Sage Therapeutics™

Investor Presentation

June 2020

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”, “goal”, “potential,” or “continue,” and other similar expressions.
- Forward-looking statements in this presentation include statements regarding: our plans and expectations for ZULRESSO, including our revenue expectations and the factors that may impact revenues; our expectations as to the development and regulatory path forward and filing requirements for zuranolone; our development plans, goals and strategy for our product candidates and the potential results of our development efforts; the anticipated timing of clinical trial initiation and reporting of results, including our belief as to our ability to mitigate the possible impact of the COVID-19 pandemic on our clinical development timelines; the potential profile and benefit of our product candidates; our belief in the potential of our product candidates in various indications; the estimated number of patients with the disorders and diseases we are studying or plan to study; our financial expectations, including with respect to year-end cash; our belief that existing cash will support operations into 2022; and our expectations as to the goals, opportunity and potential for our business.
- 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 never be able to generate meaningful revenues from sales of ZULRESSO or to generate revenues at levels necessary to justify our investment; the impact of the COVID-19 pandemic on sales of ZULRESSO may last longer than we expect or may reoccur in waves; our post-restructuring focus on geographies where there are existing, active ZULRESSO treating sites may not be sufficient for us to achieve success from the sale of ZULRESSO or to generate revenues at meaningful levels or at levels necessary to justify our investment even after the impact of the COVID-19 pandemic lessens; we may not be able to overcome the barriers to treatment with ZULRESSO or we may continue to encounter other issues or challenges in commercializing ZULRESSO which could further limit the potential of ZULRESSO and the timing and amount of future.
  - 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.
  - We may encounter delays in initiation or conduct of our planned clinical trials, including slower than expected site initiation or enrollment or other delays or problems, including problems with our data, that may impact our ability to meet our expected time-lines or require the need for additional analysis or data. Such issues with any trial could cause delay in completion of the trial, availability of results and timing of future activities and could result in an increase in costs.
  - We may not be able to mitigate the impact of COVID-19 on our clinical development timelines and the impact may be more significant than we expect and may negatively impact expected site initiation or enrollment in our clinical trials, or cause us to pause trials or not be able to use data, in each case which may significantly impact our ability to meet our expected time-lines or may significantly impact the integrity or sufficiency of the data from our trials or increase our costs or cause us to have to change our plans.
  - Success in pre-clinical studies or in prior 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 regulatory filing, review or approval, despite prior regulatory advice, and regulatory authorities may ask for additional trials or data.
  - The number of people with the disorders or diseases we are studying or plan to study, or the unmet need for additional treatment options, may be significantly smaller than we expect. 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, including, for our product candidates, as a result of an increase in dosing in clinical trials or co-initiation with other 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 which could cause us to change our plans. Our expectations as to expenses, year-end cash and cash needs may prove not to be correct for other reasons such as changes in plans or actual events being different than our assumptions. We may also be opportunistic in our future financing plans even if available cash is sufficient;
  - 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™

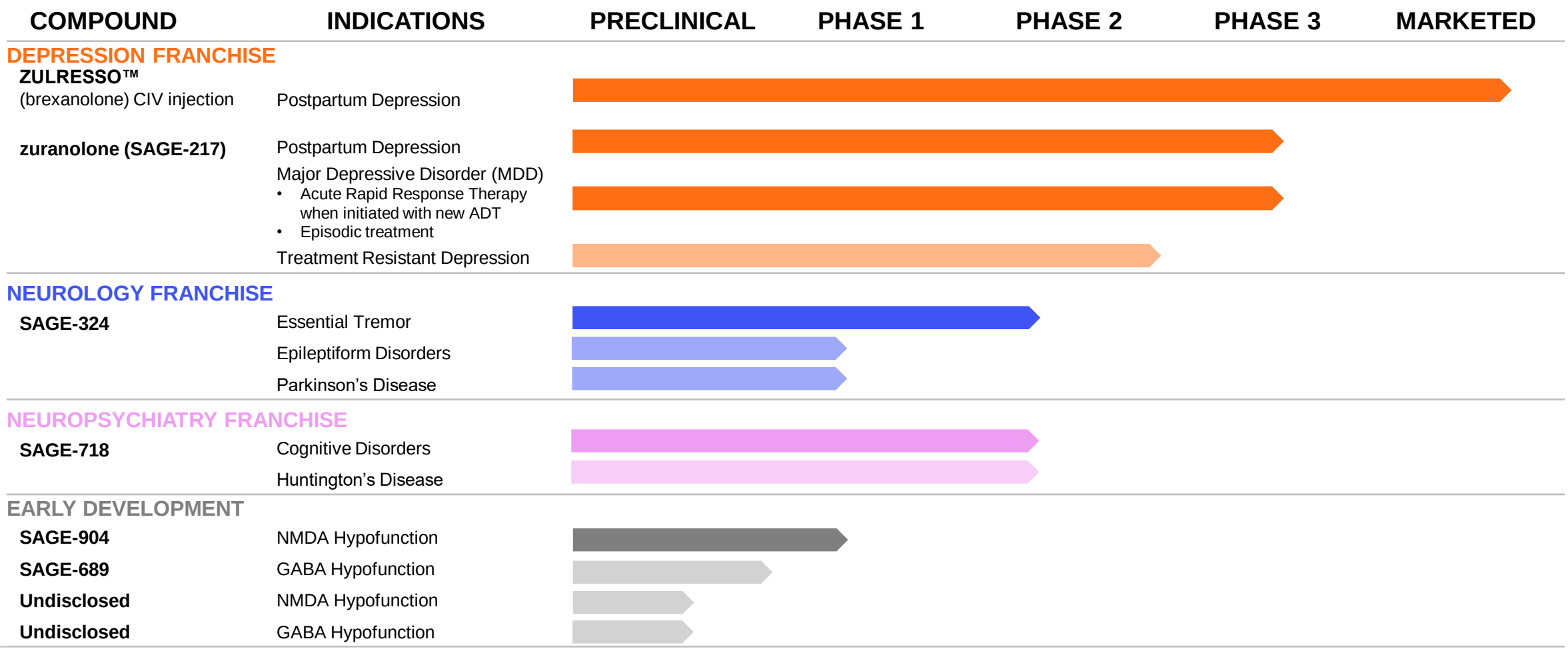
Who We Are: Sage Therapeutics

- Developing innovative treatment options with the potential to transform the lives of people with brain health disorders
- We continue to advance an industry-leading pipeline of novel brain health assets:
  - **First and only** product approved specifically for postpartum depression
  - **5** NCE clinical candidates across **8** indications
  - In-house library of **>6K** proprietary compounds
  - **$875M** cash-on-hand as of March 31, 2020

