with the same active moiety is determined to be safer, more effective, or represents a major contribution to patient care.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties. If we commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

our customers ability to obtain reimbursement for our product candidates in foreign markets;

our inability to directly control commercial activities because we are relying on third parties;

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the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;

different medical practices and customs in foreign countries affecting acceptance in the marketplace;

import or export licensing requirements;

longer accounts receivable collection times;

longer lead times for shipping;

language barriers for technical training;

reduced protection of intellectual property rights in some foreign countries;

the existence of additional potentially relevant third party intellectual property rights;

foreign currency exchange rate fluctuations; and

the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

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.

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 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. Our owned and licensed patent applications relate to SAGE-547, $GABA_A$ receptor modulators, including

genus and species claims to SAGE-689 and NMDA receptor modulators.

We currently have no issued patents covering any of our lead product candidates, SAGE-547, SAGE-689, or SAGE-217. We cannot provide any assurances that any of our pending patent applications will mature into issued patents and, if they do, that such patents will include, claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. For example, the patent applications that may provide coverage for SAGE-547, only cover particular formulations and particular methods of using such formulations to treat seizure conditions, such as SE. As a result, if a patent issues from such patent applications, it would not prevent third-party competitors from creating, making and marketing alternative formulations, that fall outside the scope of our patent claims or practicing alternative methods. There can be no assurance that any such alternative formulations will not be equally effective as our formulation of SAGE-547. 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 inventories.

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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, ex parte reexamination, or inter partes 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. 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 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 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 United States, 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.

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 candidates are invalidated or found unenforceable, our financial position and results of operations would 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 would 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, will include claims having a scope sufficient to protect our 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 successfully commercialize our product candidates, if approved, before our relevant patents expire;

we were the first to make the inventions covered by each of our patents and pending patent applications;

we were the first to file patent applications for these inventions;

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others will not develop similar or alternative technologies that do not infringe our patents;

others will not use pre-existing technology to effectively compete against us;

any of our patents, if issued, will be found to ultimately 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 rely upon unpatented trade secrets, 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 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 our product candidates, if approved.

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties.

The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our 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 and, if approved, commercialize our current product candidates and future product candidates, 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 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, 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. 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 candidates.

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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. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, intellectual property litigation or claims could force us to do one or more of the following:

- cease developing, selling or otherwise commercializing our product candidates;
- pay substantial damages for past use of the asserted intellectual property;
- obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and
- in the case of trademark claims, 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.

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, outside scientific collaborators, sponsored researchers 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 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.

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.

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 non-compliance with these requirements.

The U.S. Patent and Trademark Office, or U.S. PTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other 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

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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 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 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 United States.

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 candidates could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent, if and when issued, covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, 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 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 United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review and equivalent proceedings in foreign jurisdictions, e.g., opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. 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 our 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, 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 United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. 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 United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions

in and into the United States or other jurisdictions. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our

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patent applications. For the patent families related to SAGE-547, SAGE-689 and SAGE-217, as well as for most of the patent families that we own or license, the relevant statutory deadlines have not yet expired. Thus, for each of the patent families that we believe provide coverage for our lead product candidates, we will need to decide whether and where to pursue protection outside the United States.

Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. 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 United States. 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. 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. For example, 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 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.

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 our product candidates, if approved. If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates or technology from third parties or, in certain cases, we fail to meet certain development deadlines, we could lose license rights that are important to our business.

We are a party to a number of license agreements under which we are granted rights to intellectual property that are important to our business and we expect that we may need to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose on us, various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. See Business Licenses for a description of our

license agreements, which includes a description of the termination provisions of these agreements.

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

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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. In that event, 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 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 develop and commercialize the affected product candidates.

We have entered into several licenses to support our various programs. We completed an exclusive license agreement with Washington University, or WU, under certain patent families that comprise a variety of small molecule allosteric modulators of $GABA_A$ receptors and for which we have the worldwide right to develop and commercialize. A patent family that discloses and claims SAGE-689 is licensed to us under this agreement. We are obligated to pay WU certain clinical/regulatory milestones and single-digit royalties on products developed from this technology. Termination of our license agreement with WU would have a material adverse impact on our ability to develop and commercialize SAGE-689.

We have also entered into an exclusive license agreement with CyDex Pharmaceuticals, Inc., or CyDex, a wholly owned subsidiary of Ligand Pharmaceuticals, Inc., to use its Captisol technology to develop SAGE-547 for the field of use, which includes all fields for the treatment, prevention or diagnosis of any disease or symptom in humans or animals. We are obligated to pay CyDex certain clinical/regulatory milestones and single-digit royalties on SAGE-547. In addition, we entered into a supply agreement with CyDex, pursuant to which they supply us with

Captisol to formulate SAGE-547. Absent an alternative agreement by the parties, our rights under our exclusive license agreement terminate in the event that the supply agreement terminates. Currently, our SAGE-547 product candidate in clinical development is formulated in Captisol. Termination of our license agreement with CyDex would have a material adverse impact on our ability to develop and commercialize SAGE-547 in its current formulation.

We also entered into a non-exclusive license with The Regents of the University of California, or the Regents. Pursuant to this agreement the Regents granted us a non-exclusive, non-transferable license under all personal property rights of the Regents covering the tangible personal property in an IND application package owned by the Regents, or the Data, and a specified quantity of cGMP grade allopregnanolone, or the Material, to (i) use the Data for reference or incorporation in an IND for use of the Material as a treatment of SE, essential

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tremor and/or postpartum depression and (ii) use the Material or modifications of the Material to develop a pharmaceutical formulation for clinical trials for SE, essential tremor and/or postpartum depression. This agreement requires us to pay milestone payments in connection with the first derived product, which would include SAGE-547, that meets the relevant milestones and we must also pay single-digit royalties for each derived product for a period of 15 years following the first commercial sale of such derived product. Termination of our license agreement with the Regents would have a material adverse impact on our ability to develop and commercialize derived products, which would include SAGE-547.

We may enter into additional license(s) 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, as is the case for the Washington University license, 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, our licensor(s) may allege that we have breached our license agreement and may accordingly seek to terminate our license with them. In addition, future licensor(s) may decide to terminate our license 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 and commercialize a product candidate or product, if approved, 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 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 agreements with WU and the Regents 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 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 it 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 United States. 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 United States or that under the circumstances domestic manufacture is not

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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.

We currently do not plan to apply for additional U.S. government funding, but if we do, and we discover compounds or drug 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 additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent terms and obtaining data exclusivity for our product candidates, our business may be materially harmed.

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 under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. For example, we may not be granted an extension if the active ingredient of SAGE-547, allopregnanolone, is used in another drug company s product candidate and that product candidate is the first to obtain FDA approval. 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, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected.

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

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing 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 will be 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, recent 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. The full impact of these decisions is not yet known. For example, on March 20, 2012 in Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al. v. Prometheus Laboratories, Inc., the 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, on June 13, 2013 in Association for Molecular Pathology v. Myriad Genetics, Inc., the 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. The effect of

the decision on patents for other isolated natural products is uncertain. However, on March 4, 2014, the U.S. PTO issued a memorandum to patent examiners providing guidance for examining claims that recite laws of nature, natural phenomena or natural products under the Myriad and Prometheus decisions. This guidance did not limit the application of Myriad to DNA but, rather, applied the decision to other natural products.

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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.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Our employees have 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.

Although we are not aware of any claims currently pending against us, we may be subject to claims that we or our employees, advisors or consultants have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third party. We have and may in the future also 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 claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying monetary claims, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our product candidates, which would materially adversely affect our commercial development efforts.

Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- others may be able to develop and/or practice technology that is similar to our technology or aspects of our technology but that is not covered by the claims of patents, should such patents issue from our patent applications;
- we might not have been the first to make the inventions covered by a pending patent application that we own;
- we might not have been the first to file patent applications covering an invention;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;

pending patent applications that we own or license may not lead to issued patents;

patents, if issued, that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;

third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;

we may not be able to obtain and/or maintain necessary or useful licenses on reasonable terms or at all;

third parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights over that intellectual property;

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we may not develop or in-license additional proprietary technologies that are patentable; and

the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business and results of operations.

General Company-Related Risks

As our product candidates reach later stage clinical development, we will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

As of January 31, 2015, we had 31 full-time employees and no part-time employees, and as our product candidates reach later stage clinical development, we expect to increase our number of employees and the scope of our operations. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure; give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

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

We are highly dependent on Dr. Jeffrey M. Jonas, our President and Chief Executive Officer. We have entered into an employment agreement with Dr. Jonas, but he may terminate his employment with us at any time. Although we do not have any reason to believe that we will lose the services of Dr. Jonas in the foreseeable future, the loss of his services might impede the achievement of our research, development and commercialization objectives. We also do not have any key-man life insurance on Dr. Jonas. We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us and may not be subject to our standard non-compete agreements. Recruiting and retaining qualified scientific personnel and sales and marketing personnel will also be 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 may make it more challenging to recruit and retain qualified scientific personnel.

Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and applicable non-U.S. regulators, provide accurate information to the FDA and applicable non-U.S. regulators, comply with healthcare fraud and abuse

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laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of conduct, but 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 to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

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

The use of our product candidates in clinical trials and the sale of our product candidates, if approved, exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others selling or otherwise coming into contact with our product candidates. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. 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, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of patients from our clinical trials;
- substantial monetary awards to patients or other claimants;
- decreased demand for our product candidates or any future product candidates following marketing approval, if obtained;
- 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

the inability to successfully commercialize our product candidates or any future product candidates, if approved.

We maintain product liability insurance coverage for our clinical trials with a $10 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. If and when we obtain marketing approval for our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may not be able to obtain this product liability insurance on commercially reasonable terms. 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

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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.

We will incur increased costs as a result of operating as a public company, and our management team will be required to devote substantial time to new compliance initiatives.

Now that we are a public company, and particularly after we are no longer considered an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission and The NASDAQ Stock Market have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

As we continue to grow, we will need to hire additional qualified accounting and financial personnel with appropriate public company experience.

As we continue to grow our organization, we will need to establish and maintain effective disclosure and financial controls and make changes in our corporate governance practices. We will need to hire additional accounting and financial personnel with appropriate public company experience and technical accounting knowledge, and it may be difficult to recruit and maintain such personnel. Even if we are able to hire appropriate personnel, our existing operating expenses and operations will be impacted by the direct costs of their employment and the indirect consequences related to the diversion of management resources from product development efforts.

Our ability to use our net operating loss carryforwards and certain tax credit carryforwards may be subject to limitation.

As of December 31, 2014, we had federal and state net operating loss carryforwards of $55.8 million and $55.4 million, respectively, which begin to expire in 2031. As of December 31, 2014, we also had federal and state research and development tax credit carryforwards of $0.7 million and $0.3 million, respectively, which begin to expire in 2031 and 2027, respectively. As of December 31, 2014, we had federal orphan drug tax credit carryforwards of $3.6

million, which begin to expire in 2034. Under Section 382 of the Internal Revenue Code of

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1986, as amended, or the Code, changes in our ownership may limit the amount of our net operating loss carryforwards and tax credit carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and tax credit carryforwards before they expire. Any such limitation, whether as the result of future offerings, prior private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us in the future, could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the recent global financial crisis, could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party CMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business.

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

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption 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.

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We may acquire businesses or products, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions.

We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

Risks Related to Our Financial Position and Need for Capital

We are a biopharmaceutical company with a limited operating history and have not generated any revenue from product sales. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

We are a biopharmaceutical company with a limited operating history on which to base your investment decision. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We were incorporated in April 2010. Our operations to date have been limited primarily to organizing and staffing our company, raising capital and conducting research and development activities for our product candidates. We have never generated any revenue from product sales. We have not obtained regulatory approvals for any of our product candidates.

We have funded our operations to date through proceeds from sales of redeemable convertible preferred stock and the issuance of convertible notes and the sale of common stock in our IPO. As of December 31, 2014, our cash and cash equivalents were $127.8 million. We have incurred net losses in each year since our inception, and we have an accumulated deficit of $66.9 million as of December 31, 2014. Our net losses were $36.1 million, $18.3 million and $9.6 million for the years ended December 31, 2014, 2013 and 2012, respectively. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from 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 deficit and working capital. We expect our research and development expenses to significantly increase in connection with our clinical trials of our product candidates. In addition, if we obtain marketing approval for our product candidates, we will incur significant sales, marketing and outsourced-manufacturing expenses. As a public company, we incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from our lead product candidates, SAGE-547, SAGE-689 and SAGE-217, and we do not know when, or if, we will generate any revenue. We do not expect to generate significant revenue unless and until we obtain marketing approval of, and begin to sell, SAGE-547, SAGE-689 or SAGE-217. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

initiate and successfully complete clinical trials that meet their clinical endpoints;

initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for our product candidates;

commercialize our product candidates, if approved, by developing a sales force or entering into collaborations with third parties; and

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achieve market acceptance of our product candidates in the medical community and with third-party payors.

