Sage Therapeutics™

Investor Presentation

November 2019

Sage Therapeutics™

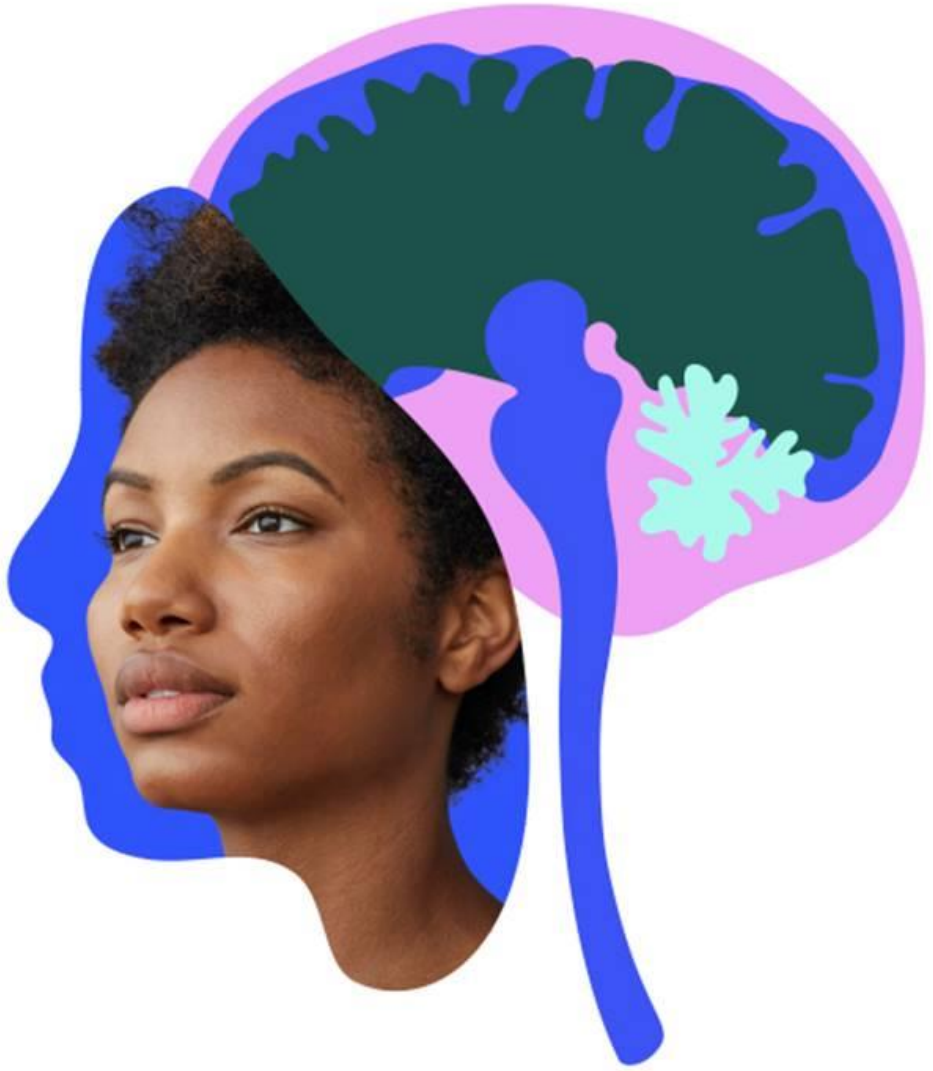
Safe Harbor Statement

- The slides presented today and the accompanying oral presentations contain forward-looking statements, which may be identified by the use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “opportunity”, “potential,” or “continue,” and other similar expressions.
- Forward-looking statements in this presentation include statements regarding: our commercial launch of ZULRESSO and its long-term potential; the potential timing for sites to become ready to administer ZULRESSO; expectations regarding an increase in the number of activated sites; the potential timing of revenue momentum; the potential for favorable reimbursement of ZULRESSO; the estimated number of patients with certain disorders; our development plans, goals and strategy and the potential timing and results of our development efforts; our belief in the potential of our product candidates in various indications; the potential profile and benefit of our product candidates; the potential of our collaboration with Shionogi; the goals, opportunity and potential for our business; and our expectations regarding our cash position at year-end.
- These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risk that:
  - We may encounter issues or other challenges in commercializing ZULRESSO and achieving our revenue expectations, including: issues related to market acceptance by healthcare providers, healthcare settings and women with PPD; issues related to the willingness of sites to administer ZULRESSO; issues related to reimbursement, issues related to the requirements of the REMS; and challenges associated with execution of our sales and patient support activities, which in each case could limit the potential of ZULRESSO and the timing and amount of future revenues.
  - Results achieved with use of ZULRESSO in the treatment of PPD in commercial use may be different than observed in clinical trials, and may vary among patients.
  - The number of women with PPD or the unmet need for additional treatment options may be significantly smaller than we expect.
  - Success in pre-clinical studies or in early stage clinical trials of our product candidates may not be repeated or observed in ongoing or future studies involving the same compound or other product candidates, and future non-clinical and clinical results for our product candidates may not support further development of the product candidate or regulatory approval on the timelines we expect or at all or may require additional clinical trials or nonclinical studies.
  - Even if our planned development programs are successful, we still may not achieve review or approval, despite prior regulatory advice, and regulatory authorities may ask for additional trials or data.
  - We may experience slower than expected enrollment in our clinical trials or may encounter other delays or problems, including in analyzing data or requiring the need for additional analysis, data or patients, and such issues with any trial could cause delay in completion of the trial, availability of results and timing of future activities.
  - Even if our products are successfully developed and approved, the number of patients with the diseases or disorders our products treat, and the actual market for such products may be smaller than our current estimates; or we may not achieve market acceptance or reimbursement at acceptable levels.
  - We may encounter unexpected safety or tolerability issues with respect to any of our product candidates or marketed products.
  - We may not be able to obtain and maintain adequate intellectual property protection or other forms of data and marketing exclusivity for its products, or to defend ours patent portfolio against challenges from third parties.
  - We may face competition from others developing products for similar uses as those for which our products are being developed.
  - Our operating expenses may be higher than forecasted, and we may also face unexpected expenditures or decide to expand our activities.
  - Funding to support operations may not be available, when needed, on reasonable terms or at all, or may result in significant dilution to existing shareholders.
  - We may not be able to establish and maintain key business relationships with third parties on we may encounter technical and other unexpected hurdles in the manufacture and development of our products.
- For additional disclosure regarding these and other risks Sage faces, see the disclosure contained in the "Risk Factors" section of our most recent quarterly report, and in our other public filings with the Securities and Exchange Commission, available on the SEC's website at http://www.sec.gov. Any forward-looking statement represent our views only as of today, and should not be relied upon as representing our views as of any subsequent date. We undertake no obligation to update or revise the information contained in this presentation, whether as a result of new information, future events or circumstances or otherwise.

Sage Therapeutics™

Sage Therapeutics: Who We Are

- Founded in 2011, Sage Therapeutics is committed to developing innovative therapies with the potential to transform the lives of people with debilitating disorders of the brain.
- Our depression, neurology and neuropsychiatry franchise programs are pursuing new pathways to brain health with a goal of changing how brain disorders are thought about and treated.
- Our mission is to make medicines that matter so people can get better, sooner.



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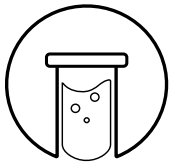
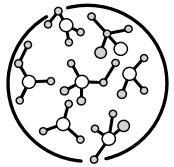
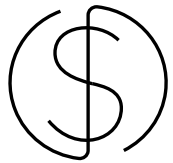
Successfully Establishing a Leading Brain Health Company in 8 Years

	APPROVED PRODUCTS	CLINICAL CANDIDATES	CLINICAL INDICATIONS	LIBRARY COMPOUNDS	FINANCING
2011	0	0	0	0	$35M Series A
2014	0	1	1	>1K	$104M IPO
2019	1	5	8*	>6K	~$7.6B** Market Cap $2.3B Gross proceeds to date