Sage Therapeutics™

Abbreviations: NCE = new chemical entity

A Leading Brain Health Portfolio



Light shades indicate trials in the planning or evaluation stage

Depression Franchise

Psychiatry as Medicine

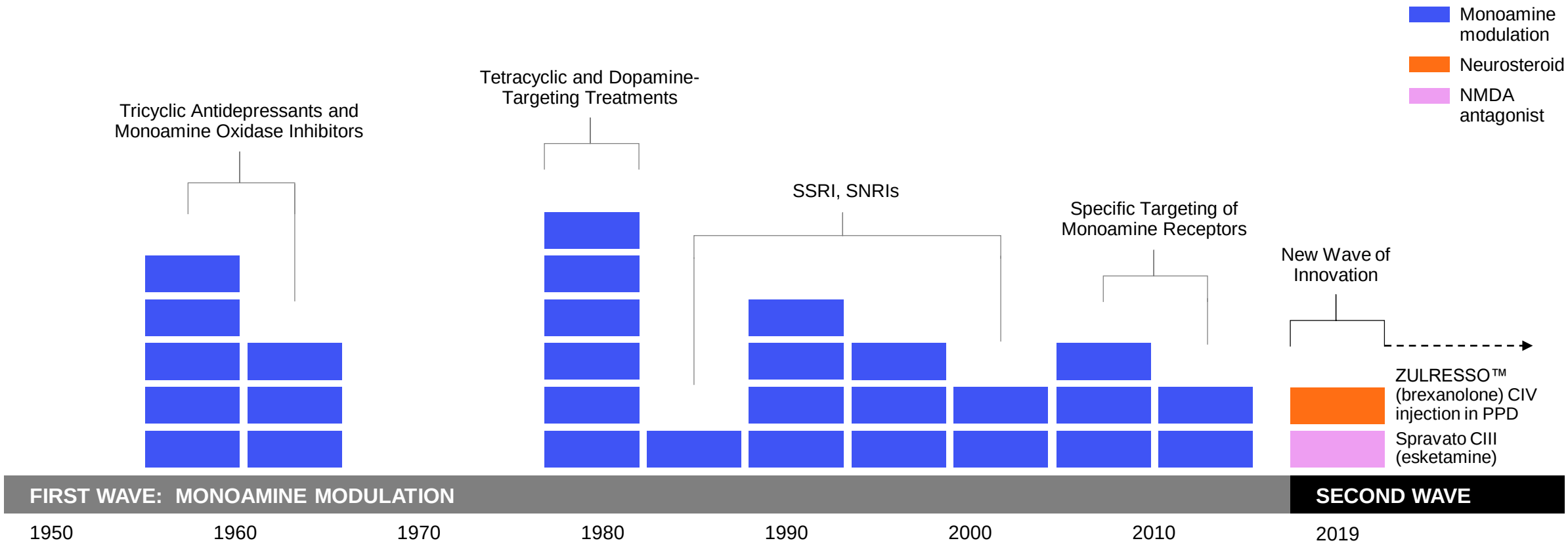
Our goal is to develop medicines to treat depression with potentially unique efficacy and tolerability profiles that:

- Allow treating-as-needed
- Act rapidly
- Reduce stigma

Sage Therapeutics™

Sage Leading Second Wave of Neuropsych Innovation

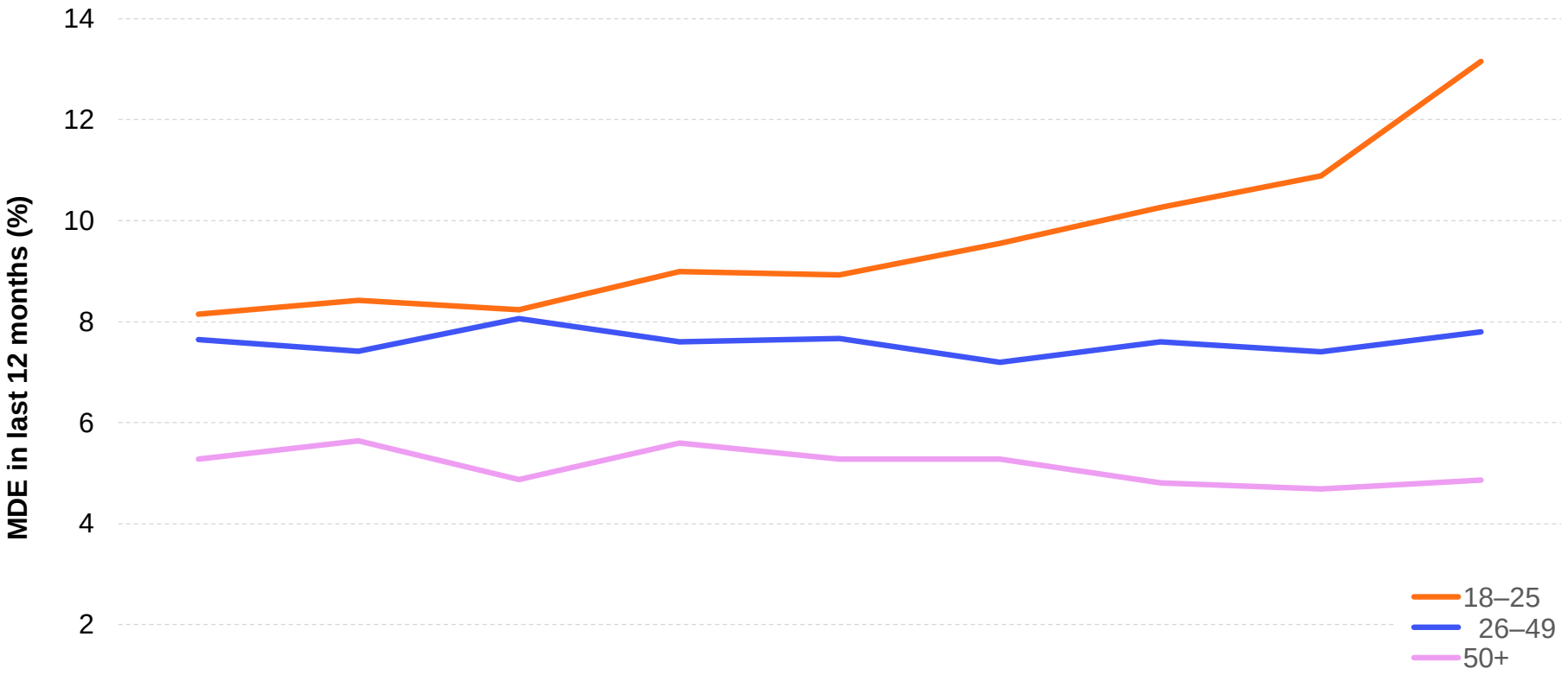
First new MOA in 60 years



Sage Therapeutics™

Source: Thomas, D., & Wessel, C. (2017). The State of Innovation in Highly Prevalent Chronic Diseases: Volume I: Depression Therapeutics. BIO.

Depression Remains an Area of Significant Unmet Need, Reflecting Lack of Innovation



Despite substantial increases in therapies for depression during the first wave (i.e., monoamine modulation), rates of major depressive episodes (MDE) have increased from 2009 to 2017

FIRST WAVE: MONOAMINE MODULATION | **SECOND WAVE**

2009 2017 2019

Sage Therapeutics™

Sources: J Abnorm Psychol. 2019 Apr;128(3):185-199. doi: 10.1037/abn0000410. Epub 2019 Mar 14.

Zuranolone's (SAGE-217) Landscape Program

Potential to reshape the depression landscape

STUDY	PPD-201	SKYLARK (PPD-301)	MDD-201	MOUNTAIN (MDD-301)	WATERFALL (MDD-301B)	REDWOOD (MDD-302)	SHORELINE (MDD-303)	RAINFOREST (MDD-304)	MDD-305
Indication	**PPD**	**PPD**	**MDD**	**MDD**	**MDD**	**MDD**	**MDD**	**Co-morbid MDD and Insomnia**	**MDD**
Phase	Pivotal Ph. 2	Pivotal Ph. 3	Pivotal Ph. 2	Pivotal Ph. 3	Pivotal Ph. 3	Pivotal Ph. 3	Pivotal Ph. 3	Pivotal Ph. 3	Pivotal Ph. 3
Objective	Efficacy in the treatment of PPD compared to placebo	Efficacy in the treatment of PPD compared to placebo	Efficacy in the treatment of MDD compared to placebo	Efficacy in the treatment of MDD compared to placebo	Efficacy in the treatment of MDD compared to placebo	Efficacy of a fixed, repeated treatment regimen in the prevention of relapse	Safety, tolerability of as-needed repeat treatment over a 1-year period	Efficacy in the treatment of sleep efficiency	Efficacy, compared to placebo, in the treatment of MDD when co-initiated with open-label SSRI
Status	Complete	Planned 2020 initiation; topline data in 2021	Complete	Complete	Ongoing; topline data in 2021	Enrollment paused; future re-evaluation planned	Enrollment for 30 mg cohort complete, with topline data by year-end 2020; ongoing enrollment for 50 mg cohort with topline data in 2021	Enrollment paused; future re-evaluation planned	Planned 2020 initiation; topline data in 2021

Sage Therapeutics™

Abbreviations: MDD = major depressive disorder, PPD = postpartum depression

Development Plan for Zuranolone Creates Flexibility to Pursue an Efficient and Expedited Pathway to Filing

Potential for 3 distinct indications

ORAL POSTPARTUM DEPRESSION (PPD) THERAPY	**SKYLARK (PPD-301):** Placebo-controlled trial evaluating a two-week course of zuranolone 50 mg in women with PPD, with additional *short-term* follow-up	+	Previously completed studies; no additional long-term follow-up expected to be required
ACCUTE RAPID RESPONSE (RRT) IN MAJOR DEPRESSIVE DISORDER (MDD) WHEN COINITIATED WITH NEW ADT	**MDD-305:** Placebo-controlled trial evaluating a two-week course of zuranolone 50 mg, when co-initiated with an open-label SSRI, in patients with MDD, with additional *short-term* follow-up	+	Previously completed studies; no additional long-term follow-up expected to be required
EPISODIC THERAPY IN PATIENTS WITH MDD	**WATERFALL (MDD-301B):** Placebo-controlled trial evaluating a two-week course of zuranolone 50 mg in patients with MDD, with additional *short-term* follow-up	+	Previously completed acute treatment studies and long-term safety data, including data from REDWOOD (MDD-302)

Distinct indications enable Sage to efficiently pursue NDA filing for zuranolone and, if successful, bring this treatment to patients quickly

Sage is also currently evaluating the ongoing zuranolone clinical pharmacology and safety program and plans to finalize requirements to support a potential future NDA with the FDA.