Absent our entering into a collaboration or partnership agreement, we expect to incur significant sales and marketing costs as we prepare to commercialize our product candidates. Even if we initiate and successfully complete pivotal clinical trials of our product candidates, and our product candidates are approved for commercial sale, and despite expending these costs, our product candidates may not be a commercially successful drug. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate product revenue, we will not become profitable and may be unable to continue operations without continued funding.

Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We are currently advancing our product candidates through non-clinical and clinical development. Developing small molecule products is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidate in clinical trials. Depending on the status of regulatory approval or, if approved, commercialization of our product candidates, as well as the progress we make in selling our product candidates, we may require additional capital to fund operating needs thereafter. We may also need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for our product candidates or otherwise expand more rapidly than we presently anticipate.

As of December 31, 2014, our cash and cash equivalents were $127.8 million. We expect that our existing cash and cash equivalents will be sufficient to fund our current operations for at least the next 12 months. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. In any event, we will require additional capital to obtain regulatory approval for, and to commercialize, our product candidates. Raising funds in the current economic environment may present additional challenges. 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 if we have specific strategic considerations.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and 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 sale of additional equity or convertible securities would dilute all of our stockholders. 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 candidate or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

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 product candidate 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.

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Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights.

We may seek additional capital through a combination of private and public equity offerings, debt financings, collaborations and strategic and licensing arrangements. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, your ownership interest in our company will be diluted. In addition, the terms of any such securities may include liquidation or other preferences that materially adversely affect your rights as a stockholder. 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.

Risks Related to Our Common Stock

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

Our IPO was completed on July 23, 2014 therefore, there only has been a public market for our common stock for only a short period of time.

The market price for our common stock, similar to other biopharmaceutical companies, is likely to be 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:

- plans for, progress of or results from non-clinical studies and clinical trials of our product candidates;
- the failure of the FDA to approve our product candidates;
- announcements of new products, technologies, commercial relationships, acquisitions or other events by us or our competitors;
- the success or failure of other CNS therapies;
- regulatory or legal developments in the United States and other countries;
- failure of our product candidates, if approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;

general market conditions and overall fluctuations in U.S. equity markets;

variations in our quarterly operating results;

changes in our financial guidance or securities analysts estimates of our financial performance;

changes in accounting principles;

our ability to raise additional capital and the terms on which we can raise it;

sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;

additions or departures of key personnel;

discussion of us or our stock price by the press and by online investor communities; and

other risks and uncertainties described in these risk factors.

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We have a significant stockholder, which will limit your ability to influence corporate matters and may give rise to conflicts of interest.

A fund affiliated with Third Rock Ventures, or TRV, is our largest stockholder. As of December 31, 2014, TRV beneficially owned approximately 45.3% of our common stock. Accordingly, TRV exerts and will continue to exert significant influence over us and any action requiring the approval of the holders of our common stock, including the election of directors and amendments to our organizational documents, such as increases in our authorized shares of common stock and approval of significant corporate transactions. Furthermore, the interests of TRV may not always coincide with your interests or the interests of other stockholders and TRV may act in a manner that advances its best interests and not necessarily those of other stockholders, including seeking a premium value for its common stock, which might affect the prevailing market price for our common stock.

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.

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.

We are an emerging growth company, and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act, and we have taken advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. Since we have chosen not to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, our auditors are not required to attest to the effectiveness of our internal control over financial reporting. As a result, investors may become less comfortable with the effectiveness of our internal controls and the risk that material weaknesses or other deficiencies in our internal controls go undetected may increase. Since we have chosen to provide reduced disclosures in our periodic reports and proxy statements while we are an emerging growth company, investors have access to less

information and analysis about our executive compensation, which may make it difficult for investors to evaluate our executive compensation practices. We cannot predict if investors will find our common stock less attractive because we have chosen to rely on these

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exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (a) the last day of the fiscal year following the fifth anniversary of the completion of our IPO, (b) the last day of the fiscal year in which we have total annual gross revenue of at least $1.0 billion, (c) the date on which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th , and (d) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

We do not intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which you purchased them.

If equity research analysts do not publish research or reports about our business or if they issue unfavorable commentary or downgrade our common stock, the price of our common stock could decline.

The trading market for our common stock relies in part on the research and reports that equity research analysts publish about us and our business. We do not control these analysts. The price of our common stock could decline if one or more equity research analysts downgrade our common stock or if analysts issue other unfavorable commentary or cease publishing reports about us or our business.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters and clinical development operations are located in Cambridge, Massachusetts, which consists of 13,300 square feet. Our lease expires on February 28, 2017. We expect to lease additional space prior to expiration of our existing lease to meet the needs of the business.

Item 3. Legal Proceedings

We are not a party to any legal proceedings and we are not aware of any claims or actions pending or threatened against us. In the future, we might from time to time become involved in litigation relating to claims arising from our ordinary course of business.

Item 4. Mine Safety Disclosures

Not applicable.

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PART II

Item 5. Market for Registrant s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

On July 18, 2014, our common stock began trading on the NASDAQ Global Market under the symbol SAGE . Prior to that time, there was no public market for our common stock. Shares sold in our initial public offering on July 17, 2014 were priced at $18.00 per share.

On March 2, 2015, the closing price for our common stock as reported on the NASDAQ Global Market was $43.89. The following table sets forth the high and low sales prices per share of our common stock as reported on the NASDAQ Global Market for the period indicated.

Year Ended December 31, 2014	High	Low
Third Quarter (from July 18, 2014)	$ 33.40	$ 25.86
Fourth Quarter	$ 43.75	$ 30.50

Stockholders

As of January 31, 2015, there were 37 stockholders of record, which excludes stockholders whose shares were held in nominee or street name by brokers. We believe that, when our record holders and stockholders whose shares are held in nominee or street name by brokers are combined, we have in excess of 124 beneficial holders of our common stock.

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Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return for our common stock since July 18, 2014, which is the date our shares began trading, to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of $100 on July 18, 2014, in our common stock, the stocks comprising the NASDAQ Composite Index, and the stocks comprising the NASDAQ Biotechnology Index. Historical stockholder return is not necessarily indicative of the performance to be expected for any future periods.

Comparison of Five Month Cumulative Total Return*

Among Sage Therapeutics, Inc., the NASDAQ Composite Index and the NASDAQ Biotechnology Index

* $100 invested on July 18, 2014 in stock or index. Fiscal Year ended December 31, 2014.
The performance graph shall not be deemed to be incorporated by reference by means of any general statement incorporating by reference this Form 10-K into any filing under the Securities Act of 1933, as amended or the Exchange Act, except to the extent that we specifically incorporate such information by reference, and shall not otherwise be deemed filed under such acts.

Dividend Policy

We have never paid or declared any cash dividends on our common stock, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon a number of factors, including our results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors our board of directors deems relevant.

Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12. of Part III of this Annual Report on Form 10-K.

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Recent Sales of Unregistered Securities

Set forth below is information regarding securities sold by us during the year ended December 31, 2012 that were not registered under the Securities Act. Also included is the consideration, if any, received by us for the securities and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

Issuances of securities

On January 7, 2014, we issued 6,666,666 shares of our Series B redeemable convertible preferred stock to two investors for net consideration of $9,995,000. On February 12, 2014, we issued an aggregate of 3,333,333 shares of our Series B redeemable convertible preferred stock to two investors for $5,000,000.

On January 24, 2014, we issued 7,936 shares of our common stock to a nonemployee advisor upon attainment of certain clinical milestones.

On March 11, 2014, we issued 8,973,905 shares of our Series C redeemable convertible preferred stock to 13 investors for aggregate consideration of $38,000,000.

On March 26, 2014, we issued 7,936 shares of our common stock to a nonemployee advisor upon attainment of certain clinical milestones.

No underwriters were used in the foregoing transactions. All sales of securities described above were made in reliance upon the exemption from registration provided by Section 4(2) of the Securities Act (and/or Regulation D promulgated thereunder) for transactions by an issuer not involving a public offering. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

Grants of stock options and restricted stock

During the year ended December 31, 2014, we granted stock options to purchase an aggregate of 680,939 shares of our common stock, with exercise prices ranging from $1.36 to $8.92 per share, to employees, directors and consultants pursuant to our stock option plan. During the year ended December 31, 2014, we did not grant any shares of restricted stock. The issuances of these securities were exempt either pursuant to Rule 701, as a transaction pursuant to a compensatory benefit plan, or pursuant to Section 4(2), as a transaction by an issuer not involving a public offering.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Use of Proceeds from Registered Securities

On July 23, 2014, we closed the sale of 5,750,000 shares of common stock to the public at an initial public offering price of $18.00 per share, including the exercise in full by the underwriters of their over-allotment option, pursuant to which we sold an additional 750,000 shares of common stock at a price of $18.00 per share. The offer and sale of the shares in the IPO was registered under the Securities Act pursuant to registration statements on Form S-1 (File No. 333-196849), which was filed with the SEC on June 17, 2014 and amended subsequently and declared effective

on July 17, 2014. Following the sale of the shares in connection with the closing of our IPO, the offering terminated. The offering did not terminate before all the securities registered in the registration statements were sold. The underwriters of the offering were JP Morgan and Goldman Sachs & Co. acting as joint book-running managers for the offering and as representatives of the underwriters. Leerink Partners and Canaccord Genuity acted as co-managers for the offering.

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We raised approximately $94.0 million in net proceeds after deducting underwriting discounts and commissions of approximately $7.3 million and other offering expenses of approximately $2.3 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

To date, we have not yet used the net proceeds from our IPO. We invested the funds received in cash equivalents in accordance with our investment policy. None of such payments were direct or indirect payments to any of our directors or officers (or their associates), to persons owning ten percent or more of our common stock or to any other affiliates. As described in our final prospectus filed with the SEC on July 17, 2014 pursuant to Rule 424(b) under the Securities Act, we expect to use the net proceeds from our IPO to fund the costs of our Phase 1/2 clinical development of SAGE-547, to fund the IND-enabling activities and Phase 1 clinical development of SAGE-689, to fund the IND-enabling activities for SAGE-217, as well as for working capital and general corporate purposes, including funding the costs of operating as a public company.

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Item 6. Selected Consolidated Financial Data

The selected financial data set forth below is derived from our audited consolidated financial statements and may not be indicative of future operating results. The following selected consolidated financial data should be read in conjunction with Item 7, Management s Discussion and Analysis of Financial Condition and Results of Operations and the consolidated financial statements and the notes thereto included elsewhere in this report. The selected financial data in this section are not intended to replace our consolidated financial statements and the related notes. Our historical results are not necessarily indicative of our future results.

	Year Ended December 31,		
	2014	2013	2012
	(in thousands, except for per share data)		
Consolidated statements of operations data:			
Operating expenses:			
Research and development	$ 24,100	$ 14,357	$ 7,229
General and administrative	9,710	3,922	2,402
Total operating expenses	33,810	18,279	9,631
Loss from operations	(33,810)	(18,279)	(9,631)
Interest income (expense), net	8	1	
Other income (expense), net	(9)	(3)	(1)
Net loss and comprehensive loss	(33,811)	(18,281)	(9,632)
Accretion of redeemable convertible preferred stock to redemption value	(2,294)	(7)	(4)
Net loss attributable to common stockholders	$ (36,105)	$ (18,288)	$ (9,636)
Net loss per share attributable to common stockholders basic and diluted(1)	$ (1.67)	$ (12.26)	$ (8.62)
Weighted average number of common shares used in net loss per share attributable to common stockholders basic and diluted(1)	21,574,347	1,492,288	1,118,288

	Year Ended December 31,		
	2014	2013	2012
	(in thousands)		
Consolidated balance sheet data:			
Cash and cash equivalents	$ 127,766	$ 8,066	$ 2,802
Working capital(2)	121,706	6,092	1,407
Total assets	129,665	8,532	2,995
Redeemable convertible preferred stock		37,709	14,970

Common stock and additional paid-in capital	188,730	139	
Total stockholders equity (deficit)	121,885	(31,536)	(13,394)

(1) See Note 8 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for further details on the calculation of basic and diluted net loss per share attributable to common stockholders.

(2) We define working capital as current assets less current liabilities.

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Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operation

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report, including those set forth under Item 1A. Risk Factors and under Forward-Looking Statements in this Annual Report on Form 10-K.