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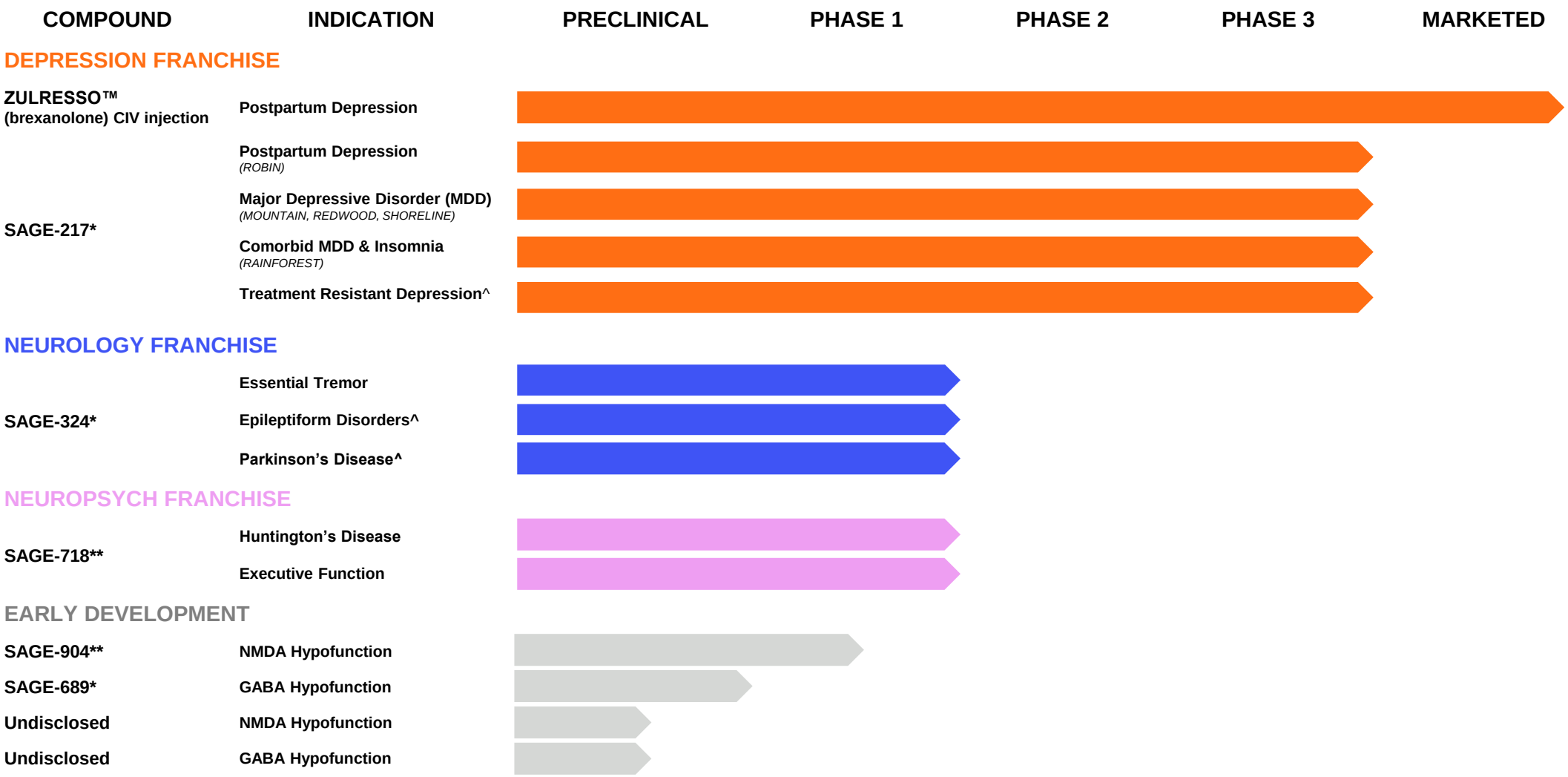
*Planned or ongoing clinical studies

**As of market close on Friday, November 8, 2019

Advancing a Leading Brain Health Portfolio



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KEY: * GABA; ** NMDA; ^ Planned Initiation

Depression Franchise

Psychiatry as Medicine
Medicalizing Depression

Our goal is to develop medicines that:

- Treat-as-needed
- Act rapidly
- Reduce stigma
- Enable durable treatment-free intervals

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Opportunity to Take on Stigma of PPD

Sage is taking on the challenge of breaking the stigma around PPD through product and portfolio candidates

- PPD is one of the most common medical complications during and after pregnancy[1-7]
- PPD can lead to devastating consequences for a woman[8-12] and for her family[13-15]
- Suicide is a leading cause of pregnancy related mortality[16-18]

Estimated

400k **Women experience PPD** each year in the US[1,16]

~50% of patients are currently diagnosed and treated[17]

20–30% **are severe**[18-20, a]

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References available in appendix

ZULRESSO™ (brexanolone) CIV Injection

Continuing to Execute on Key Priorities

Enable Pathways to Care

- Support healthcare facilities in advancing through the four key actions required to be treatment-ready:
  - Establish protocols for administering ZULRESSO
  - Certify under the ZULRESSO REMS
  - Achieve formulary approval
  - Secure satisfactory reimbursement from payers

Support Access and Reimbursement

- Drive strong payer coverage enabling access for women with PPD and satisfactory reimbursement from payers.

Focus on Patient Experience

- Support women with PPD and their families through Sage Central, Sage's national patient support center, by providing customized case management services and access to a range of patient resources

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ZULRESSO is only available at certified healthcare settings through a restricted program called the ZULRESSO REMS due to the risk of serious harm resulting from excessive sedation or sudden loss of consciousness.

ZULRESSO™ (brexanolone) CIV Injection

Indicators of long-term potential are encouraging

Enable Pathways to Care

- **140+** ZULRESSO REMS-certified sites of care across **66 of the top 140** Metropolitan Statistical Areas in the U.S., covering **54**% of potential patients
- Anticipate 6 – 9 months, or more, for sites to be treatment-ready
- **11** sites of care accelerated through the four actions required to treat

Support Access and Reimbursement

- **75%** of aggregated lives have **favorable coverage with no to light restrictions** across commercial and Medicaid plans

Focus on Patient Experience

- **200+** patient start forms and referrals from **150+** HCPs
- More than **90%** of treatment-ready patients are utilizing Sage Central's resources, exceeding best-in-class benchmarks

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ZULRESSO is only available at certified healthcare settings through a restricted program called the ZULRESSO REMS due to the risk of serious harm resulting from excessive sedation or sudden loss of consciousness.

*All metrics as of September 30, 2019

SAGE-217's Potential to Reshape Depression Landscape

Broad Program Underway Across Numerous Studies, Indications

STUDY	MDD-201	PPD-201	BPD-201	MDD-301	MDD-302	MDD-303	MDD-304	TRD
Indication	MDD	PPD	Bipolar Depression	MDD	MDD	MDD	Co-morbid MDD and Insomnia	Treatment Resistant Depression
Phase	Pivotal Ph. 2	Pivotal Ph. 2	Ph. 2	Pivotal Ph. 3	Pivotal Ph. 3	Pivotal Ph. 3 (Open-Label)	Pivotal Ph. 3	Pivotal Ph. 3
Status	Complete	Complete	Complete	Enrollment Complete	Enrolling	Enrollment Complete	Enrolling	Planned

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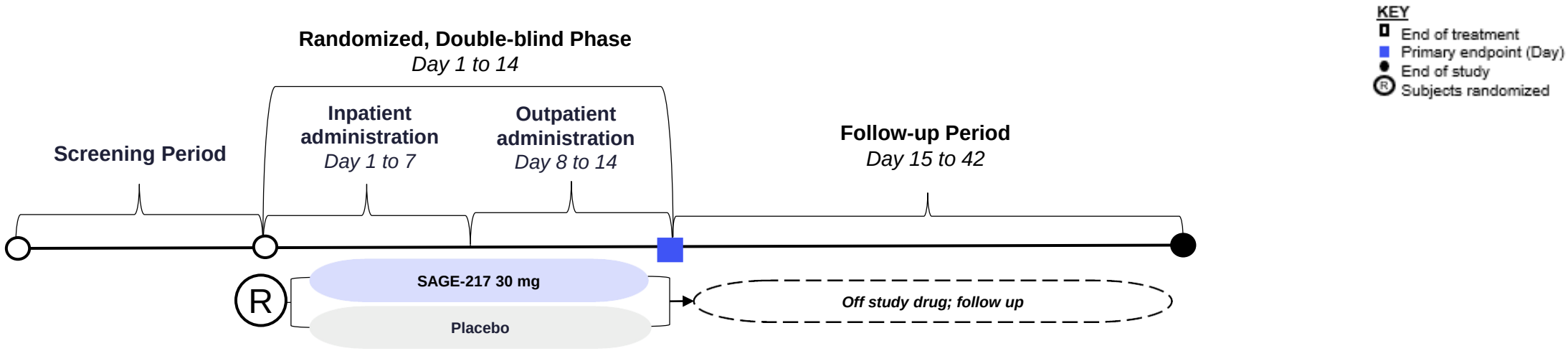
SAGE-217 MDD-201 (Part 2b)

Pivotal Phase 2 Placebo-controlled Efficacy and Safety Study



STUDY OVERVIEW

Arms

Randomization: 1:1
- SAGE-217 30 mg
- Placebo

Dosing Regimen

2-week, once-nightly

Inclusion Criteria

- Diagnosis of MDD with symptoms that have been present for at least a 4-week period

Exclusion Criteria

- History of suicide attempt
- Active psychosis
- Medical history of seizures, bipolar disorder, schizophrenia, and/or schizoaffective disorder
- History of treatment-resistant depression, defined as persistent depressive symptoms despite treatment with adequate doses of antidepressants from two different classes for an adequate amount of time

Primary Endpoint

- Change from baseline in HAM-D*

Secondary Endpoints

- Safety and tolerability of SAGE-217 as assessed by:
  - Frequency and severity of AE/SAE**
  - Physical examination**
  - Clinical laboratory measures, vital signs, electrocardiograms, suicidal ideation using C-SSRS*
  - Stanford Sleepiness Scale (SSS) score*
- Reduction in depressive symptoms, compared to placebo, as assessed by:
  - Change in the 17-item HAM-D total score from baseline at all time points**
  - HAM-D response, HAM-D remission**
  - Change from baseline in MADRS total score, HAM-A total score, at Day 15 and all other time points**
  - HAM-D subscale and individual item scores at all time points**
  - CGI-I response**