Sage Therapeutics™

ZULRESSO™ (brexanolone) CIV Injection

Commercial efforts primarily focused on geographies that have existing, active treating sites

- **<u>Support in existing geographies:</u>** Primary focus on working with healthcare providers and supporting women with PPD in geographies with active ZULRESSO treating sites

- **<u>Customized case management:</u>** Sage Central, Sage's national patient support center, continuing to provide customized case management support to women with PPD

SAGE CENTRAL™
PATIENT SUPPORT

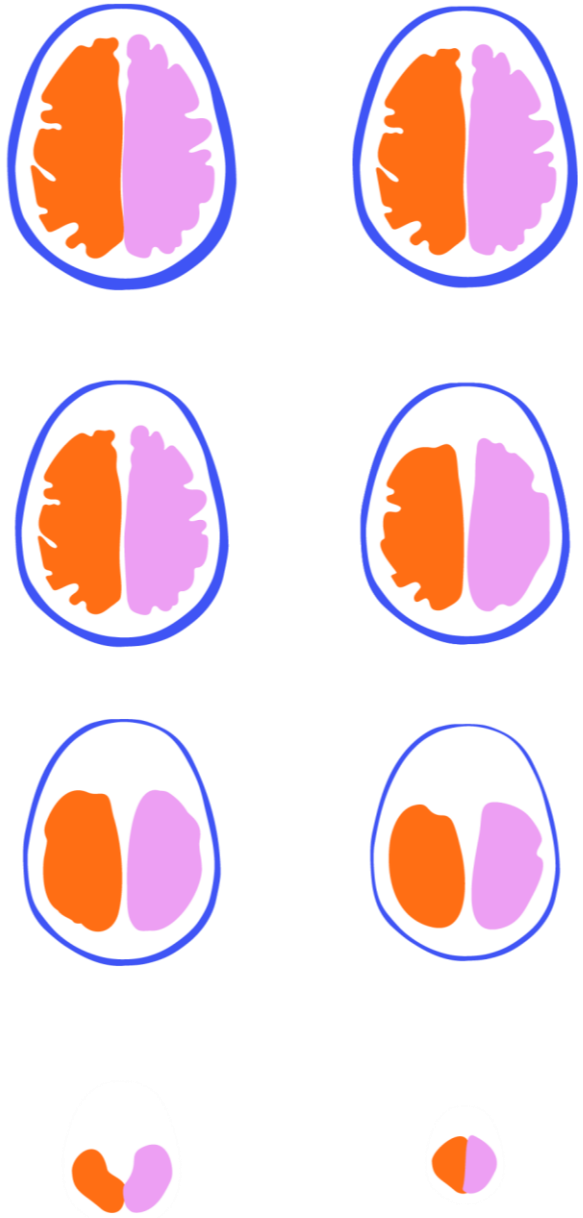
ZULRESSO is only available at certified healthcare settings through a restricted program called the ZULRESSO REMS due to the risk of serious harm resulting from excessive sedation or sudden loss of consciousness

Sage Therapeutics™

Neurology Franchise

Next-generation Asset Positioned for Neurological Conditions

- **SAGE-324**
  - Novel next-generation positive allosteric modulator (PAM) of $GABA_A$ receptors
  - Chronic dosing: long half-life provides consistent plasma concentrations with minimal daily fluctuations after multiple doses
  - Potential therapy for neurological conditions, such as essential tremor, epilepsy and Parkinson's disease



Sage Therapeutics™

SAGE-324 in Essential Tremor

On-track to initiate Phase 2 placebo-controlled study

Essential tremor (ET) is the most common movement disorder where standard of care may be inadequate for many

- Symptoms progressively worsen over time and can significantly impair activities of daily living and independence
- Patients with tremor resulting in impaired functioning or disability are treated with pharmacotherapeutic interventions[1]
- Approximately 50% of diagnosed patients receive pharmacotherapy for ET[2]

SAGE-324 well-suited for development in ET

- Pathophysiology of ET is associated with reduced GABAergic tone in regions of the brain controlling motor function – GABA PAMs mechanistically have the potential to address that deficit by improving GABA receptor function
- Long half-life supports low peak-to-trough ratio and provides flexibility in dosing paradigms – beneficial for ET where stable levels are a clinical challenge

Estimated

6M+ **people have ET** in the U.S.

Up to

1M

people with ET seek treatment

50% of patients seeking care **do not respond** or have a **sub-optimal response to standard of care**[3]

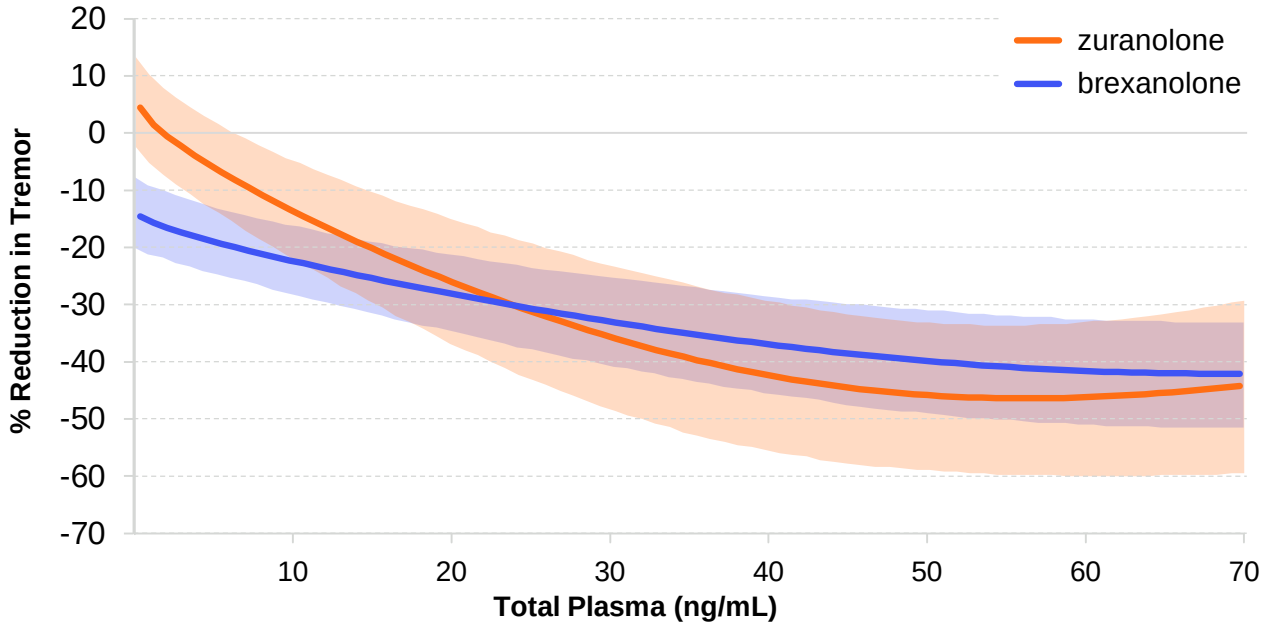
Sage Therapeutics™

1. Rajput AH, Rajput A. Medical treatment of essential tremor. Journal of Central Nervous System Disease 2014:6. 2. Louis ED. Medication non-adherence in essential tremor. Parkinsonism Relat Disord. 2015 February ; 21(2): 138–141. 3. Louis ED, Rios E, Henchcliffe C. How are we doing with the treatment of essential tremor (ET)? Eur J Neurol. 2010;17(6):882–884.