Overview

We are a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat life-threatening, rare central nervous system, or CNS, disorders, where there are inadequate or no approved existing therapies. We are targeting CNS indications where patient populations are easily identified, acute treatment is typically initiated in the hospital setting, clinical endpoints are well-defined and development pathways are feasible. This focus allows us to make highly informed decisions when advancing our product candidates through the development process. Our initial product candidates, which are summarized in the following table, are aimed at treating different stages of status epilepticus, or SE, a life-threatening condition in which the brain is in a state of persistent seizure, as well as other seizure and non-seizure disorders.

The lead product candidate in our SE program, SAGE-547, is an intravenous, or IV, agent in Phase 1/2 clinical development as an adjunctive therapy, a therapy combined with current therapeutic approaches, for the treatment of super-refractory SE, or SRSE. The current standard of care for SRSE is empiric, and there are no therapies at present that have been specifically approved for this indication. We thus believe there is a significant medical need for SAGE-547.

In addition, we continue to use SAGE-547 to establish proof of principle in clinical trials for essential tremor, a debilitating neurological disorder that causes involuntary, rhythmic shaking with no known cause, and severe postpartum depression, a distinct and readily identified form of major depressive disorder estimated to affect 15% to 20% of women following childbirth. We plan to use the data from these exploratory studies to help guide the design of a second-generation molecule for the chronic treatment of these diseases.

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SAGE-689 and SAGE-217 are two additional product candidates in our pipeline, which are currently in IND-enabling toxicology and safety pharmacology testing. SAGE-689 is being developed as an adjunctive second-line therapy for the treatment of SE. We are currently conducting IND-enabling studies of SAGE-689, with a plan to file an IND in late 2015 and to begin a Phase 1 clinical trial thereafter. SAGE-217 is being developed as an oral monotherapy for orphan epilepsies, such as Dravet and Rett syndromes. We are currently conducting IND-enabling studies of SAGE-217 with a plan to file an IND by late 2015 and to begin a Phase 1 clinical trial thereafter.

Since our inception in April 2010, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, identifying and developing our product candidates, preparing to conduct and conducting non-clinical and clinical trials of our product candidates, providing general and administrative support for these operations and protecting our intellectual property. We have funded our operations to date through sales of common stock, redeemable convertible preferred stock and, to a lesser extent, the issuance of convertible notes, and proceeds from our initial public offering, or IPO.

We have not generated any revenue to date. We have incurred net losses in each year since our inception, and we have an accumulated deficit of $66.9 million as of December 31, 2014. Our net losses were $36.1 million, $18.3 million, and $9.6 million for the years ended December 31, 2014, 2013, and 2012, respectively. These losses have resulted principally from costs incurred in connection with research and development activities and general and administrative costs associated with our operations. We expect to incur significant expenses and increasing operating losses for the foreseeable future.

We expect that our expenses will increase substantially in connection with our ongoing activities, as we:

- advance clinical development of SAGE-547, our lead product candidate in our SE program, including completing our planned Phase 3 clinical trial for Sage-547 in SRSE, late stage non-clinical studies of SAGE-547, initial preparations for commercial launch, and clinical trials to establish proof of principle in additional indications including severe PPD and essential tremor;

- advance development of SAGE-689 as an adjunctive second-line therapy for the treatment of SE, including completing the IND-enabling toxicology and safety pharmacology testing currently underway, filing an Investigational New Drug Application, or IND, in late 2015 and conducting a Phase 1 clinical trial thereafter;

- advance development of SAGE-217 as an oral monotherapy for orphan epilepsies such as Dravet and Rett syndromes, including completing the IND-enabling toxicology and safety pharmacology testing currently underway and filing an IND in late 2015;

- continue our research and development efforts for other drug candidates in the treatment of CNS disorders including on our early-stage novel allosteric modulators for NMDA;

- seek regulatory approvals for our product candidates;

add personnel, including personnel to support our product development and future commercialization;

add operational, financial and management information systems;

maintain, leverage and expand our intellectual property portfolio; and

operate as a public company.

As a result, we will need additional financing to support our continuing operations. Until such time that we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity or debt financings or other sources, which may include collaborations with third parties. Arrangements with collaborators or others may require us to relinquish rights to certain of our technologies or product candidates. In addition, we may never successfully complete development of any of our product candidates, obtain adequate patent protection for our technology, obtain necessary regulatory approval

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for our product candidates or achieve commercial viability for any approved product candidates. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We will need to generate significant revenue to achieve profitability, and we may never do so.

Financial Operations Overview

Revenue

We have not generated any revenue from product sales since our inception and do not expect to generate any revenue from the sale of products in the near future. If our development efforts result in clinical success and regulatory approval or collaboration agreements with third parties for our product candidates, we may generate revenue from those product candidates.

Operating Expenses

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

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, related benefits, stock-based compensation and related travel expenses for employees engaged in scientific research and development functions;
- expenses incurred under agreements with contract research organizations, or CROs, and investigative sites that conduct our non-clinical studies and clinical trials;
- expenses associated with manufacturing clinical study materials and developing external manufacturing capabilities;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- other expenses related to our non-clinical studies and expenses related to our regulatory activities; and
- payments made under our third-party licensing agreements.

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 SAGE-547, SAGE-689 and SAGE-217 and focusing on other research and development programs related to exploratory efforts, target validation, 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, or CMOs in connection with our non-clinical studies and clinical trials; third-party license fees related to our product candidates; fees paid to outside consultants who perform work on our programs; and costs related to manufacturing or purchasing clinical trial materials. 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 research and development expenses.

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The following table summarizes our research and development expenses by program:

	2014	2013	2012
		(in thousands)	
SAGE-547	$ 9,137	$ 3,918	$ 125
SAGE-689	3,058	2,772	1,047
SAGE-217	2,764	1,129	
Other research and development programs	3,088	3,388	3,495
Unallocated expenses	6,053	3,150	2,562
Total research and development programs	$ 24,100	$ 14,357	$ 7,229

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 initiate clinical trials for certain product candidates and pursue later stages of clinical development of our product candidates.

We cannot determine with certainty the duration and completion costs of the current or future clinical trials of our product candidates or if, when, or to what extent we will generate revenue from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any 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, rate of progress, and expense of our ongoing as well as any additional non-clinical studies, clinical trials and other research and development activities;
- future clinical trial results;
- uncertainties in clinical trial enrollment rate or design;
- significant and changing government regulation; and
- the timing and receipt of any regulatory approvals.

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 if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel costs, consisting of salaries, related benefits, stock-based compensation and related travel expenses of our executive, finance, business and corporate development and other administrative functions. General and administrative expenses also include expenses incurred under agreements with third parties relating to initial commercial evaluation and planning; facilities and other expenses, including rent, depreciation, maintenance of facilities, insurance and supplies; and professional fees for audit, tax and legal services, including legal expenses to pursue patent protection of our intellectual property.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support the expected growth in our research and development activities and the potential commercialization of our product candidates. We also anticipate increased expenses associated with being a public company, including costs related to audit, legal, regulatory and tax-related services associated with

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maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs. Additionally, if and when we believe that a regulatory approval of the first product candidate appears likely, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidates.

Other Income (Expense)

Interest income (expense), net. Interest income (expense), net consists of interest earned on our cash and cash equivalents and interest expense on prior debt. Our interest income has not been significant due to low interest earned on invested balances. We anticipate that our interest income will increase in the future due to increased balances from the net proceeds of $146.8 million we received from our Series B and Series C preferred stock financings in the first quarter of 2014 and our IPO on July 23, 2014.

Other income (expense), net. Other income (expense), net consists of the realized and unrealized net gains and losses from foreign currency-denominated vendor payables.

Critical Accounting Policies and Significant Judgments and Estimates

Our financial statements are prepared in accordance with generally accepted accounting principles in the United States. The preparation of our financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. We believe that the estimates and assumptions involved in the accounting policies described below may have the greatest potential impact on our financial statements and, therefore, consider these to be our critical accounting policies. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing research and development services on our behalf;
- investigative sites or other providers in connection with clinical trials;

vendors in connection with non-clinical development activities; and

vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven

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payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting expenses that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We measure stock-based awards granted to our employees and nonemployee directors at fair value on the date of grant and recognize the corresponding compensation expense of those awards, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. Generally, we issue stock options and restricted stock with only service-based vesting conditions and record the expense for these awards using the straight-line method. We have historically granted stock options with exercise prices equivalent to the fair value of our common stock as of the date of grant.

We measure stock-based awards granted to nonemployee consultants at the fair value of the award on the date at which the related service is complete. Compensation expense is recognized over the period during which services are rendered by such nonemployee consultants until completed. At the end of each financial reporting period prior to the completion of the service, the fair value of these awards is re-measured using, for options, the then-current fair value of our common stock and updated assumptions in the Black-Scholes option-pricing model and using, for restricted stock, the then-current fair value of our common stock.

The fair value of each stock option grant is estimated using the Black-Scholes option-pricing model. Until July 18, 2014, we were a private company and we lacked company-specific historical and implied volatility information. Considering this and the short history of being a public company, we estimate our expected volatility based on the historical volatility of our publicly traded peer companies and expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded stock price. The expected term of our options has been determined utilizing the simplified method for awards that qualify as plain-vanilla options, while the expected term of our options granted to consultants and nonemployees has been determined based on the contractual term of the options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

The assumptions we used to determine the fair value of stock options granted to employees and directors are as follows, presented on a weighted average basis:

	Year Ended December 31,		
	2014	**2013**	**2012**
Expected dividend yield	0.00%	0.00%	0.00%
Expected volatility	98.86%	99.89%	0.00%

Risk free interest rate	1.95%	1.66%	0.00%
Expected life of option	6.38 years	6.04 years	

These assumptions represented our best estimates, but the estimates involve inherent uncertainties and the application of our judgment. As a result, if factors change and we use significantly different assumptions or estimates when valuing our stock options, our stock-based compensation expense could be materially different. We recognize compensation expense for only the portion of awards that are expected to vest. In developing a

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forfeiture rate estimate for pre-vesting forfeitures, we have considered our historical experience of actual forfeitures. If our future actual forfeiture rate is materially different from our estimate, our stock-based compensation expense could be significantly different from what we have recorded in the current period.

During the years ended December 31, 2014 and 2013, we recognized stock-based compensation expense of $2,512 and $61, respectively, of which $1,093 and $38, respectively, was recorded as research and development expense and $1,419 and $23, respectively, was recorded as general and administrative expense in our statement of operations. During the year ended December 31, 2012, we did not record any stock-based compensation expense, as the amounts were inconsequential.

JOBS Act

On April 5, 2012, the Jumpstart Our Business Startups Act, or the JOBS Act, was signed into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an emerging growth company. As an emerging growth company, we are electing not to take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards and, as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Section 107 of the JOBS Act provides that our decision not to take advantage of the extended transition period is irrevocable.

In addition, we intend to rely on the other exemptions and reduced reporting requirements provided by the JOBS Act. Subject to certain conditions set forth in the JOBS Act, if as an emerging growth company we intend to rely on such exemptions, we are not required to, among other things, (i) provide an auditor s attestation report on our system of internal controls over financial reporting pursuant to Section 404, (ii) provide all of the compensation disclosure that may be required of non-emerging growth public companies under the Dodd-Frank Wall Street Reform and Consumer Protection Act, (iii) comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor s report providing additional information about the audit and the financial statements (auditor discussion and analysis), and (iv) disclose certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the Chief Executive Officer s compensation to median employee compensation. These exemptions will apply for a period of five years following the date of our IPO or until we no longer meet the requirements of being an emerging growth company, whichever is earlier.

Our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

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Results of Operations

Comparison of the Years Ended December 31, 2014 and 2013

The following table summarizes our results of operations for the years ended December 31, 2014 and 2013:

	Year Ended December 31,		Increase (Decrease)
	2014	2013	
	(in thousands)		
Operating expenses:			
Research and development	$ 24,100	$ 14,357	$ 9,743
General and administrative	9,710	3,922	5,788
Total operating expenses	33,810	18,279	15,531
Loss from operations	(33,810)	(18,279)	(15,531)
Interest income (expense), net	8	1	7
Other income (expense), net	(9)	(3)	(6)
Net loss	$ (33,811)	$ (18,281)	$ (15,530)

Research and development expenses

	Year Ended December 31,		Increase (Decrease)
	2014	2013	
	(in thousands)		
SAGE-547	$ 9,137	$ 3,918	$ 5,219
SAGE-689	3,058	2,772	286
SAGE-217	2,764	1,129	1,635
Other research and development programs	3,088	3,388	(300)
Unallocated expenses	6,053	3,150	2,903
Total research and development programs	$ 24,100	$ 14,357	$ 9,743

Research and development expenses for the fiscal year ended December 31, 2014 were $24.1 million, compared to $14.4 million for the year ended December 31, 2013. The increase of $9.7 million period over period was primarily due to the following:

an increase of $5.2 million in expenses of our SAGE-547 program. We initiated the Phase 1/2 clinical trial of SAGE-547 in SRSE in early 2014;

an increase of $0.3 million in expenses of our SAGE-689 program with advancement of the lead optimization program into IND-enabling non-clinical development (e.g. toxicology studies, process development, and drug substance manufacturing);

an increase of $1.6 million in expenses of our SAGE-217 program with advancement of the lead optimization program into IND-enabling non-clinical development (e.g. toxicology studies, process development, and drug substance manufacturing);

a net decrease of $0.3 million in expenses of our other research and development programs reflecting a focus on advancing SAGE-689 and SAGE-217 into IND-enabling non-clinical development, portfolio priorities, and timing of investment in certain research programs; and

an increase of $2.9 million in employee related spending to support the growth in our research and development activities, reflecting the effects of hiring additional, full-time employees during 2014.