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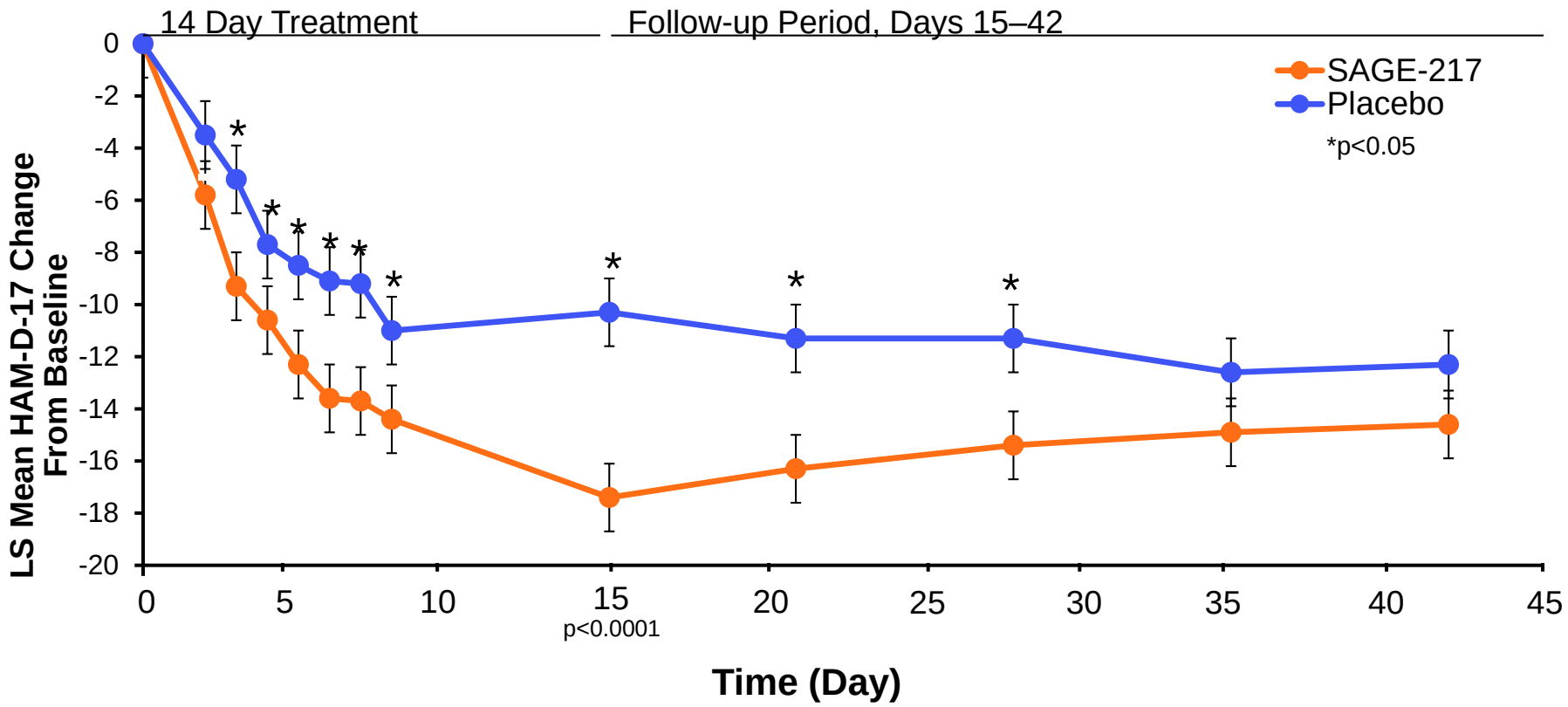
*During double-blind phase; **During double-blind and follow-up periods

NCT03000530. Available from: clinicaltrials.gov [accessed November 2019]

SAGE-217 MDD-201 Positive Pivotal Results

Demonstrated Rapid and Durable Treatment Response



SAGE-217 was generally well-tolerated in the study

The most common AEs included headache, dizziness, nausea, and somnolence

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SAGE-217 MDD-201

Statistically Significant Primary & Secondary Endpoints

	PRIMARY ENDPOINT	SECONDARY ENDPOINTS					
	HAM-D-17 Change from Baseline	**HAM-D-17 Change from Baseline**	**HAM-D-17 Response**	**HAM-D-17 Remission**	**MADRS Change from Baseline**	**HAM-A Change from Baseline**	**CGI-I Response**
SAGE-217	Day 15: -17.4	Day 42: -14.6	Day 15: 79%	Day 15: 64%	Day 15: -22.5	Day 15: -13.2	Day 15: 79%
			Day 42: 62%	Day 42: 45%	Day 42: -19.1	Day 42: -11.8	Day 42: 69%
PLACEBO	Day 15: -10.3	Day 42: -12.3	Day 15: 40%	Day 15: 26%	Day 15: -15.0	Day 15: -8.6	Day 15: 45%
			Day 42: 56%	Day 42: 33%	Day 42: -17.2	Day 42: -9.6	Day 42: 59%
DIFFERENCE	**Day 15: -7.0 (p<0.0001)**	**Day 42: p>0.05***	**Day 15: p=0.0002****	**Day 15: p=0.0005****	**Day 15: p=0.0021****	**Day 15: p=0.0008****	**Day 15: p=0.0007****

SAGE-217 was generally well-tolerated in the study

The most common AEs included headache, dizziness, nausea, and somnolence

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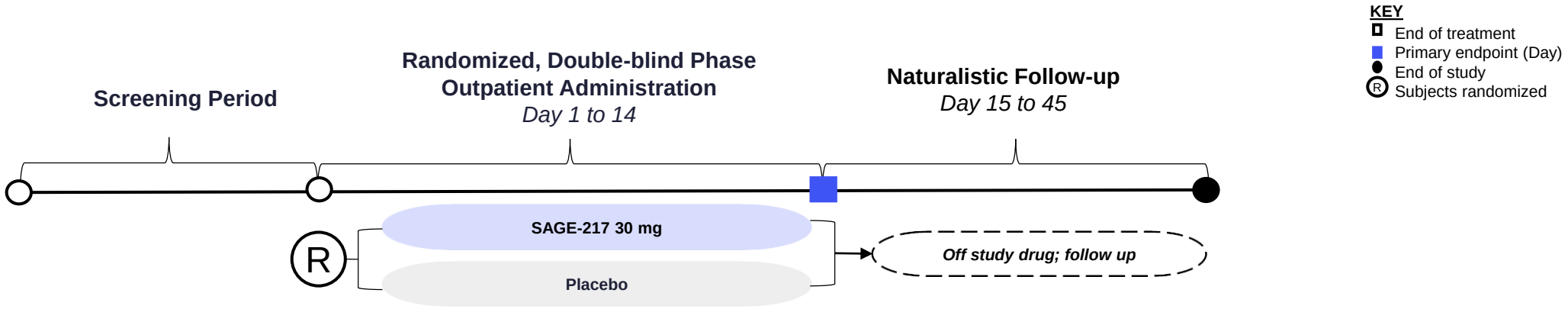
Gunduz-Bruce, H., et. al. (2019). Trial of SAGE-217 in Patients with Major Depressive Disorder. *New England Journal of Medicine*, *381*(10), 903–911. doi: 10.1056/nejmoa1815981

*Lasser, R. GABAergic Mode of Action and GABAa receptor positive allosteric modulators in Major Depressive Disorder. Presented at: 27th European Congress of Psychiatry; 2019; Madrid, Spain.

**Kanes, S. Neuroactive steroids as rapid-acting antidepressants: the story of brexanolone and SAGE-217. Presented at: The International College of Neuropsychopharmacology; 2019; Athens, Greece.

ROBIN Study (SAGE-217 PPD-201)

Pivotal Phase 2 Efficacy and Safety Study



STUDY OVERVIEW

Arms	Randomization: 1:1 • SAGE-217 30 mg • Placebo	**Key Inclusion Criteria**	• Major Depressive Episode that began no earlier than the third trimester and no later than the first 4 weeks following delivery, as diagnosed by the SCID-I • Subject is ≤ six months postpartum • Ceased lactating at screening or, if still lactating or actively breastfeeding at screening, must agree to temporarily cease giving breast milk to her infant(s)	**Primary Endpoint**	• Change from baseline in HAM-D total score*

Dosing Regimen	2-week, once-nightly	**Key Exclusion Criteria**	• Active psychosis
			• Attempted suicide associated with current episode of PPD (Note, suicidal ideation is not an exclusion; other protocol-defined inclusion/exclusion criteria may apply)
			• Medical history of seizures, bipolar disorder, schizophrenia, and/or schizoaffective disorder
				Secondary Endpoints	• Safety and tolerability compared with placebo as assessed by:
					  • Incidence of AEs, vital signs, clinical laboratory evaluations, ECG parameters**
					  • C-SSRS**