On-Track to Initiate Phase 2 Study in Essential Tremor

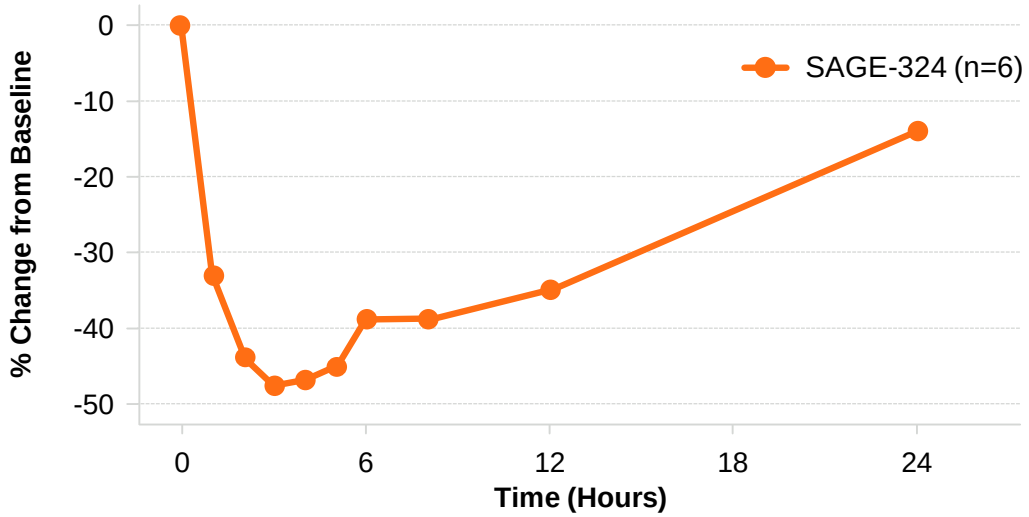
Phase 1 open-label study evaluating the safety and pharmacokinetics of SAGE-324 in patients with ET

SAGE GABA PAMs REDUCE TREMOR



SAGE-324 EFFECT OBSERVED AFTER A SINGLE DOSE

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



SAGE-324 was well-tolerated in Phase 1 studies; most common AEs (≥5%) included somnolence, dizziness, and feeling of relaxation