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General and administrative expenses

	Year Ended December 31, 2014	2013	Increase (Decrease)
		(in thousands)	
Personnel related	$ 4,337	$ 1,764	$ 2,573
Professional fees	3,788	1,253	2,535
Facilities	370	364	6
Other	1,215	541	674
Total general and administrative expenses	$ 9,710	$ 3,922	$ 5,788

General and administrative expenses for the year ended December 31, 2014 were $9.7 million, compared to $3.9 million for the year ended December 31, 2013. The increase of $5.8 million in general and administrative expenses was primarily due to the $2.6 million increase in personnel related costs due to the effects of hiring additional, full-time employees during 2014 to support operations, finance, human resources, and early commercial planning activities as well as an increase in stock compensation expense costs and $2.5 million increase in professional fees associated with being a public company, including costs related to audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, and investor relations costs.

Other income (expense), net

Interest income (expense), net and other income (expense), net were insignificant for the years ended December 31, 2014 and 2013.

Comparison of the Years Ended December 31, 2013 and 2012

The following table summarizes our results of operations for the years ended December 31, 2013 and 2012:

	Year Ended December 31, 2013	2012	Increase (Decrease)
		(in thousands)	
Operating expenses:			
Research and development	$ 14,357	$ 7,229	$ 7,128
General and administrative	3,922	2,402	1,520
Total operating expenses	18,279	9,631	8,648
Loss from operations	(18,279)	(9,631)	(8,648)
Interest income (expense), net	1		1
Other income (expense), net	(3)	(1)	(2)
Net loss	$ (18,281)	$ (9,632)	$ (8,649)

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Research and development expenses

	Year Ended December 31, 2013	2012	Increase (Decrease)
		(in thousands)	
SAGE-547	$ 3,918	$ 125	$ 3,793
SAGE-689	2,772	1,047	1,725
SAGE-217	1,129		1,129
Other research and development programs	3,388	3,495	(107)
Unallocated expenses	3,150	2,562	588
Total research and development programs	$ 14,357	$ 7,229	$ 7,128

Research and development expenses for the year ended December 31, 2013 were $14.4 million, compared to $7.2 million for the year ended December 31, 2012. The increase of $7.1 million year over year was primarily due to the following:

an increase of $3.8 million in expenses of our SAGE-547 program, consisting primarily of external clinical and drug manufacturing costs associated with the preparation of our Phase 1/2 clinical trial of SAGE-547, as compared to only $0.1 million being spent on the program in 2012;

an increase of $1.7 million in expenses of our SAGE-689 program, consisting primarily of external costs related to IND-enabling toxicology and safety pharmacology testing and manufacturing activities that were incurred as that program progressed into non-clinical studies during the second half of 2013;

$1.1 million of expenses of our SAGE-217 program, consisting primarily of costs for external drug discovery efforts;

a net decrease $0.1 million in expenses of our other research and development programs, which consist of our chemistry platform-related work and other research programs;

an increase of $0.6 million in employee related spending to support the growth in our research and development activities, reflecting increases in salaries and bonus expenses, including the effects of hiring additional, full-time employees during 2013.

General and administrative expenses

	Year Ended December 31, 2013	2012	Increase (Decrease)

	(in thousands)		
Personnel related	$ 1,764	$ 899	$ 865
Professional fees	1,253	929	324
Facilities	364	266	98
Other	541	308	233
Total general and administrative expenses	$ 3,922	$ 2,402	$ 1,520

General and administrative expenses for the year ended December 31, 2013 were $3.9 million, compared to $2.4 million for the year ended December 31, 2012. The increase of $1.5 million in general and administrative expenses was primarily due to increased personnel related costs of $0.9 million, which were principally due to employee salary and bonus increases of $0.5 million, including the effects of hiring additional, full-time employees during 2013 to support operations, finance and business development activities. The increase year over year in general and administrative expenses was also due to a $0.3 million increase in professional fees.

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Other income (expense), net

Interest income (expense), net and other income (expense), net were insignificant for the years ended December 31, 2013 and 2012.

Liquidity and Capital Resources

Since our inception in April 2010, we have not generated any revenue and have incurred recurring net losses. As of December 31, 2014, we had an accumulated deficit of $66.8 million. From our inception through December 31, 2014, we have received net proceeds of $90.7 million from the sales of redeemable convertible preferred stock, and to a lesser extent, the issuance of convertible notes, and proceeds from our IPO.

In July 2014, we completed our IPO pursuant to a registration statement on Form S-1. In the IPO, we issued and sold an aggregate of 5,750,000 shares of common stock, including the underwriters exercise in full of their over-allotment option, under the registration statement at a public offering price of $18.00 per share. Net proceeds were approximately $94.0 million, after deducting underwriting discounts and commissions and offering expenses.

As of December 31, 2014, our primary sources of liquidity were our cash and cash equivalents, which totaled $127.8 million. We invest our cash equivalents and investments in highly liquid, interest-bearing investment-grade and government securities to preserve principal.

The following table summarizes the primary sources and uses of cash for the periods presented below:

	Years Ended December 31,		
	2014	2013	2012
	(in thousands)		
Net cash provided by (used in):			
Operating activities	$ (27,042)	$ (17,516)	$ (8,926)
Investing activities	(128)	(3)	(111)
Financing activities	146,870	22,783	8,997
Net increase in cash and cash equivalents	$ 119,700	$ 5,264	$ (40)

Operating Activities

Operating activities used $27.0 million of cash during the year ended December 31, 2014. The cash flow used in operating activities resulted primarily from our net loss of $33.8 million for the period and cash used for changes in our operating assets and liabilities of $4.1 million and by non-cash charges of $2.7 million. Our net loss was primarily attributable to research and development activities related to our lead programs in development and our general and administrative expenses, as we had no revenue in the period. Our net non-cash charges during the year ended December 31, 2014 primarily consisted of stock-based compensation expenses of $2.5 million and non-cash licensing fees paid in shares of our common stock of $0.1 million. Net cash used in changes in our operating assets and liabilities consisted primarily of an increase in accrued expenses and other liabilities of $4.4 million offset by an increase in prepaid expenses and other current assets of $0.7 million. Our prepaid expenses and other current assets, accounts payable and accrued expense balances were affected by the timing of vendor invoicing and payments.

During the year ended December 31, 2013 operating activities used $17.5 million of cash, primarily resulting from our net loss of $18.3 million, partially offset by cash provided by changes in our operating assets and liabilities and non-cash charges totaling $0.8 million. Our net loss was primarily attributed to research and development activities related to our lead programs in development and our general and administrative expenses. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2013

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consisted primarily of an increase in accrued expenses and accounts payable of $0.9 million partially offset by an increase in prepaid expenses and other current assets of $0.3 million. Our prepaid expenses and other current assets, accounts payable and accrued expense balances were affected by the timing of vendor invoicing and payments.

Investing Activities

During the year ended December 31, 2014, we used $0.1 million of cash for purchases of property and equipment. During the year ended December 31, 2013, we had no significant purchases of property and equipment.

Financing Activities

During the years ended December 31, 2014 and 2013, net cash provided by financing activities was $146.9 million and $22.8 million, respectively. Net cash provided by financing activities in the year ended December 31, 2014 consisted of $94.0 million in net proceeds from our IPO on July 23, 2014 and $52.9 million from the issuance of Series B and Series C redeemable preferred stock and from the exercise of stock options. Net cash provided by financing activities in the year ended December 31, 2013 consisted of $22.8 million from the issuance of Series A redeemable convertible preferred stock and from the exercise of stock options.

Operating Capital Requirements

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize one of our current or future product candidates. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates and begin to commercialize any approved products. We expect to incur additional costs associated with operating as a public company. In addition, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing and manufacturing. Accordingly, we anticipate that we will need substantial additional funding in connection with our continuing operations.

Based on our current operating plan, we expect that our existing cash and cash equivalents as of December 31, 2014, including the net proceeds from our IPO which closed on July 23, 2014, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. In that time, we expect that our expenses will increase substantially as we advance clinical development of SAGE-547 including completing our Phase 3 clinical trial, fund IND-enabling activities and Phase 1 clinical development for SAGE-689, fund IND-enabling activities for SAGE-217, fund new and ongoing research and development activities and working capital, and fund other general corporate purposes. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development and commercialization of our product candidates.

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

- the costs, timing, and outcome of regulatory reviews and approvals;

the ability of our product candidates to progress through clinical development successfully;

the initiation, progress, timings, costs, and results of non-clinical studies and clinical trials for our other programs and potential product candidates;

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the number and characteristics of the product candidates we pursue;

the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;

the extent to which we acquire or in-license other products and technologies; and

our ability to establish any future collaboration arrangements on favorable terms, if at all.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. 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 your rights as a common stockholder. 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 your ownership interest. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or research programs or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings 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

The following table summarizes our contractual obligations at December 31, 2014 and the effect such obligations are expected to have on our liquidity and cash flow in future periods:

	Payments Due by Period				
	Total	Less Than 1 year	1-3 Years	3-5 Years	More Than 5 years
			(in thousands)		
Operating lease commitments [1]	$ 575	$ 262	$ 313	$	$
Total [2][3][4]	$ 575	$ 262	$ 313	$	$

(1) We lease office space in Cambridge, Massachusetts under an operating lease agreement that initially expires on February 28, 2017. The minimum lease payments in the table do not include related common area maintenance charges or real estate taxes, which costs are variable.

(2) We have acquired exclusive and non-exclusive rights to use, research, develop and offer for sale certain products and patents under three separate licensing agreements, including amendments entered into in April and May 2014, with Washington University, CyDex Pharmaceuticals, Inc. and The Regents of the University of California.

The licensing rights obligate us to make payments to the licensors for license fees, milestones, license maintenance fees and royalties. We are obligated to make future milestone payments under these agreements of up to $29.8 million upon achieving certain pre-commercialization milestones, such as clinical trials and regulatory approvals. We reasonably anticipate that we may be required to pay $0.5 million of milestone payments in 2015, provided various development milestones are achieved. Amounts related to contingent milestone payments are not considered contractual obligations as they are contingent on the successful achievement of certain milestones. These milestones may not be achieved. Because the achievement of these milestones had not occurred as of December 31, 2014, no liabilities for such contingencies have been recorded in our financial statements. In addition, under the licensing agreements, we will owe single-digit royalties on sales of commercial products, if any, developed using the licensed technologies. Under two of these license agreements, we are obligated to pay to the licensors a

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percentage of fees received if and when we sublicense the technologies. As of December 31, 2014, we had not developed a commercial product using the licensed technologies and we had not entered into any sublicense agreements for the technologies. We have not included any of these amounts in the table as we cannot estimate or predict when, or if, these amounts will become due.

(3) We enter into contracts in the normal course of business with CROs for clinical trials, non-clinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts generally provide for termination upon notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

(4) Under a January 2014 consulting agreement, we are obligated to make milestone payments of up to $2.0 million and to issue up to 126,984 shares of our common stock to a nonemployee consultant upon achieving certain clinical trial milestones and regulatory approval milestones. As of December 31, 2014, we paid $50,000 and issued 15,872 shares of common stock relating to this consulting agreement. We have not included remaining amounts in the table as we cannot estimate or predict when, or if, these amounts will become due.

Off-Balance Sheet Arrangements

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

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We had cash and cash equivalents of approximately $127.8 million at December 31, 2014. 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 equivalents, we believe that a sudden change in market interest rates would not be expected to have a material impact on our financial condition and/or results of operation. We do not have any foreign currency or other derivative financial instruments.

We do not believe that our cash and cash equivalents have significant risk of default or illiquidity. While we believe our cash and cash equivalents 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 and cash equivalents at one or more financial institutions that are in excess of federally insured limits.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the year ended December 31, 2014.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

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Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities and 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 Chief Financial Officer, who is also our principal financial and accounting officer, to allow timely decisions regarding required disclosure.