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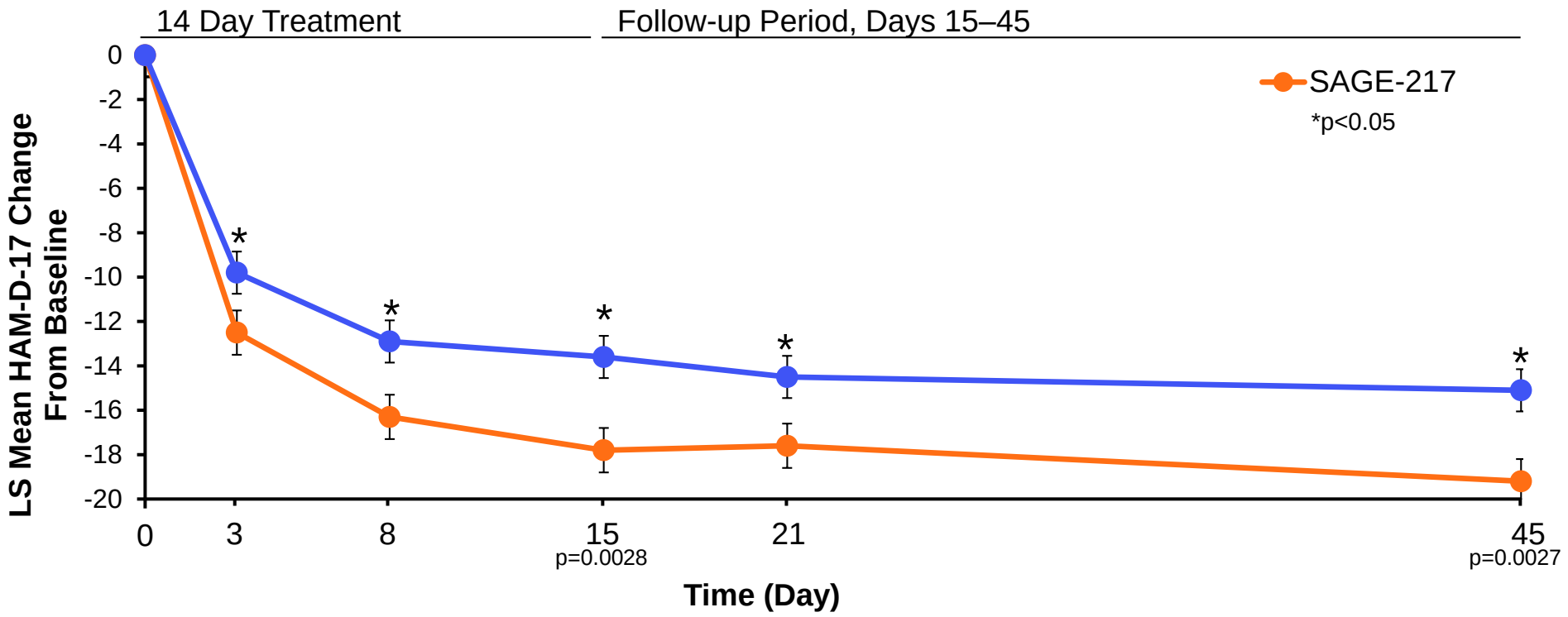
*During double-blind phase; **During double-blind and follow-up periods
NCT02978326. Available from: clinicaltrials.gov [accessed November 2019]

SAGE-217 ROBIN Study Positive Phase 3 Results

Statistically Significant HAM-D Improvement Observed on Day 3; Maintained through Day 45



SAGE-217 was generally well-tolerated in the study

The most common AEs included somnolence, headache, dizziness, upper respiratory tract infection, diarrhea, and sedation

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ROBIN Study (SAGE-217 PPD-201)

Secondary Endpoints were Statistically Significant and Consistent with the Primary Endpoint

	PRIMARY ENDPOINT	SECONDARY ENDPOINTS				
	HAM-D Change from baseline	**HAM-D Change from baseline**	**HAM-D Remission (total score ≤7)**	**HAM-D Response (≥50% reduction in total score)**	**MADRS Change from baseline**	**HAM-A Change from baseline**
SAGE-217	Day 15: -17.8	Day 45: -19.2	Day 15: 45% Day 45: 53%	Day 15: 72% Day 45: 75%	Day 15: -22.1 Day 45: -24.8	Day 15: -16.6 Day 45: -18.6
PLACEBO	Day 15: -13.6	Day 45: -15.1	Day 15: 23% Day 45: 30%	Day 15: 48% Day 45: 57%	Day 15: -17.6 Day 45: -19.0	Day 15: -12.7 Day 45: -13.6
DIFFERENCE	**Day 15: -4.2 (p=0.003)**	**Day 45: p=0.003**	**Day 15: p=0.011** **Day 45: p=0.009**	**Day 15: p=0.005** **Day 45: p=0.022**	**Day 15: p=0.018** **Day 45: p=0.002**	**Day 15: p=0.006** **Day 45: p<0.001**

SAGE-217 was generally well-tolerated in the study

The most common AEs included somnolence, headache, dizziness, upper respiratory tract infection, diarrhea, and sedation

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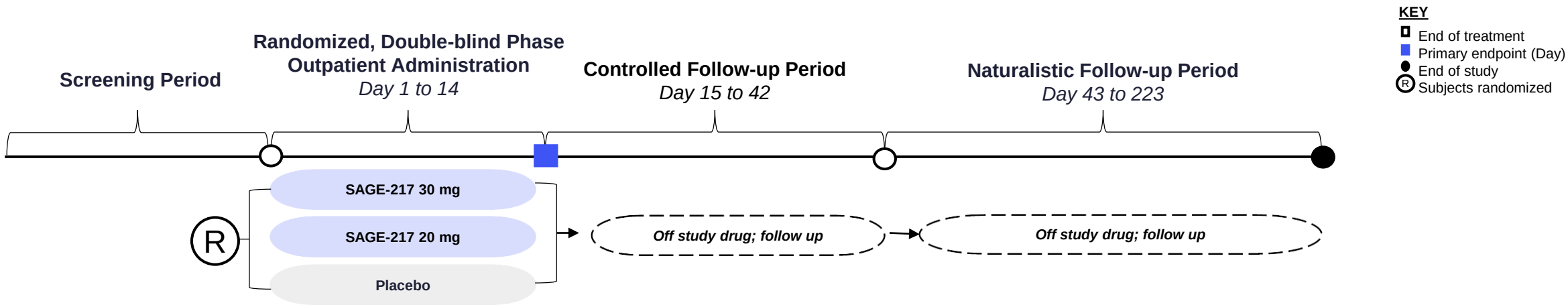
Gunduz-Bruce, H. A Phase 3, Double-Blind, Placebo-Controlled Trial of SAGE-217 in Postpartum Depression. Presented at: Massachusetts General Hospital CTNI VII Annual Symposium; June, 2019; Rome, Italy

MOUNTAIN Study (SAGE-217 MDD-301)

Pivotal Phase 3 Efficacy and Safety Study



STUDY OVERVIEW

Status	Enrollment Complete (3Q 2019)	**Inclusion Criteria**	• Diagnosis of MDD with symptoms that have been present for at least a 4-week period • MADRS total score ≥32 and HAM-D total score ≥22 at screening and Day 1 (prior to dosing)
Data Timing	4Q 2019	**Exclusion Criteria**	• Active psychosis • Attempted suicide associated with the current episode of MDD • Medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder
Arms	Randomization: 1:1:1 • SAGE-217 20 mg • SAGE-217 30 mg • Placebo	**Primary Endpoint**	• Change from baseline in HAM-D*
Dosing Regimen	2-week, once-nightly	**Secondary Endpoints**	• Change from baseline in HAM-D, HAM-A, MADRS, CGI-I, CGI-S** • Incidence and severity of AE/SAE**

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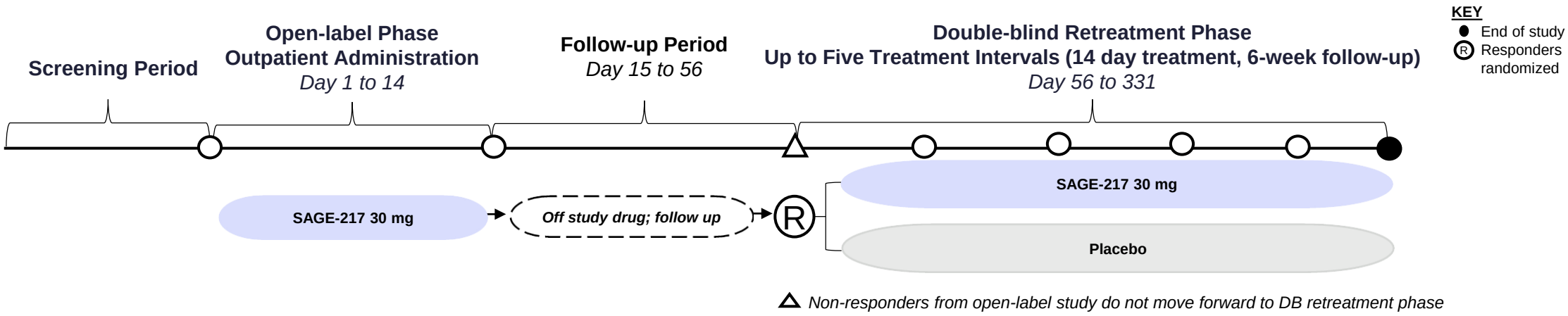
*During double-blind phase; **During double-blind and follow-up periods