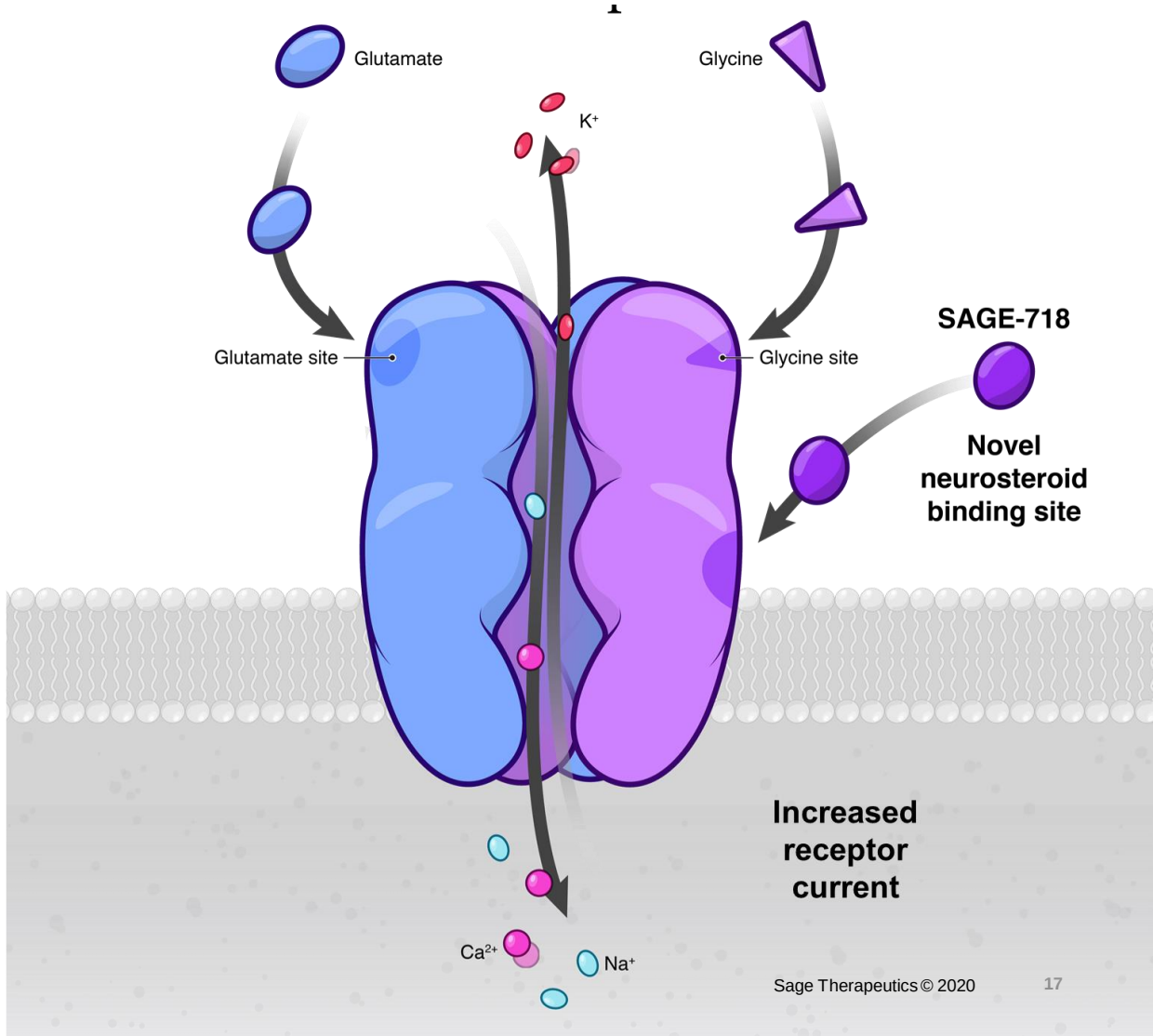
Abbreviations: AEs = adverse events

Neuropsychiatry Franchise

Sage's First-in-Class NMDA PAM

- NMDA receptors are thought to play a key role in a host of cognitive and behavioral processes
- Sage identified an endogenous modulator of the NMDA receptor (24S-hydroxycholesterol)
  - Yields potential biomarkers for activity and drug development
- Sage has built a library of thousands of novel NMDA modulators, with unique profiles, that are in various stages of development, the first of these being SAGE-718

Endogenous & Exogenous Ligands at the NMDA Receptor

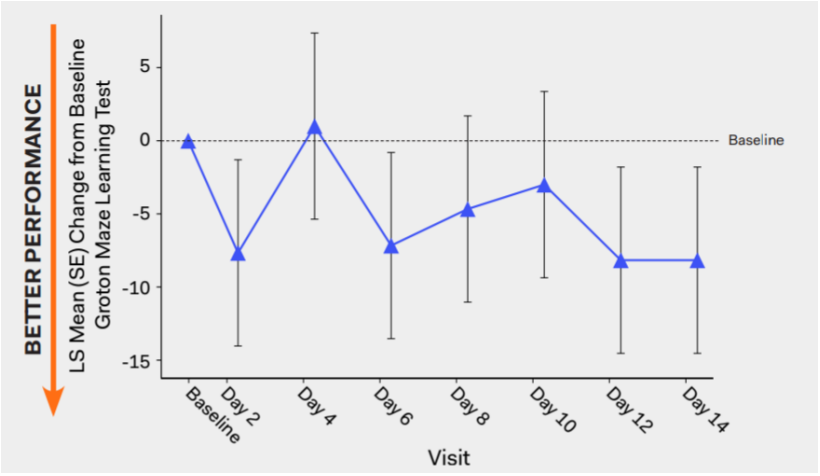


Sage Therapeutics™

In Phase 1 HD Cohort, SAGE-718 Demonstrated Consistent Activity on Executive Functioning

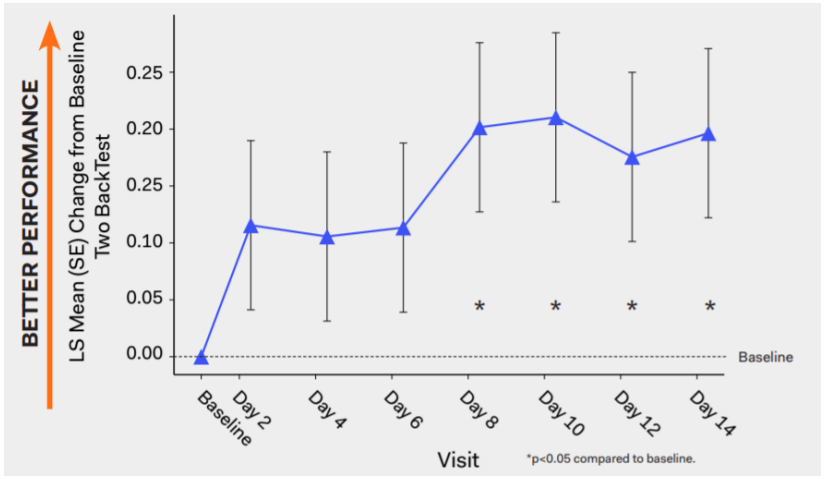
Improvement on two tests of executive functioning, not driven by performance on other domains

GROTON MAZE TEST *(Executive Function)*



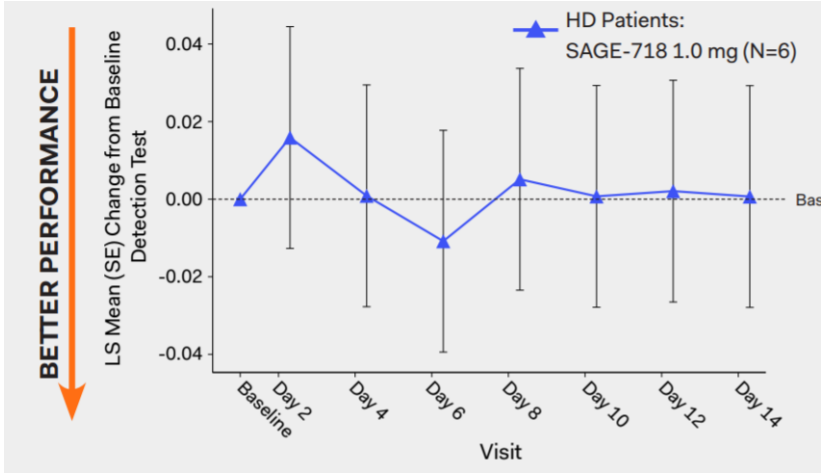
HD subjects demonstrated numerical improvement on the Groton Maze Test at all post-baseline visits, with the exception of Day 4.

TWO-BACK TEST *(Complex Working Memory and Executive Function)*



HD subjects demonstrated numerical improvement on the Two-Back test at all post-baseline visits, and demonstrated statistically-significant ($p<0.05$) improvement compared to baseline on Days 8, 10, 12 and 14.