As of December 31, 2014, 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 (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities and Exchange Act of 1934). 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 December 31, 2014, our disclosure controls and procedures were effective at the reasonable assurance level.

Management s Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include a report of management s assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There were no changes to our internal control over financial reporting that occurred during the period covered by this report that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not applicable.

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PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2015 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 11. Executive Compensation

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2015 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2015 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2015 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

Item 14. Principal Accounting Fees and Services

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2015 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are filed as part of this report:

(1) Financial Statements:

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits. The exhibits filed as part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately following our consolidated financial statements. The Exhibit Index is incorporated herein by reference.

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SIGNATURES

Pursuant to the requirements of the Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

SAGE THERAPEUTICS, INC.

Date: March 6, 2015

By: /s/ Jeffrey M. Jonas

Jeffrey M. Jonas, M.D.
Chief Executive Officer, President and Director
(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed by the following persons in the capacities indicated below and on the dates indicated:

Signature	Title	Date
/s/ Jeffrey M. Jonas Jeffrey M. Jonas, M.D.	Chief Executive Officer, President and Director (Principal Executive Officer)	March 6, 2015
/s/ Kimi Iguchi Kimi Iguchi	Chief Financial Officer (Principal Financial and Accounting Officer)	March 6, 2015
/s/ Robert T. Nelsen Robert T. Nelsen	Director	March 6, 2015
/s/ Steven Paul Steven Paul, M.D.	Director	March 6, 2015
/s/ Kevin P. Starr Kevin P. Starr	Director	March 6, 2015
/s/ Howard Pien Howard Pien	Director	March 6, 2015
/s/ James Frates James Frates	Director	March 6, 2015

/s/ Michael F. Cola	Director	March 6, 2015
Michael F. Cola		

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of

Sage Therapeutics, Inc.:

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations and comprehensive loss, of changes in redeemable convertible preferred stock and shareholders equity (deficit) and of cash flows present fairly, in all material respects, the financial position of Sage Therapeutics, Inc. and its subsidiary at December 31, 2014 and December 31, 2013 and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2014 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts

March 6, 2015

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Sage Therapeutics, Inc. and Subsidiary

Consolidated Balance Sheets

(in thousands, except share and per share data)

	December 31, 2014	December 31, 2013
Assets		
Current assets:		
Cash and cash equivalents	$ 127,766	$ 8,066
Prepaid expenses and other current assets	1,056	341
Total current assets	128,822	8,407
Property and equipment, net	163	86
Restricted cash	39	39
Deferred tax assets	641	
Total assets	$ 129,665	$ 8,532
Liabilities, Redeemable Convertible Preferred Stock and Stockholders Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 2,429	$ 1,988
Accrued expenses	4,687	327
Deferred tax liabilities	641	
Total current liabilities	7,757	2,315
Other liabilities	23	44
Total liabilities	7,780	2,359
Commitments and contingencies (Note 4)		
Redeemable convertible preferred stock (Series A, B and C), $0.0001 par value; no shares and 37,750,000 shares authorized at December 31, 2014 and 2013, respectively; no shares and 37,750,000 shares issued and outstanding at December 31, 2014 and 2013, respectively; liquidation preference of $0 and $40,663 at December 31, 2014 and 2013, respectively		37,709
Stockholders equity (deficit):		
Preferred stock, $0.0001 par value; 5,000,000 and no shares authorized at December 31, 2014 and 2013, respectively; no shares issued or outstanding at December 31, 2014 and 2013, respectively		
Common stock, $0.0001 par value; 120,000,000 and 66,000,000 shares authorized at December 31, 2014 and 2013, respectively; 25,621,791 and 1,622,761 shares issued and outstanding at December 31, 2014 and 2013, respectively	3	

Additional paid-in capital	188,727	139
Accumulated deficit	(66,845)	(31,675)
Total stockholders equity (deficit)	121,885	(31,536)
Total liabilities, redeemable convertible preferred stock and stockholders equity (deficit)	$ 129,665	$ 8,532

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

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Sage Therapeutics, Inc. and Subsidiary

Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except share and per share data)

	2014	2013	2012
Operating expenses:			
Research and development	$ 24,100	$ 14,357	$ 7,229
General and administrative	9,710	3,922	2,402
Total operating expenses	33,810	18,279	9,631
Loss from operations	(33,810)	(18,279)	(9,631)
Interest income (expense), net	8	1	
Other income (expense), net	(9)	(3)	(1)
Net loss and comprehensive loss	(33,811)	(18,281)	(9,632)
Accretion of redeemable convertible preferred stock to redemption value	(2,294)	(7)	(4)
Net loss attributable to common stockholders	$ (36,105)	$ (18,288)	$ (9,636)
Net loss per share attributable to common stockholders basic and diluted	$ (1.67)	$ (12.26)	$ (8.62)
Weighted average number of common shares used in net loss per share attributable to common stockholders basic and diluted	21,574,347	1,492,288	1,118,288

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

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Sage Therapeutics, Inc. and Subsidiary

Consolidated Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders Equity (Deficit)

(in thousands, except share data)

	Series A, B and C Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders Equity (Deficit)
	Shares	Amount	Shares	Amount			
Balances at December 31, 2011	6,000,000	$ 5,972	680,560	$	$	$ (3,761)	$ (3,761)
Issuance of Series A Preferred Stock, net of issuance costs of $6	9,000,000	8,994					
Issuance of common stock from exercise of stock options			5,555				
Vesting of restricted stock			709,158		3		3
Accretion of Series A Preferred Stock issuance costs		4			(3)	(1)	(4)
Net loss						(9,632)	(9,632)
Balances at December 31, 2012	15,000,000	14,970	1,395,273			(13,394)	(13,394)
Issuance of Series A Preferred Stock, net of issuance costs of $18	22,750,000	22,732					
Issuance of common stock from exercise of stock options			3,174		1		1
Vesting of restricted stock			176,695		20		20
Accretion of Series A Preferred Stock issuance costs		7			(7)		(7)
Issuance of common stock in payment of licensing fees			47,619		64		64
Stock-based compensation expense					61		61
Net loss						(18,281)	(18,281)

Balances at December 31, 2013	37,750,000	37,709	1,622,761		139	(31,675)	(31,536)
Issuance of Series B Preferred Stock, net of issuance costs of $30	9,999,999	14,970					
Issuance of Series C Preferred Stock, net of issuance costs of $110	8,973,905	37,890					
Issuance of common stock from exercise of stock options			87,475		40		40
Vesting of restricted stock			138,108		14		14
Issuance of common stock in payment of consultant fees			15,872		127		127
Stock-based compensation expense					2,512		2,512
Accretion of redeemable convertible preferred stock to redemption value		2,294			(935)	(1,359)	(2,294)
Conversion of redeemable convertible preferred stock to common stock	(56,723,904)	(92,863)	18,007,575	2	92,861		92,863
Initial public offering of common stock, net of offering costs			5,750,000	1	93,969		93,970
Net loss						(33,811)	(33,811)
Balances at December 31, 2014		$	25,621,791	$ 3	$ 188,727	$ (66,845)	$ 121,885

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

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Sage Therapeutics, Inc. and Subsidiary

Consolidated Statements of Cash Flows

(in thousands)

	Year Ended December 31,		
	2014	**2013**	**2012**
Cash flows from operating activities			
Net loss	$ (33,811)	$ (18,281)	$ (9,632)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	2,512	61	
Licensing or consulting fees paid in common stock	127	64	
Depreciation and amortization	51	47	44
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(715)	(317)	71
Accounts payable	441	674	609
Accrued expenses	4,374	236	(18)
Other liabilities	(21)		
Net cash used in operating activities	(27,042)	(17,516)	(8,926)
Cash flows from investing activities			
Purchase of property and equipment	(128)	(3)	(111)
Net cash used in investing activities	(128)	(3)	(111)
Cash flows from financing activities			
Proceeds from the issuance of Series A preferred stock, net of issuance costs		22,732	8,994
Proceeds from the issuance of Series B preferred stock, net of issuance costs	14,970		
Proceeds from the issuance of Series C preferred stock, net of issuance costs	37,890		
Proceeds from the issuance of common stock and restricted stock, net	40	51	3
Proceeds from initial public offering of common stock, net of commissions and underwriting discounts	96,255		
Payment of offering costs	(2,285)		
Net cash provided by financing activities	146,870	22,783	8,997
Net increase in cash and cash equivalents	119,700	5,264	(40)
Cash and cash equivalents at beginning of period	8,066	2,802	2,842
Cash and cash equivalents at end of period	$ 127,766	$ 8,066	$ 2,802
Supplemental disclosure of non-cash investing and financing activities			
Accretion of redeemable convertible preferred stock to redemption value	$ 2,294	$ 7	$ 4

Conversion of redeemable convertible preferred stock to common stock	$ 92,863	$	$

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

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SAGE THERAPEUTICS, INC. AND SUBSIDIARY

Notes to Consolidated Financial Statements

(Amounts in thousands, except share and per share data)

1. Nature of the Business

Sage Therapeutics, Inc. (Sage or the Company) is a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat life-threatening, rare central nervous system (CNS) disorders, where there are inadequate or no approved existing therapies. The Company is targeting CNS indications where patient populations are easily identified, acute treatment is typically initiated in the hospital setting, clinical endpoints are well-defined, and development pathways are feasible. This focus allows the Company to make highly informed decisions when advancing its product candidates through the development process. The Company s initial product candidates are aimed at treating different stages of status epilepticus, a life-threatening condition in which the brain is in a state of persistent seizure.

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. under its second Amended and Restated Certificate of Incorporation.

The Company is subject to risks and uncertainties common to early-stage companies in the biotech industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel protection of proprietary technology, compliance with government regulations, and ability to secure additional capital to fund operations.

We have incurred losses and negative cash flows from operations since our inception. As of December 31, 2014, we had an accumulated deficit of $66.9 million. From our inception through December 31, 2014, we raised aggregate net proceeds of $90.6 million from the issuance of Series A, Series B and Series C redeemable convertible preferred stock. In July 2014, we raised gross proceeds of $96.3 million from the sale of common stock in our initial public offering. We believe our cash balance of $127.8 million as of December 31, 2014 will be sufficient to fund our anticipated level of operations for at least the next 12 months. The future viability of the Company is largely dependent on its ability to raise additional capital to finance its operations. Management expects that future sources of funding may include new or expanded partnering arrangements and sales of equity or debt securities. Adequate additional funding may not be available to the Company on acceptable terms or at all. The failure to raise capital as and when needed could have a negative impact on the Company s financial condition and ability to pursue business strategies. The Company may be required to delay, reduce the scope of or eliminate research and development programs, or obtain funds through arrangements with collaborators or others that may require the Company to relinquish rights to certain product candidates that the Company might otherwise seek to develop or commercialize independently.

2. Summary of Significant Accounting Policies

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

Basis of Presentation

The accompanying consolidated financial statements include those of the Company and its subsidiary, Sage Securities Corporation, after elimination of all intercompany accounts and transactions. The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (GAAP).

Use of Estimates

The preparation of 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 financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from those estimates.

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Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents.

Restricted Cash

A deposit of $39 was restricted from withdrawal as of December 31, 2014 and 2013. The restriction is related to securing the Company s facility lease and expires in 2017 in accordance with the operating lease agreement. This balance is included in restricted cash on the accompanying balance sheets.

Property and Equipment

Property and equipment are recorded at cost and depreciated over their estimated useful lives using the straight-line method. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is credited or charged to income. Repairs and maintenance costs are expensed as incurred.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any impairment losses on long-lived assets.

Research and Development

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.

Research Contract Costs and Accruals

The Company has entered into various research and development contracts with research institutions and other companies both inside and outside of the United States. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company s estimates. The Company s historical accrual estimates have not been materially different from the actual costs.

Patent Costs

The Company expenses patent costs as incurred and classifies such costs as general and administrative expenses in the accompanying statements of operations and comprehensive loss.

Stock-Based Compensation

The Company recognizes compensation expense for all stock-based awards made to employees and nonemployee directors, including grants of stock options and restricted stock, based on estimated fair value on date of grant, over the requisite service period.

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For stock options and restricted stock issued to nonemployee consultants, the Company recognizes the fair value of such instruments as an expense over the period in which the related services are received. The fair value of the awards and measurement of related stock-based compensation is subject to periodic adjustments as the underlying equity instruments vest.