NCT03672175. Available from: clinicaltrials.gov [accessed November 2019]

REDWOOD Study (SAGE-217 MDD-302)

Pivotal Phase 3 Efficacy and Long-Term Safety of Fixed Repeated Dosing



STUDY OVERVIEW

Status	Initiated (3Q 2019)	**Inclusion Criteria**	• MDD, as diagnosed by SCID-5-CT, with symptoms that have been present for at least a 4-week period • At least 1 prior MDE in the 5 years prior to screening • Willingness to delay antidepressant, anxiolytic, insomnia, psychostimulant, prescription opioid regimens, and new psychotherapy (including Cognitive Behavioral Therapy for Insomnia [CBT-I]) until after study completion
Arms	Randomization: 1:1^ • SAGE-217 30 mg • Placebo ^Double-blind phase only	**Exclusion Criteria**	• Attempted suicide associated with the current episode of MDD • Subject has treatment-resistant depression, defined as persistent depressive symptoms despite treatment with adequate doses of antidepressants within the current episode of MDD (excluding antipsychotics) from two different classes for at least 4 weeks of treatment • Positive pregnancy test as screening or on Day 1 prior to dosing
Dosing Regimen	2-week, once-nightly	**Primary Endpoint**	• Prevention of relapse: time to relapse during DB phase (days; from first dose of study drug in DB Phase to relapse during the DB Phase)
		Secondary Endpoints	• % of subjects who relapse during DB phase • HAM-D response (≥50% reduction) and remission (HAM-D total score ≤7) in DB phase at Day 15 • Change from baseline in HAM-D, CGI-response, CGI-S, PHQ-9 at Day 15 in DB phase • Time to relapse during DB phase for subjects who achieved HAM-D remission in OL phase • Incidence and severity of AE/SAE

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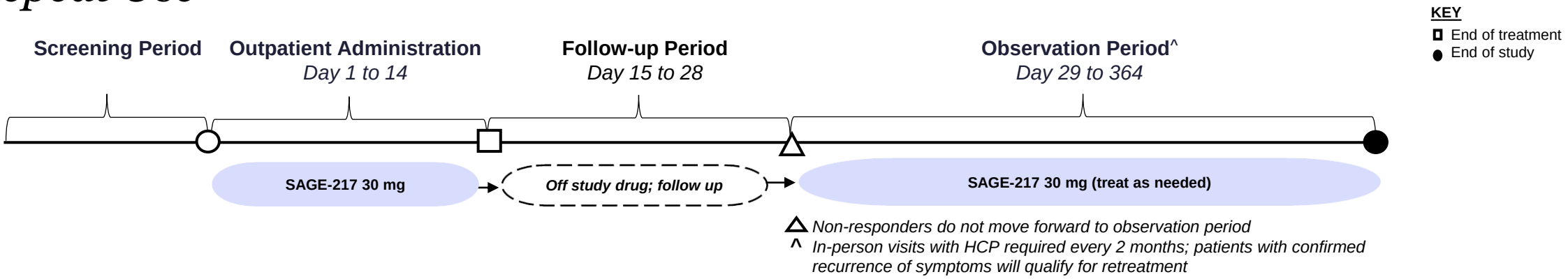
NCT04007367. Available from: clinicaltrials.gov [accessed November 2019]

SHORELINE (SAGE-217 MDD-303)

Pivotal Phase 3 Open-Label, Non-Randomized, Long-Term Safety Study, Repeat Use



STUDY OVERVIEW

Status	Enrollment Complete (3Q 2019)	**Inclusion Criteria**	• MDD, as diagnosed by SCID-5-CT, with symptoms that have been present for at least a 4-week period • Subject is in good physical health and has no clinically significant findings, as determined by the Investigator, on physical examination, 12-lead ECG, or clinical laboratory tests
Data Timing	2020	**Exclusion Criteria**	• Attempted suicide associated with the current episode of MDD • Medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder • Subject has had vagus nerve stimulation, electroconvulsive therapy, or has taken ketamine (including esketamine) within the current major depressive episode
Arms	Non-randomized; SAGE-217 30 mg	**Primary Endpoint**	• Safety and tolerability of the initial treatment and re-treatment as assessed by: incidence and severity of AEs; suicidal ideation and behavior using C-SSRS*

Dosing Regimen	2-week, once-nightly	**Secondary Endpoints**	• Need for re-treatment, as assessed by time to first re-treatment, number of subjects achieving the requirements for re-treatment, number of re-treatment cycles for each subject*
			• Response of initial treatment and/or retreatment, as assessed by:
			  • Change from baseline in HAM-D, CGI-S*
			  • Percent of subjects achieving: HAM-D response (≥50% reduction) and HAM-D remission (HAM-D total score ≤7) at the end of each 14-day treatment period*
			  • Percent of subjects achieving CGI-I*

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*During double-blind and follow-up periods

NCT03864614. Available from: clinicaltrials.gov [accessed November 2019]

Neurology Franchise

Next-generation $GABA_A$ PAM Positioned for Neurological Conditions

- SAGE-324, a next-generation Positive Allosteric Modulator (PAM) of $GABA_A$ receptors, is in development as a potential therapy for neurological conditions, such as essential tremor (ET), epilepsy and Parkinson's disease
- Pharmacodynamic markers (β-EEG) support dose ranging in Phase 2 to explore efficacy and tolerability of SAGE-324 in ET
- SAGE-324's long half-life provides consistent plasma concentrations with minimal daily fluctuations after multiple doses

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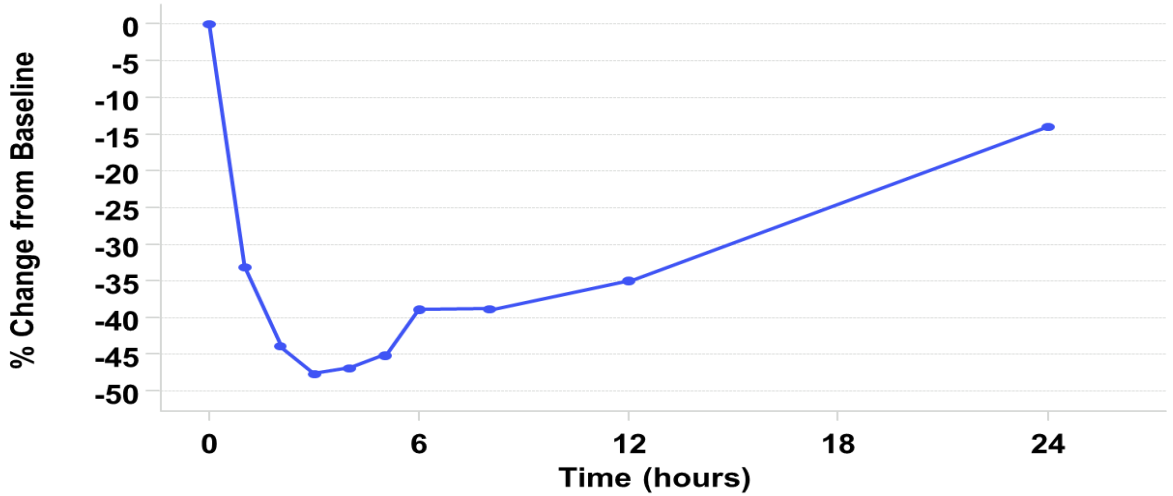
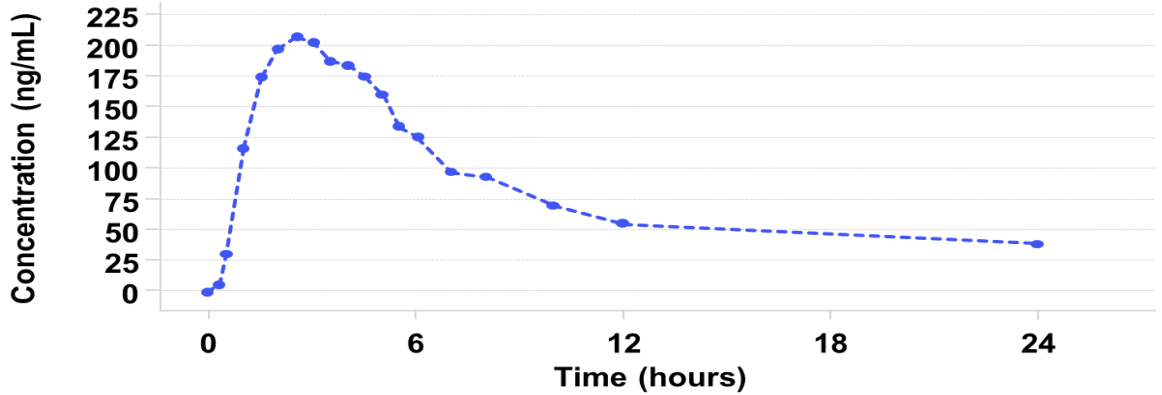
SAGE-324 Tremor Reduction in ET Patients Observed After a Single Dose

Total upper limb combined score change after SAGE-324 dosing in 6 people with ET as measured by accelerometer