DETECTION TEST *(Psychomotor Speed)*



Improvement on tests of executive functioning was not driven by performance on simpler tests of cognitive performance, as demonstrated by consistent performance on the detection test, a test of psychomotor speed.

In Phase 1 studies of SAGE-718 no serious adverse events or deaths have occurred, and most treatment-emergent adverse events have been mild in severity.

Sage Therapeutics™

Abbreviations: HD = Huntington's disease

First Quarter 2020 & First Quarter 2019 Financial Results

Strong financial position with $875M in cash

Item	1Q '20	1Q '19
Revenue: • *Zulresso* • *Collaboration*	$2.3M • *2.3M* • *-*	$0.5M • *-* • *0.5M*
R&D Expense	$63.6M	$86.4M
SG&A Expense	$70.1M	$83.9M
COGS	$0.2M	-
Total Operating Costs and Expenses	$139.9M	$170.3M
Net Loss	($126.7M)	($163.4M)
Cash and Marketable Securities	$875M	$1.4B

- Sage anticipates a cash balance of at least $550 million at end of 2020, which the Company anticipates will support operations into 2022 based on current operating plans.
- The Company expects de minimis revenues from sales of ZULRESSO in the second quarter of 2020. The Company does not plan to provide revenue guidance for the balance of 2020.

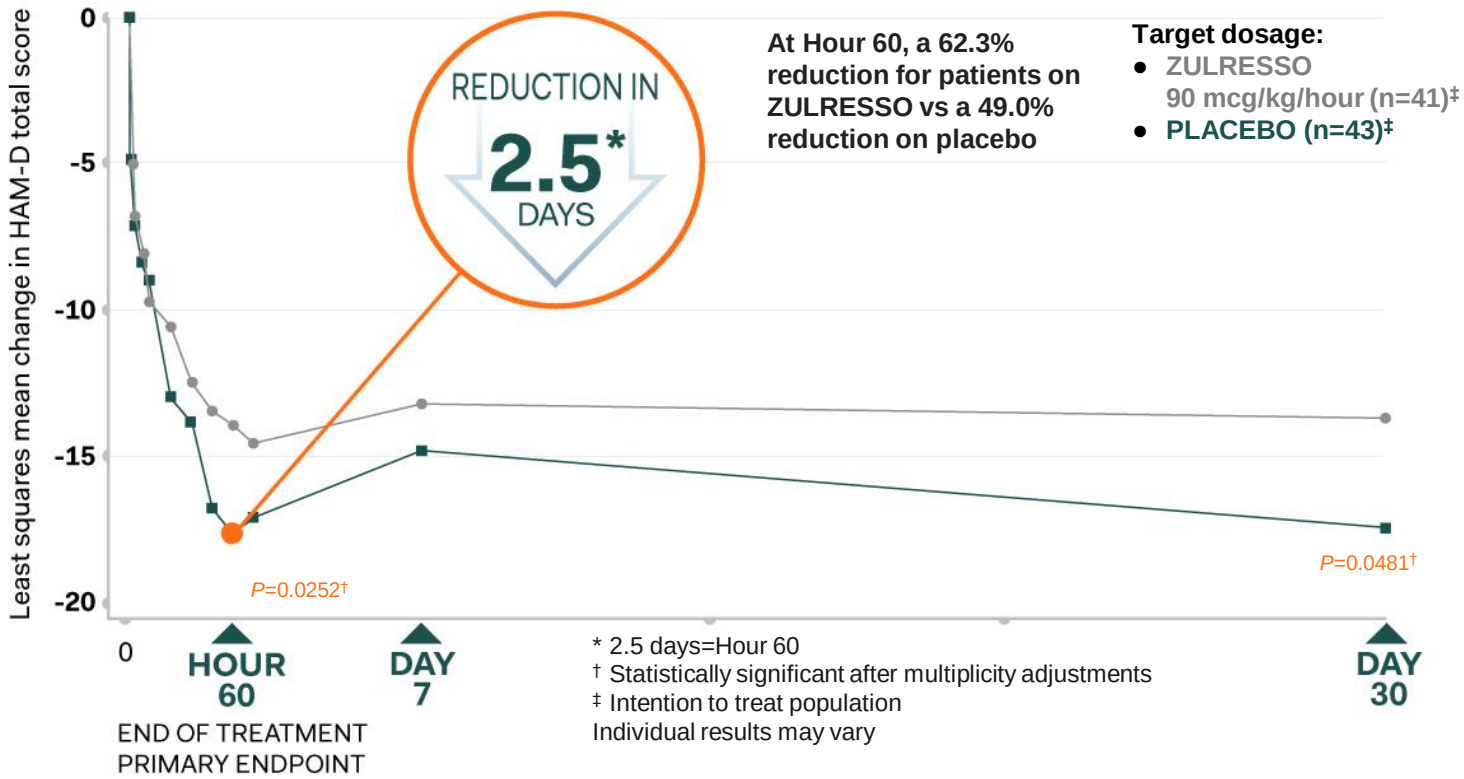
Sage Therapeutics™

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)[i,ii]



Durable therapeutic effect

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

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

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

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

ZULRESSO is only available through the ZULRESSO Risk Evaluation and Mitigation Strategy (REMS), a safety program to manage the risk of serious harm resulting from excessive sedation and sudden loss of consciousness during the ZULRESSO infusion. To administer ZULRESSO, sites of care must be certified in the ZULRESSO REMS[iii]

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

Sage Therapeutics™

Sources: i. ZULRESSO Prescribing Information. Cambridge, MA: Sage Therapeutics, Inc., ii. Meltzer-Brody S et al. Lancet. 2018;392(10152):1058-1070, iii. ZULRESSO REMS. https://zulressorems.com/#Public

ZULRESSO™ (brexanolone) CIV Injection

Boxed warning

WARNING: EXCESSIVE SEDATION AND SUDDEN LOSS OF CONSCIOUSNESS

See full prescribing information for complete boxed warning.