The fair value of each option grant is estimated using the Black-Scholes option-pricing model. Through July 2014, the Company was a private company and lacks sufficient Company-specific historical and implied volatility information. Therefore, the Company estimates expected volatility based on the historical volatility of publicly traded peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its traded stock price. The expected term of the Company s options has been determined utilizing the simplified method for awards that qualify as plain-vanilla options, while the expected term of its options granted to consultants and nonemployees has been determined based on the contractual term of the options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

The Company also applies a forfeiture rate in order to calculate stock-based compensation expense. To the extent actual forfeitures differ from the estimates, the difference will be recorded as a cumulative adjustment in the period the estimates are revised. The Company recognizes compensation expense for only the portion of awards that are expected to vest. Expected forfeitures are based on the Company s historical experience and management s expectations of future forfeitures.

Basic and Diluted Net Income (Loss) Per Share

Upon the closing of the Company s IPO in July 2014, all of the Company s outstanding redeemable convertible preferred shares were converted into shares of common stock. Prior to this conversion, the Company followed the two-class method when computing net income (loss) per share as the Company had issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common shareholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed. The Company s redeemable convertible preferred shares contractually entitled the holders of such shares to participate in dividends, but did not contractually require the holders of such shares to participate in losses of the Company. Accordingly, the two-class method did not apply for periods in which the Company reported a net loss or a net loss attributable to common shareholders resulting from dividends or accretion related to its redeemable convertible preferred shares.

Basic net income (loss) per share attributable to common shareholders is computed by dividing the net income (loss) attributable to common shareholders by the weighted average number of common shares outstanding for the period. Diluted net income (loss) per share attributable to common shareholders is computed by dividing the diluted net income (loss) attributable to common shareholders by the weighted average number of common shares outstanding for the period, including potential dilutive common shares assuming the dilutive effect of outstanding stock options and unvested restricted common shares, as determined using the treasury stock method. For periods in which the Company has reported net losses, diluted net loss per common share attributable to common shareholders is the same as basic net loss per common share attributable to common shareholders, since dilutive common shares are not assumed to have been issued if their effect is antidilutive.

The Company reported a net loss attributable to common stockholders for the years ended December 31, 2014, 2013 and 2012.

Risks and Uncertainties

The product candidates developed by the Company require approvals from the U.S. Food and Drug Administration or foreign regulatory agencies prior to commercial sales. There can be no assurance that the

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Company s current and future product candidates will receive the necessary approvals. If the Company is denied approval or approval is delayed, it may have a material adverse impact on the Company s business and its financial statements.

The Company is subject to risks common to companies in the development stage including, but not limited to, dependency on the clinical and commercial success of its product candidates, ability to obtain regulatory approval of its product candidates, the need for substantial additional financing to achieve its goals, uncertainty of broad adoption of its approved products, if any, by physicians and consumers, significant competition and untested manufacturing capabilities.

Concentration of Credit Risk and of Significant Suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company has all cash and cash equivalents balances at two accredited financial institutions, in amounts that exceed federally insured limits. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on third-party manufacturers to supply products for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

Income Taxes

The Company accounts for income taxes under the asset and liability method. Under this method, deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted rates in effect for the year in which these temporary differences are expected to be recovered or settled. Valuation allowances are provided if based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

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 to be classified and disclosed in one of the following three categories:

Level 1	Quoted market prices in active markets for identical assets or liabilities. At December 31, 2014 and 2013, the Company s Level 1 assets consisted of money market funds totaling $127,766 and $8,066, respectively.
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. At December 31, 2014 and 2013, the Company had no Level 2 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. At December 31, 2014 and 2013, the Company had no Level 3 assets or liabilities.

The Company s financial instruments generally consist of cash equivalents, accounts payable and accrued expenses. The carrying amounts for the applicable financial instruments reported in the balance sheets approximate their fair values at December 31, 2014 and 2013, respectively.

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Deferred Offering Costs

The Company capitalizes certain legal, accounting and other third-party fees that are directly associated with in-process equity financings as other assets until such financings are consummated. After consummation of the equity financing in July 2014, $2,285 of these costs were recorded in stockholders equity (deficit) as a reduction of additional paid-in capital generated as a result of the initial public offering.

Segment Data

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company s singular focus is on advancing medicines to treat central nervous system disorders, where there are inadequate or no approved existing therapies, including status epilepticus. All tangible assets are held within the U.S.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders equity (deficit) that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2014, 2013 and 2012, there was no difference between net loss and comprehensive loss.

Government Grants

The Company records amounts received under grants as a reduction to research and development expense in the period it has incurred the expenditures in compliance with the specific restrictions of the grant. The Company recorded $129, $96 and $0 for the years ended December 31, 2014, 2013 and 2012, respectively.

Initial Public Offering

On July 23, 2014, the Company completed the sale of 5,750,000 shares of its common stock in its initial public offering (the IPO), at a price to the public of $18.00 per share, resulting in net proceeds to the Company of $94.0 million after deducting underwriting discounts and commissions and offering costs paid by the Company. The shares began trading on Nasdaq Global Market on July 18, 2014.

In connection with preparing for the IPO, the Company s board of directors and stockholders approved a 1-for-3.15 reverse stock split of the Company s common stock effective July 2, 2014. All share and per share amounts in the financial statements contained herein and notes thereto have been retroactively adjusted, where necessary, to give effect to this reverse stock split. In connection with the closing of the IPO, all of the Company s outstanding redeemable convertible preferred stock automatically converted into shares of common stock as of July 23, 2014, resulting in the issuance by the Company of an additional 18,007,575 shares of common stock. The significant increase in common stock outstanding in July 2014 will impact the year-over-year comparability of the Company s net loss per share calculations over the next year.

Recently Issued Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, (FASB), issued Accounting Standards Update (ASU) 2014-09, Revenue from Contracts with Customers (Topic 606), (ASU 2014-09). ASU 2014-09 outlines a new, single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. This new revenue

recognition model provides a five-step analysis in determining when and how revenue is recognized. The new model will require revenue recognition to depict the transfer of promised goods or services to customers in an amount that reflects the consideration a company expects to receive in exchange for those goods or services. ASU 2014-09 is effective for public entities for annual reporting periods beginning after December 15, 2016 and interim periods within those periods. Early adoption is not permitted. Companies may

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use either a full retrospective or a modified retrospective approach to adopt ASU 2014-09. The Company is currently assessing the method of adoption and the impact this new accounting guidance will have on its financial statements and footnote disclosures.

In June 2014, the Financial Accounting Standard Board, or FASB, issued amended accounting guidance for development stage entities. The amendment eliminates certain financial reporting requirements for development stage entities, specifically, the presentation of inception-to-date information, the development stage entity label on the financial statements, the description of the activities in which the entity is engaged, and disclosure in the first year that the entity is no longer a development stage entity that it had been in prior years. The amendment is effective retrospectively for annual reporting periods beginning after December 15, 2014, and interim periods therein with early adoption permitted. The Company elected to early adopt this standard in the period ended June 30, 2014. Other than a change in presentation, the adoption of this guidance did not have an impact on the Company s financial statements.

In August 2014, the FASB issued ASU 2014-15, Presentation of Financial Statements Going Concern (Subtopic 205-40). The new guidance addresses management s responsibility to evaluate whether there is substantial doubt about an entity s ability to continue as a going concern and to provide related footnote disclosures. Management s evaluation should be based on relevant conditions and events that are known and reasonably knowable at the date that the financial statements are issued. The standard will be effective for the first interim period within annual reporting periods beginning after December 15, 2016. Early adoption is permitted. The Company is evaluating the effect that this guidance will have on its financial statements.

3. Balance Sheet Components

Property and Equipment, net

Property and equipment, net consists of the following:

	Useful Life (Years)	December 31, 2014	December 31, 2013
Computer and office equipment	3	$ 206	$ 78
Furniture and equipment	5	103	103
		309	181
Less: Accumulated depreciation		(146)	(95)
Property and equipment, net		$ 163	$ 86

Depreciation expense for the years ended December 31, 2014, 2013 and 2012 was $51, $47, and $44, respectively.

Accrued Expenses

Accrued expenses consist of the following:

	December 31,	
	2014	2013
Employee related expenses	$ 1,279	$ 49
Development costs	2,788	57
Professional services	574	190
Other accrued expenses	46	31
	$ 4,687	$ 327

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4. Commitments and Contingencies

Operating Leases

The Company rents its 6,500 square foot office space under an operating lease that was executed in 2011 and expires in 2017. In March 2013, the Company entered into a second lease for an additional 4,100 square feet. The second lease, which commenced on August 26, 2013, has a term of 42 months and rent expense of $9 per month. Also in March 2013, the Company signed a sublease agreement to sublet 1,900 square feet. The sublease is for a term of 42 months and rental income is $4 per month.

Rent expense, net of sublease income, for the years ended December 31, 2014, 2013, and 2012 was $302, $274 and $194, respectively.

Future minimum lease payments, net of sublease income, under non-cancelable operating leases are as follows at December 31, 2014:

Years Ending December 31,	
2015	$ 262
2016	268
2017	45
	$ 575

License Agreements

CyDex License Agreement

In October 2011, the Company entered into a research and development license with CyDex Pharmaceuticals, Inc. (CyDex) for the development of drug product using licensed technology for a period of one year. Under the terms of the license agreement, the Company paid an initial licensing fee of $200 and an additional fee of $100 for CyDex to perform research and development services to evaluate the licensed technology for formulation with the Company s developmental product.

The $200 payment was recorded as research and development expense as the acquired technology was in-process research and development, and the $100 payment was recorded to research and development expense in 2011 and 2012 as services were performed.

In December 2012, the Company exercised its option to enter into a commercial license and supply agreement for CyDex s proprietary technology and paid $100 for the perpetual license, which was recorded as research and development expense.

In August 2013, the Company entered into a commercial license agreement as a result of which the December 2012 license was terminated and the December 2012 supply agreement was amended. Specifically, CyDex granted the Company an exclusive license to the CyDex technology for use in the fields of status epilepticus and traumatic brain injury. In exchange, the Company is required to pay upfront, milestone and royalty-based compensation. In addition, CyDex granted the Company a research license to Captisol for allopregnanolone for use in proof of concept studies. The August 2013 agreement will continue in effect unless and until terminated. In consideration for the amended

license rights, the Company paid $300. The Company is obligated to make milestone payments based on achievement of clinical development and regulatory milestones of $900 and $3,750, respectively. Also under this agreement, the Company is required to pay royalties in the low single digits based on levels of net sales.

Under the amended supply agreement with CyDex, the Company is required to purchase all of its supply of Captisol from CyDex and CyDex is required to supply the Company with Captisol, subject to certain limitations.

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In April 2014, the Company amended its commercial license and supply agreements with CyDex to expand the fields of use to include the treatment, prevention or diagnosis of any disease or symptom in humans or animals. In consideration for the amended terms, the Company paid $200 upfront and is obligated to make milestone payments, once per field, based on the achievement of clinical development and regulatory milestones for the development of SAGE-547 in the fields of status epilepticus and traumatic brain injury of $750 and $3,750, respectively. For the development in two additional fields, the Company is obligated to make milestone payments, once per field, based on the achievement of clinical development and regulatory milestones of $1,250 and $8,500, respectively.

As of December 31, 2014, the Company had not made any milestone or royalty payments.

Washington University License Agreement

In November 2013, the Company entered into a license agreement with Washington University whereby the Company was granted exclusive, worldwide rights to develop and commercialize a novel set of neuroactive steroids developed by Washington University. In exchange for development and commercialization rights, the Company paid an upfront, non-refundable payment of $50 and is required to pay an annual license maintenance fee of $15 on each subsequent anniversary date, until the first Phase 2 clinical study for a licensed product is initiated. The Company is obligated to make milestone payments based on achievement of clinical development and regulatory milestones of up to $650 and $500, respectively. Additionally, the Company fulfilled its obligation to issue Washington University 47,619 shares of common stock on December 13, 2013. The fair values of these shares totaling $64 were recorded as research and development expense in 2013.

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

As of December 31, 2014, the Company had not made any milestone or royalty payments.

University of California License Agreement

In October 2013, the Company entered into a non-exclusive license agreement with The Regents of the University of California whereby the Company was granted a non-exclusive license to certain clinical data and clinical material for use in the development and commercialization of biopharmaceutical products in the licensed field, including status epilepticus and post-partum 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 will be required to pay clinical development milestones of up to $100 and pay royalties of less than 1% on net sales for a period of fifteen years following the sale of the first commercial product.

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.

As of December 31, 2014, the Company had not made any milestone or royalty payments.

Consulting Agreement

In January 2014, the Company entered into a consulting agreement with a nonemployee advisor whereby the Company is obligated to make cash payments of up to $2,000 and to issue up to 126,984 shares of common stock upon attainment of certain clinical development and regulatory milestones.

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In January and March 2014, the first milestone for each of two programs included in the consulting agreement were met. Accordingly, the Company made cash payments of $50 and issued 15,872 shares of the Company s common stock. In connection with the shares of common stock issued, the Company recorded $127 as research and development expense for the year ended December 31, 2014.