PK over time in 6 people with ET dosed with SAGE-324



- Clear PK/PD relationship
- Promising signals of tremor reduction, consistent with those observed previously for brexanolone and SAGE-217
- SAGE-324 was well-tolerated in Phase 1 studies; most common adverse events were somnolence, dizziness, and feeling of relaxation

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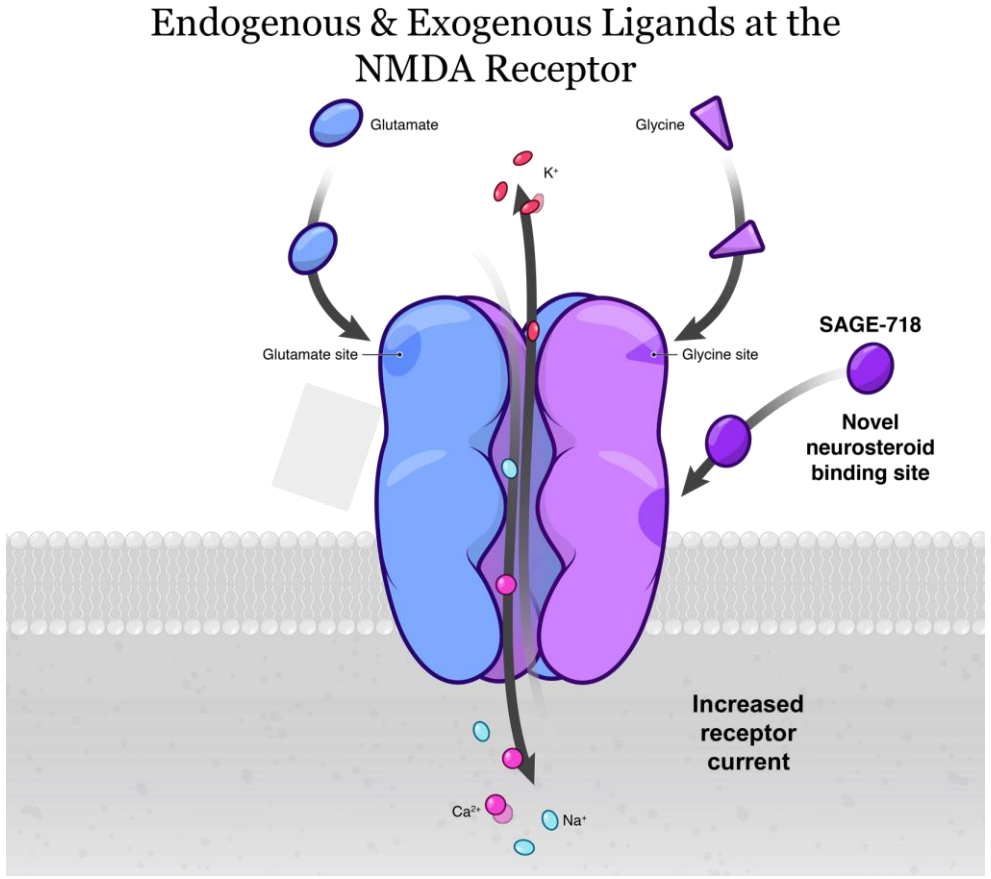
Neuropsychiatry Franchise

Sage's First-in-Class NMDA PAM

- Sage has built a library of novel oxysterol-based NMDA modulators, with unique profiles, that are in various stages of development, the first of these being SAGE-718
- NMDA receptors are ionotropic glutamate receptors that play a key role in a host of cognitive and behavioral processes
- Sage identified an endogenous modulator of the NMDAR (24S-hydroxycholesterol) and initiated a research effort to discover novel NMDAR modulators



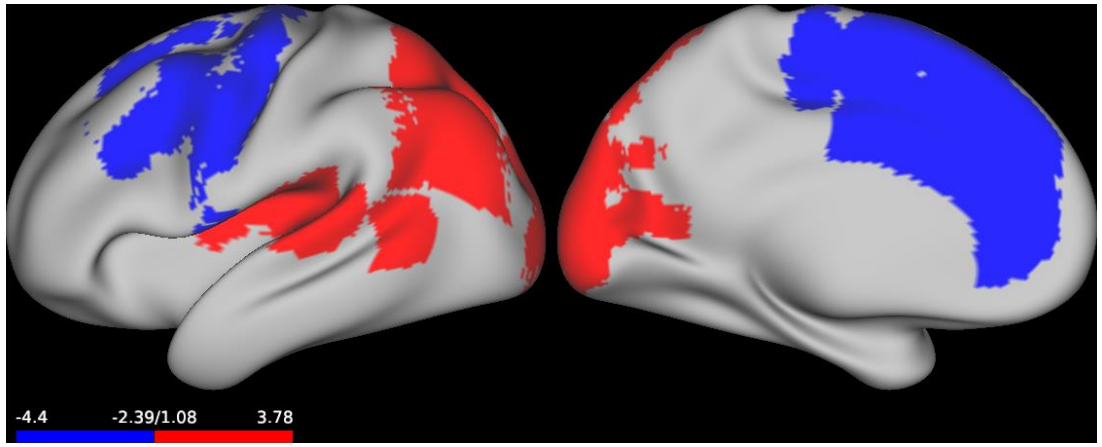
SAGE-718 Data Suggest Potentially Transformational Activity in the Brain

A suite of three experimental medicine studies was designed to investigate CNS-target engagement; results from an integrated data analysis demonstrate SAGE-718:

- Had effects on electrophysiological, functional imaging and cognitive endpoints in healthy volunteers consistent with CNS activity in these studies
- Healthy volunteers dosed with SAGE-718 exhibited superior performance on tests of working memory and complex problem solving
- Modulated the effects of ketamine on regional and global measures of resting brain activity indicating functional interaction with NMDA receptors
  - SAGE-718 was generally well-tolerated. The most commonly reported adverse event was mild orthostatic hypotension, which occurred in 2 subjects

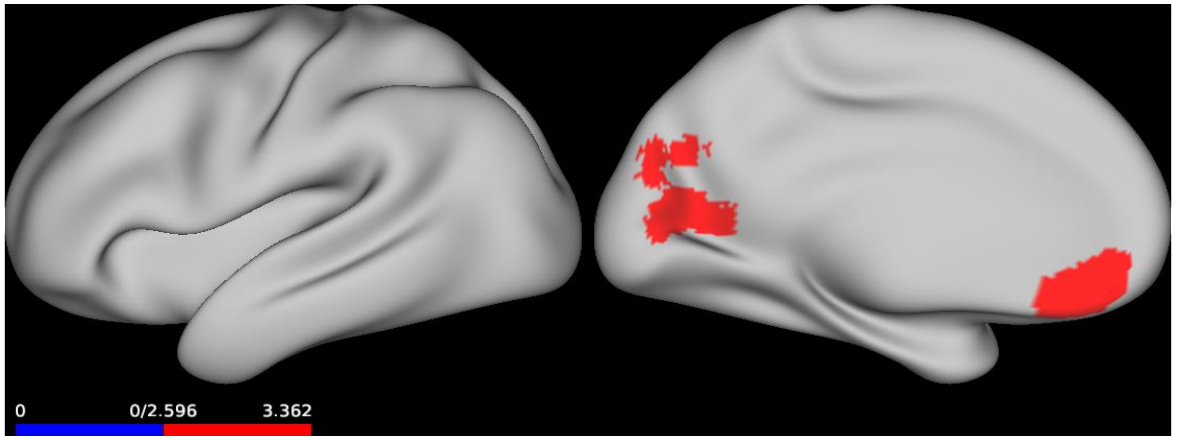
Attenuated effects of ketamine on brain circuits, in Phase 1 study

KETAMINE



*Ketamine caused regionally localized increases (**RED**) and decreases (**BLUE**) in cerebral blood flow (BOLD-MRI)*