5. Redeemable Convertible Preferred Stock

As of December 31, 2014 and 2013, the Company s Certificate of Incorporation, as amended and restated, authorizes the Company to issue no shares and 37,750,000, respectively, shares of $0.0001 par value preferred stock. In July 2014, all issued and outstanding redeemable convertible preferred stock was converted to common stock, see Note 2.

The Company had issued Series A, Series B and Series C redeemable convertible preferred stock (collectively, the Redeemable Preferred Stock). The Redeemable Preferred Stock was classified outside of stockholders equity (deficit) as of December 31, 2013 because the shares contain redemption features that are not solely within the control of the Company.

On March 18, 2013, the Company issued an additional 5,000,000 shares in the second funding of the second tranche of Series A Preferred Stock at $1.00 per share, resulting in net proceeds of $4,996.

On July 1, 2013, the Company issued an additional 5,000,000 shares in the third funding of the second tranche of Series A Preferred Stock at $1.00 per share, resulting in net proceeds of $4,999.

On September 12, 2013, the Company issued an additional 12,500,000 shares in the third tranche of Series A Preferred Stock at $1.00 per share, resulting in net proceeds of $12,487.

On October 18, 2013, the Company issued 250,000 shares of Series A Preferred Stock at $1.00 per share, resulting in net proceeds of $250.

The Company incurred issuance costs of $18 and $6 in 2013 and 2012, respectively, with the issuance of the Series A Preferred Stock which were recorded as a reduction of the proceeds received. These costs were accreted on a straight-line basis to the carrying value of preferred stock, beginning with the date of issue to the date of earliest redemption.

On October 15, 2013, the Company entered into a Stock Purchase Agreement whereby the Company would issue up to $20,000 of Series B redeemable convertible preferred stock (Series B Preferred Stock) at $1.50 per share. The initial purchase and sale in the amount of $10,000 could have occurred once certain development milestones had been successfully achieved. The second tranche of $10,000 could be issued after the initial closing and at the discretion of the Board of Directors. In November 2013, the Company met the development milestones to issue the first tranche of the Series B Preferred Stock.

On January 7, 2014, the Company issued 6,666,666 shares of Series B Preferred Stock at $1.50 per share, resulting in net proceeds of $9,995.

On February 12, 2014, the Company issued 3,333,333 shares of Series B Preferred Stock at $1.50 in a second closing, resulting in net proceeds of $5,000. At that time, the Company decided not to draw on the remaining $5,000 of the second tranche of the Series B Preferred Stock.

The Company incurred issuance costs of $30 in 2014 with the issuance of the Series B Preferred Stock which were recorded as a reduction of the proceeds received.

On March 11, 2014, the Company entered into a Stock Purchase Agreement whereby the Company issued 8,973,905 shares of Series C redeemable convertible preferred stock (Series C Preferred Stock) at $4.2345 per share for net proceeds of $37,981.

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The Company incurred issuance costs of $110 in 2014 with the issuance of the Series C Preferred Stock which were recorded as a reduction of the proceeds received.

The holders of the Redeemable Preferred Stock had the following rights and preferences:

Voting Rights

The holders of Redeemable Preferred Stock were entitled to vote, together with the holders of common stock, on all matters submitted to stockholders for a vote. Each preferred stockholder was entitled to the number of votes equal to the number of shares of common stock into which each share of Redeemable Preferred Stock was convertible at the time of such vote.

Dividends

The holders of Series A, Series B and Series C Preferred Stock were entitled to receive dividends in preference to any dividend on common stock at the rate of $0.08, $0.12 and $0.34, respectively, per share per annum. Dividends were payable only when, as, and if declared by the Board of Directors. As of December 31, 2014 and 2013, no dividends had been declared or paid by the Company.

Liquidation

In the event of any liquidation, dissolution or winding up of the affairs of the Company, the holders of the Series A, Series B and Series C Preferred Stock were entitled to receive an amount per share equal to the original issue price of $1.00, $1.50 and $4.2345, respectively, per share (the Original Issue Price), plus all accruing dividends, whether or not declared, payable in preference and priority to any payments made to the holders of the then outstanding common stock. In the event of a liquidation, dissolution or winding up of the affairs of the Company, holders of Series C Preferred Stock were to be paid their liquidation preference amounts prior to the payment to holders of Series A Preferred Stock and Series B Preferred Stock of their liquidation preference amounts on a pari passu basis. Series A Preferred Stock and Series B Preferred Stock were to be paid their liquidation preference amounts on a pari passu basis prior to the payment of any amounts to holders of common stock. If the liquidation proceeds exceeded the liquidation preferences, then holders of the Series A, Series B and Series C Preferred Stock were to participate in the excess on an as-if converted basis with the common shareholders up to $2.50, $3.75 and $10.58, respectively, per share.

Redemption Rights

Redeemable Preferred Stock was redeemable at the option of the preferred stockholders on or after September 30, 2020. If the holders of at least seventy-five percent of the then outstanding shares of Redeemable Preferred Stock exercised their redemption rights, the Company must notify all preferred stockholders of the election to exercise redemption rights. Under the terms of the Company s Certificate of Incorporation, as amended and restated on March 11, 2014, the holders of the Redeemable Preferred Stock who requested redemption of their Redeemable Preferred Stock were entitled to receive an amount per share equal to the Original Issue Price of $1.00, $1.50 or $4.2345 for each share of Series A, Series B or Series C Preferred Stock, respectively, plus all accruing dividends, whether or not declared, and were to be paid in three annual installments commencing not more than sixty days after receipt of notification by the Company.

If the Company did not have sufficient funds legally available to redeem all shares of Redeemable Preferred Stock to be redeemed at the redemption date, the Company would redeem such shares ratably to the extent possible and would

redeem the remaining shares as soon as sufficient funds are legally available.

Conversion

Each share of Redeemable Preferred Stock was convertible at any time at the option of the shareholder into fully paid and nonassessable shares of common stock determined by dividing the Original Issue Price by the

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Conversion Price in effect at the time of conversion. The initial Series A, Series B and Series C Conversion Price is $3.15, $4.725 and $13.338675, respectively, per share (the Conversion Price).

In addition to the above optional conversion feature, the Redeemable Preferred Stock included a mandatory conversion feature whereby upon either of the following events, all outstanding shares of Redeemable Preferred Stock would automatically be converted into shares of common stock at the then-effective conversion ratio: (i) Initial Public Offering resulting in a closing price of at least $14.18 per share that results in at least $30,000 in gross proceeds to the Company, or (ii) the date and time, or the occurrence of an event, specified by vote or written consent of the holders of at least 75% of the then outstanding shares of Redeemable Preferred Stock. All shares that are required to be surrendered per the provisions above will be deemed to have been retired and canceled and may not be reissued as shares of Redeemable Preferred Stock.

The Company has newly authorized preferred stock amounting to 5,000,000 shares as of December 31, 2014. The newly authorized preferred stock was classified under stockholders equity (deficit) as of December 31, 2014.

6. Common Stock

As of December 31, 2014 and 2013, the Company has authorized 120,000,000 and 66,000,000 shares, respectively, of common stock with a par value of $0.0001 per share.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company s stockholders. Common stockholders are entitled to receive dividends, as may be declared by the Board of Directors, if any, subject to the preferential dividend rights of the Series A, Series B and Series C preferred stockholders. As of December 31, 2014 and 2013, no dividends have been declared.

7. Stock-Based Compensation

2014 Stock Option Plan

On July 2, 2014, the Company s stockholders approved the 2014 Stock Option and Incentive Plan (the 2014 Stock Option Plan), which became effective upon the completion of the IPO. The 2014 Stock Option Plan provides for the grant of restricted stock awards, incentive stock options and non-statutory stock options. The 2014 Stock Option Plan replaced the Company s 2011 Stock Option and Grant Plan (the 2011 Stock Option Plan). The Company will grant no further stock options or other awards under the 2011 Stock Option Plan. Any options or awards outstanding under the 2011 Stock Option Plan remained outstanding and effective. As of December 31, 2014, the total number of shares reserved under all equity plans is 3,505,868, and the Company had 1,509,253 shares available for future issuance under such plans.

The 2014 Stock Option Plan provides for an annual increase, to be added on the first day of each fiscal year, by up to 4% of the Company s issued and outstanding shares of common stock on the immediately preceding December 31.

2014 Employee Stock Purchase Plan

On July 2, 2014, the Company s stockholders approved the 2014 Employee Stock Purchase Plan. A total of 282,000 shares of common stock were initially authorized for issuance under this plan. The 2014 Employee Stock Purchase Plan became effective upon the completion of the IPO. As of December 31, 2014, no shares have been issued under

this plan.

Terms of restricted stock awards and stock option agreements, including vesting requirements, are determined by the Board of Directors, subject to the provisions of the applicable stock option plan. Options and restricted stock awards granted by the Company generally vest based on the grantee s continued service with the Company during a specified period following grant. Awards generally vest ratably over four years, with a 25% cliff vesting at the one year anniversary for new employee awards. During 2013, the Company also granted a pool of option awards which vest ratably over one year. All awards are exercisable from the date of grant for a period of ten years.

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The stock-based compensation expense recognized during the years ended December 31, 2014, 2013, and 2012 was as follows:

	Year Ended December 31,		
	2014	2013	2012
Stock compensation expense:			
Research and development	$ 1,093	$ 38	$
General and administrative	1,419	23	
	$ 2,512	$ 61	$

During the year ended 2012, the Company did not record stock-based compensation expense as the amounts were inconsequential.

Prior to December 31, 2012, the estimated fair market value of the Company s common stock was determined solely by the Board of Directors on the date of grant. From December 31, 2012 until its IPO, the Company secured a third-party valuation to assist the Board of Directors in the determination of the estimated fair market value of the Company s common stock.

For stock option awards, the fair value of the options is estimated at the grant date using the Black-Scholes option-pricing model, taking into account the terms and conditions upon which options are granted. The fair value of the options is amortized on a straight-line basis over the requisite service period of the awards. The weighted average grant date fair value per share relating to outstanding stock options granted under the Company s stock option plans during the years ended December 31, 2014 and 2013 was $14.33 and $0.38, respectively.

The fair value of each option granted to employees and directors during the years ended December 31, 2014, 2013, and 2012 under the Company s stock option plans has been calculated on the date of grant using the following weighted average assumptions:

	Year Ended December 31,		
	2014	2013	2012
Expected dividend yield	0.00%	0.00%	0.00%
Expected volatility	98.86%	99.89%	0.00%
Risk free interest rate	1.95%	1.66%	0.00%
Expected term	6.38 years	6.04 years	

Expected dividend yield: The Company has not paid and does not anticipate paying any dividends in the foreseeable future.

Risk-free interest rate: The Company determined the risk-free interest rate by using a weighted average equivalent to the expected term based on the U.S. Treasury yield curve in effect as of the date of grant.

Expected volatility: As the Company has only been a public company since July 2014, there is not sufficient historical volatility for the expected term of the options. Therefore, the Company used an average historical share price volatility based on an analysis of reported data for a peer group of comparable companies.

Expected term (in years): Expected term represents the period that the Company s share option grants are expected to be outstanding. As the Company has only been a public company since July 2014, there is not sufficient historical term data to calculate the expected term of the options. Therefore, the Company elected to utilize the simplified method to estimate the expected term of option grants issued to employees. Under this approach, the weighted average expected life is presumed to be the average of the vesting term and the contractual term of the option.

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Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates. The Company estimates forfeitures based on historical termination behavior. For the years ended December 31, 2014, 2013 and 2012, a forfeiture rate of 10% was applied.

For options granted to nonemployees, the expected life of the option used is ten years, which is the contractual term of each such option. All other assumptions used to calculate the grant date fair value are generally consistent with the assumptions used for options granted to employees.

The table below summarizes activity related to stock options:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Life (in years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2011		$		
Granted	5,555	0.04		
Exercised	(5,555)	0.04		
Forfeited				
Outstanding as of December 31, 2012		$		
Granted	1,206,655	0.51		
Exercised	(3,174)	0.45		
Forfeited				
Outstanding as of December 31, 2013	1,203,481	$ 0.51	9.60	$ 1,038
Granted	942,513	14.34		
Exercised	(87,476)	0.46		
Forfeited	(61,903)	1.36		
Outstanding as of December 31, 2014	1,996,615	$ 7.01	8.98	$ 59,362
Vested or expected to vest as of December 31, 2014	1,782,257	$ 6.61	8.96	$ 53,670
Exercisable as of December 31, 2014	383,032	$ 0.82	8.66	$ 13,705

As of December 31, 2014, the Company had unrecognized stock-based compensation expense related to its unvested stock option awards of $9,705, which is expected to be recognized over the remaining weighted average vesting period of 3.24 years. The total fair value of shares vested for the years ended December 31, 2014, 2013 and 2012 was $988, $9, and $1, respectively. During the year ended December 31, 2014, stock option exercises resulted in proceeds of $40, and during the years ended December 31, 2013 and 2012 stock option exercises resulted in the proceeds of less than $1. The intrinsic value of stock options exercised during the year ended December 31, 2014 was $2,446 and the intrinsic value of stock options exercised during the years ended December 31, 2013 and 2012 was zero.