SAGE-718 + KETAMINE



SAGE-718 blunted ketamine's induced increases and decreases in BOLD-MRI

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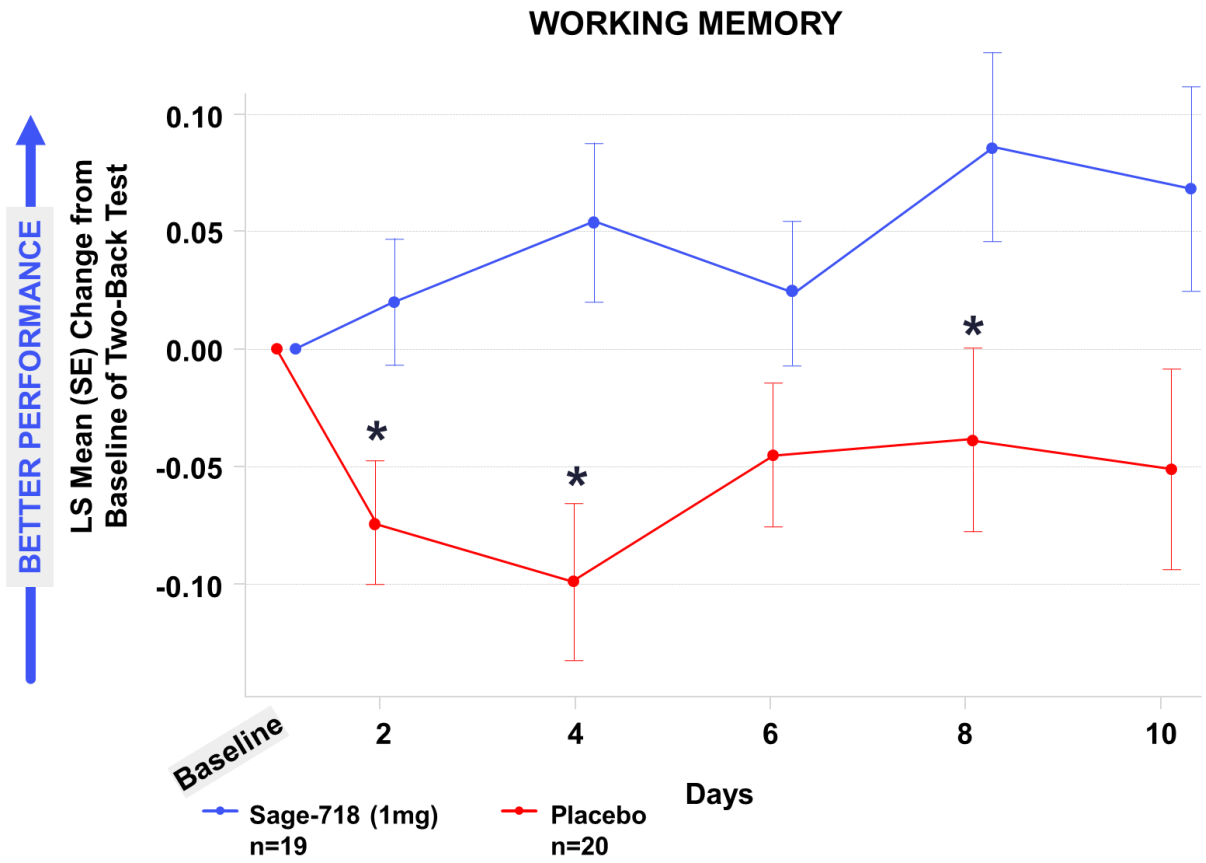
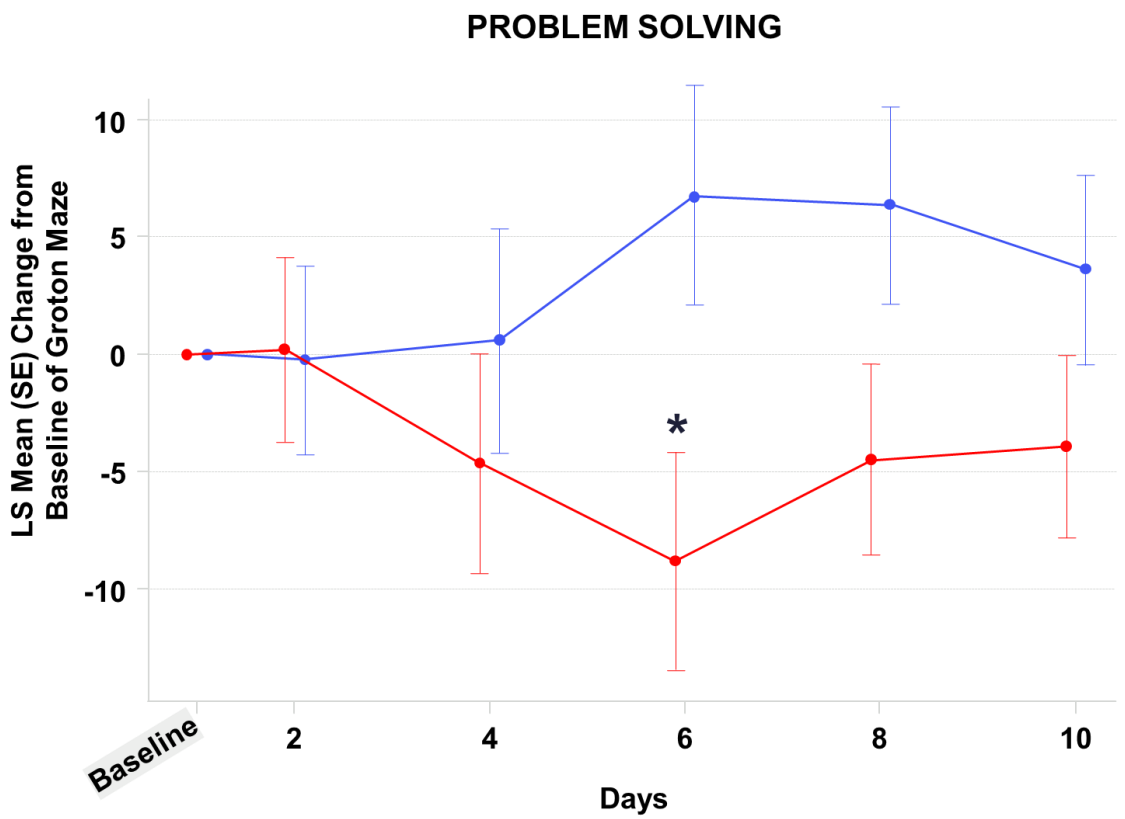
SAGE-718 Significantly Improved Executive Functioning in Phase 1 Study





*p<0.05. A MMRM model was applied with change from baseline in each cognitive assessment test score as the response variable and treatment, visit, visit-by-treatment interaction as fixed effect, baseline as covariate, and measurements within the same subject as repeated measure. Unstructured covariance structure was applied for the repeated measure.

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SAGE-718 Has the Potential to Provide Unique Cognitive Benefits Across Therapeutic Indications

- Findings suggest a potential application for cognition beyond illnesses with NMDA hypofunction

3Q 2019 Financial Results

Strong Financial Position with ~$1.1B in Cash

	3Q ‘19	4Q ’18
Cash and Marketable Securities	$1.1B	$925.1M
	3Q ’19	**3Q ’18**
Product Revenue	$1.5M	–
Collaboration Revenue	$2.1M	–
Costs of Goods Sold	$0.1M	-
Research & Development	$102.1M	$75.1M
Selling, General & Administrative	$88.5M	$53.7M
Total Operating Costs & Expenses	$190.7M	$128.7M
Net Loss	($180.0M)	($122.9M)

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3Q 2019 Financial Guidance

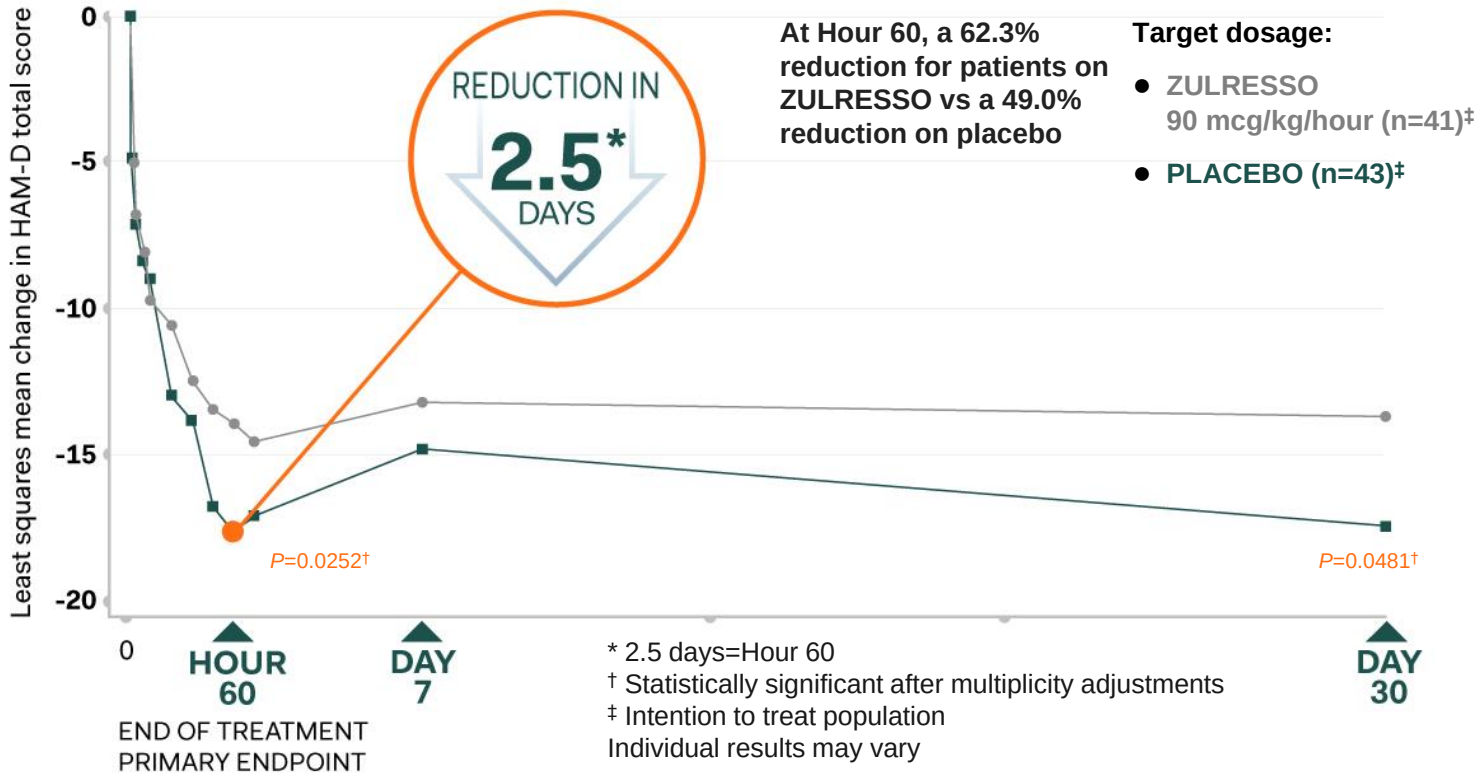
- Based on its current operating plan, Sage anticipates that its balance of cash, cash equivalents, restricted cash, and marketable securities will be at least $950 million at the end of 2019.
- Sage expects ZULRESSO revenue growth will be modest over the next few quarters and anticipates a meaningful increase in ZULRESSO revenue in the second half of 2020.

Appendix

ZULRESSO™ (brexanolone) CIV Injection

Treated Patients Experienced Rapid Improvement of Depressive Symptoms

Change from baseline in HAM-D total score over time in Study 1 with the recommended target dosage of ZULRESSO (90 mcg/kg/h)[1,2]



* 2.5 days=Hour 60
† Statistically significant after multiplicity adjustments
‡ Intention to treat population
Individual results may vary

Durable therapeutic effect

A prespecified secondary efficacy endpoint was the mean change from baseline in HAM-D total score at Day 30[1]

In Study 1, significantly greater symptom reduction vs placebo was observed at Day 30[1,2]

In Study 2, the 90 mcg/kg/hour arm maintained therapeutic effect at Day 30, but did not show a greater reduction vs placebo[2]

In a group of 38 patients in Study 1, a ZULRESSO titration to 60 mcg/kg/hour was also superior to placebo in improvement of depressive symptoms at Hour 60[2]

Please see full Prescribing Information, including Boxed Warning available with this presentation.

1. ZULRESSO Prescribing Information. Cambridge, MA: Sage Therapeutics, Inc. 2. Meltzer-Brody S et al. *Lancet*. 2018;392(10152):1058-1070.

ZULRESSO™ (brexanolone) CIV Injection
Excessive Sedation and Sudden Loss of Consciousness

Excessive Sedation and Somnolence

In clinical studies, ZULRESSO caused sedation and somnolence that required dose interruption or reduction in some patients during the infusion (5% of ZULRESSO-treated patients compared to 0% of placebo-treated patients). Some patients were also reported to have loss of consciousness (LOC) or altered state of consciousness during the ZULRESSO infusion (4% of the ZULRESSO-treated patients compared with 0% of the placebo-treated patients). Time to full recovery from loss or altered state of consciousness, after dose interruption, ranged from 15 to 60 minutes. All patients with loss of or altered state of consciousness recovered with dose interruption.

There was no clear association between loss or alteration of consciousness and pattern or timing of dose. Not all patients who experienced a loss or alteration of consciousness reported sedation or somnolence before the episode.

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Please see full Prescribing Information, including Boxed Warning available with this presentation.

ZULRESSO™ (brexanolone) CIV Injection

Adverse Reactions

The most common adverse reactions (incidence of **≥5%** and at least twice the rate of placebo):

- SEDATION/SOMNOLENCE
- DRY MOUTH
- LOSS OF CONSCIOUSNESS
- FLUSHING/HOT FLUSH

Adverse Reactions in Placebo-Controlled Studies in Patients with PPD Reported in ≥2% of ZULRESSO-Treated Patients and Greater Than Placebo-Treated Patients[1]

	ZULRESSO Maximum dosage 90 mcg/kg/hour (n=102)	ZULRESSO Maximum dosage 60 mcg/kg/hour (n=38)	PLACEBO (n=107)
Cardiac Disorders			
Tachycardia	3%	-	-
Gastrointestinal Disorders			
Diarrhea	2%	3%	1%
Dry mouth	3%	11%	1%
Dyspepsia	2%	-	-
Oropharyngeal pain	2%	3%	-
Nervous System Disorders			
Dizziness, presyncope, vertigo	12%	13%	7%
Loss of consciousness	3%	5%	-
Sedation, somnolence	13%	21%	6%
Vascular Disorders			
Flushing, hot flush	2%	5%	-

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Please see full Prescribing Information, including Boxed Warning available with this presentation.

1. ZULRESSO Prescribing Information. Cambridge, MA: Sage Therapeutics, Inc

Important safety information for ZULRESSO™ (brexanolone) CIV injection

What is ZULRESSO™?
ZULRESSO is a prescription medicine used in adults to treat a certain type of depression called Postpartum Depression.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ZULRESSO?

ZULRESSO can cause serious side effects, including:

- **Excessive sedation and sudden loss of consciousness.** ZULRESSO may cause you to feel very sleepy (excessive sedation) or pass out (loss of consciousness). Your healthcare provider should check you for symptoms of excessive sleepiness every 2 hours while you are awake.
  - During your ZULRESSO infusion, tell your healthcare provider right away if you feel like you cannot stay awake during the time you are normally awake or if you feel like you are going to pass out. Your healthcare provider may lower your dose or stop the infusion until symptoms go away.
  - You must have a caregiver or family member with you to help care for your child(ren) during your ZULRESSO infusion.
- Because of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness, ZULRESSO is only available through a restricted program called the ZULRESSO REMS.

Before receiving ZULRESSO, tell your healthcare provider about all your medical conditions, including if you:

- drink alcohol
- have kidney problems
- are pregnant or think you may be pregnant. It is not known if ZULRESSO will harm your unborn baby.
  - There is a pregnancy registry for females who are exposed to ZULRESSO during pregnancy. The purpose of the registry is to collect information about the health of females exposed to ZULRESSO and their baby. If you become pregnant during treatment with ZULRESSO, talk to your healthcare provider about registering with the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or visit https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/antidepressants/
- are breastfeeding or plan to breastfeed. ZULRESSO passes into breast milk. Talk to your healthcare provider about the risks and benefits of breastfeeding and about the best way to feed your baby while receiving ZULRESSO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

ZULRESSO and some medicines may interact with each other and cause serious side effects.

Especially tell your healthcare provider if you take other antidepressants, opioids, or Central Nervous System (CNS) depressants (such as benzodiazepines).

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine. Your healthcare provider will decide if other medicines can be taken with ZULRESSO.

How will I receive ZULRESSO?

ZULRESSO is given to you by continuous intravenous (IV) infusion into your vein. The infusion will last for a total of 60 hours (2.5 days).

What should I avoid while receiving ZULRESSO?

- ZULRESSO may make you feel dizzy and sleepy. Do not drive a car or do other dangerous activities after your ZULRESSO infusion until your feeling of sleepiness has completely gone away. See **"What is the most important information I should know about ZULRESSO?"**
- Do not drink alcohol while receiving ZULRESSO.

What are the possible side effects of ZULRESSO?

ZULRESSO can cause serious side effects, including:

- See "What is the most important information I should know about ZULRESSO?"
- **Increased risk of suicidal thoughts or actions**. ZULRESSO and other antidepressant medicines may increase suicidal thoughts and actions in some people 24 years of age and younger. Depression or other serious mental illnesses are the most important causes of suicidal thoughts or actions.

How can I watch for and try to prevent suicidal thoughts and actions?

- Pay close attention to any changes, especially sudden changes in mood, behavior, thoughts, or feelings, or if you develop suicidal thoughts or actions.
- Tell your healthcare provider right away if you have any new or sudden changes in mood, behavior, thoughts, or feelings.
- Keep all follow-up visits with your healthcare provider as scheduled. Call your healthcare provider between visits as needed, especially if you have concerns about symptoms.

Tell your healthcare provider right away if you have any of the following symptoms, especially if they are new, worse, or worry you:

- Attempts to commit suicide, thoughts about suicide or dying, new or worse depression, other unusual changes in behavior or mood

The most common side effects of ZULRESSO include:

- Sleepiness, dry mouth, passing out, flushing of the skin or face.

These are not all the side effects of ZULRESSO. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. Please see full Prescribing Information, including Boxed WARNING, and Medication Guide for ZULRESSO™ and discuss any questions you may have with your healthcare provider.

Sage Therapeutics™

Strategic SAGE-217 Collaboration with Shionogi

Potential to Accelerate Development and Commercialization of SAGE-217 in Key Asian Markets

- **Expansion of Global Footprint**
  - Goal of collaboration to accelerate development of a potentially groundbreaking medicine to patients in key Asian markets
  - Sage maintains exclusive rights to develop and commercialize SAGE-217 outside of those geographies
- **Expert Partner in Key Asian Markets**
  - Shionogi is responsible for clinical development and commercialization of SAGE-217 in Japan, Taiwan, and South Korea
  - Shionogi has strong presence in Asia in developing & commercializing therapeutics for CNS disorders
- **Attractive Terms**
  - Sage to receive tiered royalties on sales averaging in the greater than 20% range, if commercialized
  - Shionogi has also granted Sage certain rights to co-promote SAGE-217 in Japan across all indications

Sage Therapeutics™ + SHIONOGI

$90M

Upfront payment

$485M

Potential development & commercial milestones

Sage Therapeutics™

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