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Restricted Stock Awards

During the years ended December 31, 2014, 2013 and 2012, the Company granted restricted stock awards to certain officers, employees, directors, and consultants of the Company. During the years ended December 31, 2014 and 2013, the Company recorded $213 and $11, respectively, of stock-based compensation expense related to its restricted stock. There was no stock-based compensation expense for the year ended December 31, 2012. The table below summarizes activity relating to restricted stock:

	Shares	Weighted Average Grant Date Fair Value Per Share
Outstanding as of December 31, 2011	613,086	
Issued	561,104	$ 0.04
Vested	(709,158)	
Forfeited		
Repurchased	(102,777)	
Outstanding as of December 31, 2012	362,255	
Issued	130,158	$ 0.45
Vested	(176,695)	
Forfeited		
Repurchased		
Outstanding as of December 31, 2013	315,718	
Issued		
Vested	(138,108)	
Forfeited		
Repurchased	(6,778)	
Outstanding as of December 31, 2014	170,832	

As of December 31, 2014, the Company had unrecognized stock-based compensation expense related to its unvested restricted stock awards of $340, which is expected to be recognized over the remaining weighted average vesting period of 1.15 years.

During the year ended December 31, 2014, no shares of restricted stock were issued. During the years ended December 31, 2013, and 2012, current and former employees of the Company purchased a total of 130,158 and 561,104 shares of restricted stock, respectively, resulting in the proceeds of $50 and $19, respectively.

Unvested shares are subject to repurchase by the Company, at the issuance price, upon the employee s termination at the Company s sole discretion. In 2012, the Company repurchased 102,777 shares of restricted common stock issued to employees with a value of $3 in conjunction with the employees termination from the Company, and in the year ended December 31, 2014, the Company repurchased 6,778 shares of restricted common stock issued to employees at their

$0.04 original purchase price per share.

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8. Net Loss Per Share

Basic and diluted net income (loss) per share attributable to common stockholders was calculated as follows for the years ended December 31, 2014, 2013 and 2012:

	Year Ended December 31,		
	2014	2013	2012
Basic net income (loss) per share attributable to common stockholders:			
Numerator:			
Net loss	$ (36,105)	$ (18,288)	$ (9,636)
Denominator:			
Weighted average common shares outstanding basic	21,574,347	1,492,288	1,118,288
Dilutive effect of common share equivalents resulting from common share options and preferred common shares (as converted)			
Weighted average common shares outstanding diluted	21,574,347	1,492,288	1,118,288
Net loss per share attributable to common stockholders basic and diluted	$ (1.67)	$ (12.26)	$ (8.62)

The following common stock equivalents outstanding as of December 31, 2014 and 2013, were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods presented because including them would have been anti-dilutive:

	Year Ended December 31,	
	2014	2013
Options to purchase common stock	1,621,906	766,156
Restricted stock	170,067	284,129
Redeemable convertible preferred stock (presented on a weighted average basis)		8,022,175
	1,791,973	9,072,460

9. Income Taxes

There is no provision for income taxes because the Company has historically incurred operating losses and maintains a full valuation allowance against its net deferred tax assets. The reported amount of income tax expense for the years differs from the amount that would result from applying domestic federal statutory tax rates to pretax losses primarily because of changes in valuation allowance.

A reconciliation of U.S. statutory rate to the Company s effective tax rate is as follows:

	Year Ended December 31,		
	2014	2013	2012
Tax due at statutory rate	34.0%	34.0%	34.0%
State taxes, net of federal	4.5	5.2	5.2
Permanent items	(1.0)	(0.1)	(0.1)
Federal and state credits	8.5	1.5	0.8
Change in valuation allowance	(46.0)	(40.5)	(39.9)
Other		(0.1)	
	0.0%	0.0%	0.0%

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Significant components of the Company s net deferred tax asset at December 31, 2014 and 2013 are as follows:

	December 31,	
	2014	2013
Net operating losses	21,907	9,401
Capitalized start-up costs	2,514	2,694
Accounting method change	(2,020)	
Tax credit carryforwards	4,433	369
Accrued expenses	494	15
Depreciation and amortization	332	239
Stock options	623	
Others	20	21
Total net deferred tax asset before valuation allowance	28,303	12,739
Valuation allowance	(28,303)	(12,739)
Net deferred tax asset		

As of December 31, 2014, the Company had federal and state net operating loss carryforwards of $55,821 and $55,443, respectively, which begin to expire in 2031. As of December 31, 2014, the Company had federal and state research and development tax credits carryforwards of $663 and $326, respectively, which begin to expire in 2031 and 2027, respectively. As of December 31, 2014, the Company had federal orphan drug tax credit carry forwards of $3,555, which begin to expire in 2034.

As of December 31, 2014, net deferred tax assets increased approximately $15,564 primarily due to the operating loss and tax credits incurred during the year. This increase in net deferred tax assets was offset by a corresponding increase in the valuation allowance.

Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of net operating loss carryforwards and capitalized start-up costs. Under the applicable accounting standards, management has considered the Company s history of losses and concluded that it is more likely than not that the Company will not recognize the benefits of federal and state deferred tax assets. Accordingly, a full valuation allowance of $28,303 and $12,739 has been established at December 31, 2014 and 2013, respectively.

Pursuant to Section 382 of the Internal Revenue Code, certain substantial changes in the Company s ownership may result in a limitation on the amount of net operating loss carryforwards and tax carryforwards that may be used in future years. Utilization of the net operating loss (NOL) and tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company has not completed a study to assess whether an ownership change has occurred, or whether there have been multiple ownership changes since its formation, due to significant complexity and related costs associated with such a study. There could also be additional ownership changes in the future which may result in additional limitations on the utilization of NOL carryforwards and credits.

The Company applies the authoritative guidance on accounting for and disclosure of uncertainty in tax positions, which requires the Company to determine whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals of litigation processes, based on the technical merits of the position. For tax positions meeting the more likely than not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than fifty percent likelihood of being realized upon the ultimate settlement with the relevant taxing authority.

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The following is a rollforward of the Company s unrecognized tax benefits:

	Year Ended December 31,		
	2014	2013	2012
Unrecognized tax benefits as of the beginning of the year	$ 2,880	$ 1,477	$ 504
Gross increases current period tax positions		1,403	
Gross decreases tax positions of prior periods	(2,880)		973
Unrecognized tax benefits as of the end of the year	$	$ 2,880	$ 1,477

During 2014, the Company filed an application for change in accounting method with the IRS to capitalize start-up costs that were historically deducted and included as part of the NOL carryforward through December 31, 2013. As a result, the Company s unrecognized tax benefits, which historically related to start-up costs, are zero at December 31, 2014.

The Company will recognize interest and penalties related to uncertain tax positions in income tax expense when in a taxable income position. As of December 31, 2014 and 2013, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company s statement of operations.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations, and the Company s tax returns are open under statute from 2011 to the present. The Company s policy is to record interest and penalties related to income taxes as part of the tax provision.

10. Employee Benefit Plan

The Company maintains a 401(k) profit sharing plan (the Plan) for its employees. Each participant in the Plan may elect to contribute a portion of his or her annual compensation to the Plan subject to annual limits established by the Internal Revenue Service. Effective November 1, 2014, the Company instituted an employer match of 50% of eligible contributions up to 6% of employee contributions. For the year ended December 31, 2014, the Company contributed $15.

11. Related Party Transactions

Since inception, the Company has received consulting and management services from Third Rock Ventures LLC, which through its affiliates, has a controlling interest in the Company and owns 45.3% of common stock at December 31, 2014. The Company paid Third Rock Ventures LLC $282, $682 and $994 for these services for the years ended December 31, 2014, 2013 and 2012, respectively. At December 31, 2014, the Company owed Third Rock Ventures LLC $5, which is included in accrued expenses. At December 31, 2013 and 2012, the Company owed Third Rock Ventures LLC $125 and $209, respectively, which is included in accounts payable.

12. Subsequent Events

Effective January 2015, the Company signed an agreement to sublet approximately 2,700 feet of office space. The sublease term is through July 2017 and the Company will pay $9 per month.

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Exhibit List

Exhibit No.	Description
3.1	Fifth Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect (incorporated by reference to Exhibit 3.2 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
3.2	By-laws of the Registrant and the amendments thereto, as currently in effect (incorporated by reference to Exhibit 3.4 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
4.1	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
4.2	Second Amended and Restated Investors Rights Agreement by and among the Registrant and certain of its stockholders dated March 11, 2014 (incorporated by reference to Exhibit 4.2 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.1+	2014 Stock Option and Incentive Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.1 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.2*	Exclusive License Agreement by and between the Registrant and Washington University, dated November 11, 2013 (incorporated by reference to Exhibit 10.3 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.3*	Commercial License Agreement by and between the Registrant and CyDex Pharmaceuticals, Inc., dated August 21, 2013, as amended April 30, 2014 (incorporated by reference to Exhibit 10.4 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.4*	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 (incorporated by reference to Exhibit 10.5 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.5	Lease Agreement, by and between the Registrant and ARE-MA Region No. 38, LLC, dated December 11, 2011, as amended by First Amendment to Lease, by and between ARE-MA Region No. 38, LLC, dated October 26, 2012, and Second Amendment to Lease, by and between ARE-MA Region No. 38, LLC, dated May 9, 2013 (incorporated by reference to Exhibit 10.6 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.6+	Offer letter by and between the Registrant and Jeffrey M. Jonas, dated July 18, 2013 (incorporated by reference to Exhibit 10.7 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.7+	Offer letter by and between the Registrant and Albert J. Robichaud, dated September 25, 2011 (incorporated by reference to Exhibit 10.8 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.8+	

	Offer letter by and between the Registrant and Stephen J. Kanes, dated May 21, 2013 (incorporated by reference to Exhibit 10.9 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.9+	Offer letter by and between the Registrant and Kimi Iguchi, dated February 7, 2013 (incorporated by reference to Exhibit 10.10 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.10	Non-Solicitation, Confidentiality and Assignment Agreement by and between the Registrant and Jeffrey M. Jonas, dated August 19, 2013 (incorporated by reference to Exhibit 10.11 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)

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Exhibit No.	Description
10.11+	Non-Solicitation, Confidentiality and Assignment Agreement by and between the Registrant and Albert J. Robichaud, dated November 7, 2011 (incorporated by reference to Exhibit 10.12 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.12+	Non-Solicitation, Confidentiality and Assignment Agreement by and between the Registrant and Stephen J. Kanes, dated July 17, 2013 (incorporated by reference to Exhibit 10.13 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.13+	Non-Solicitation, Confidentiality and Assignment Agreement by and between the Registrant and Kimi Iguchi, dated March 8, 2013 (incorporated by reference to Exhibit 10.14 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.14+	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.15 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.15	Form of Indemnification Agreement to be entered into between the Registrant and its directors (incorporated by reference to Exhibit 10.16 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.16	Form of Indemnification Agreement to be entered into between the Registrant and its officers (incorporated by reference to Exhibit 10.17 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.17*	Supply Agreement by and between the Registrant and CyDex Pharmaceuticals, Inc., dated December 13, 2012, as amended August 21, 2013 and April 30, 2014 (incorporated by reference to Exhibit 10.18 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.18+	2014 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.19 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.19+	Offer Letter by and between the Registrant and Thomas D. Anderson, dated April 15, 2014 (incorporated by reference to Exhibit 10.20 of the Registrant s Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)
10.20+	Severance and Change In Control Agreement between the Registrant and Jeffrey M. Jonas, dated September 25, 2014
10.21+	Severance and Change In Control Agreement between the Registrant and Kimi Iguchi, dated September 30, 2014
10.22+	Severance and Change In Control Agreement between the Registrant and Stephen J. Kanes, dated September 30, 2014
10.23+	Severance and Change In Control Agreement between the Registrant and Albert J. Robichaud, dated September 25, 2014
10.24+	Severance and Change In Control Agreement between the Registrant and Thomas D. Anderson, dated September 26, 2014
21.1	Subsidiaries of the Registrant
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
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 adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification of Principle Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

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Exhibit No.	Description
32.1	Certification of Principal Executive Officer and Principle 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	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Link Document

(+) Management contract or compensatory plan or arrangement.
(*) Confidential treatment has been granted by the Securities and Exchange Commission as to certain portions.