- Patients are at risk of excessive sedation or sudden loss of consciousness during administration of ZULRESSO. (5.1)
- Because of the risk of serious harm, patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring. Patients must be accompanied during interactions with their child(ren). (5.1)
- ZULRESSO is available only through a restricted program called the ZULRESSO REMS. (5.1, 5.2)

ZULRESSO™ (brexanolone) CIV injection

Important Safety Information

What is ZULRESSO?

ZULRESSO™ is a prescription medicine used to treat Postpartum Depression in adults.

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 Zuranolone Collaboration with Shionogi

- **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 zuranolone outside of those geographies
- **Expert Partner in Key Asian Markets**
  - Shionogi is responsible for clinical development and commercialization of zuranolone 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 zuranolone in Japan across all indications

Sage Therapeutics™ + SHIONOGI

$90M

Upfront payment

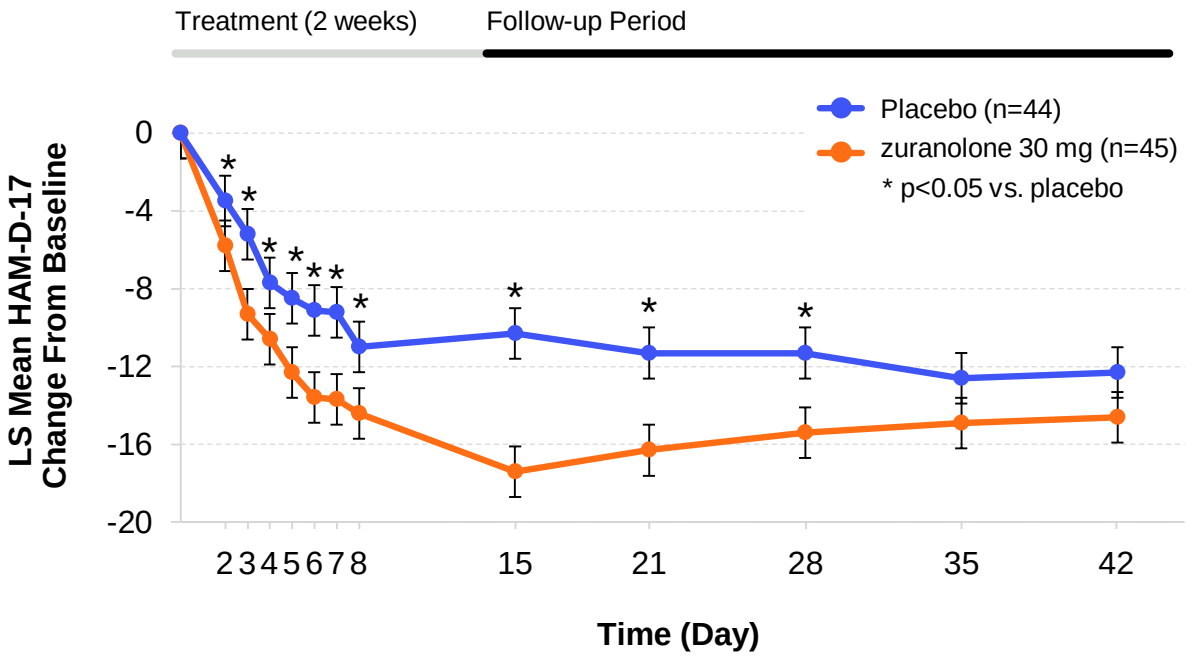
$485M

Potential development & commercial milestones

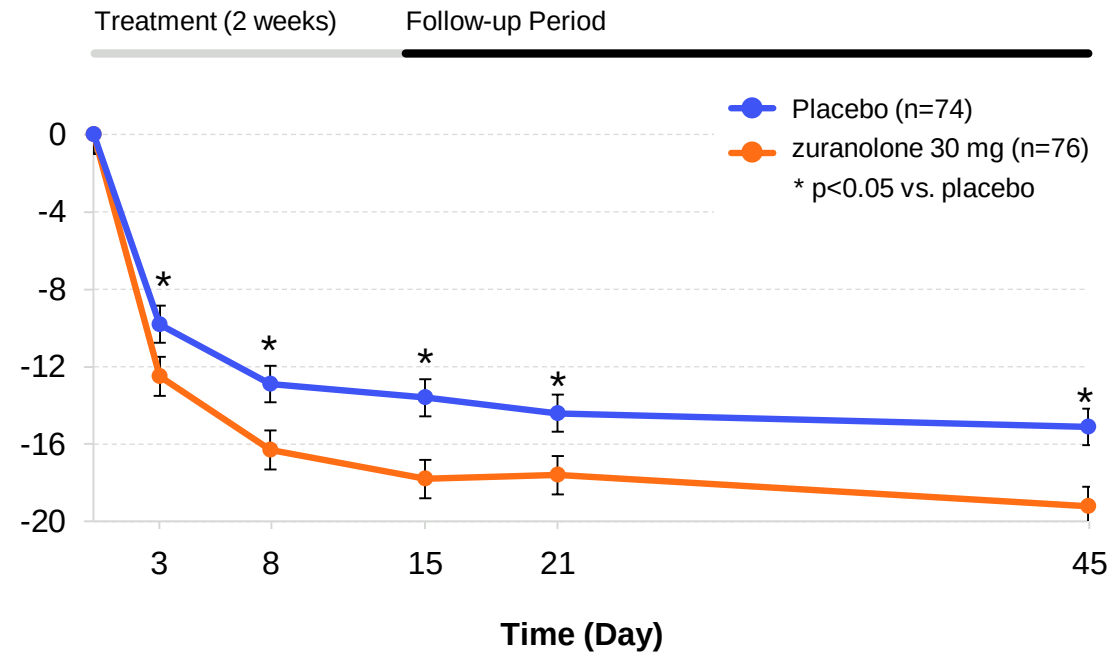
MDD-201 & ROBIN Studies

Rapid onset of activity with generally well-tolerated safety profile

MDD-201



ROBIN (PPD-201)



Zuranolone was generally well-tolerated in both studies

The most common AEs (≥5%) in the MDD-201 study included headache, dizziness, nausea, and somnolence

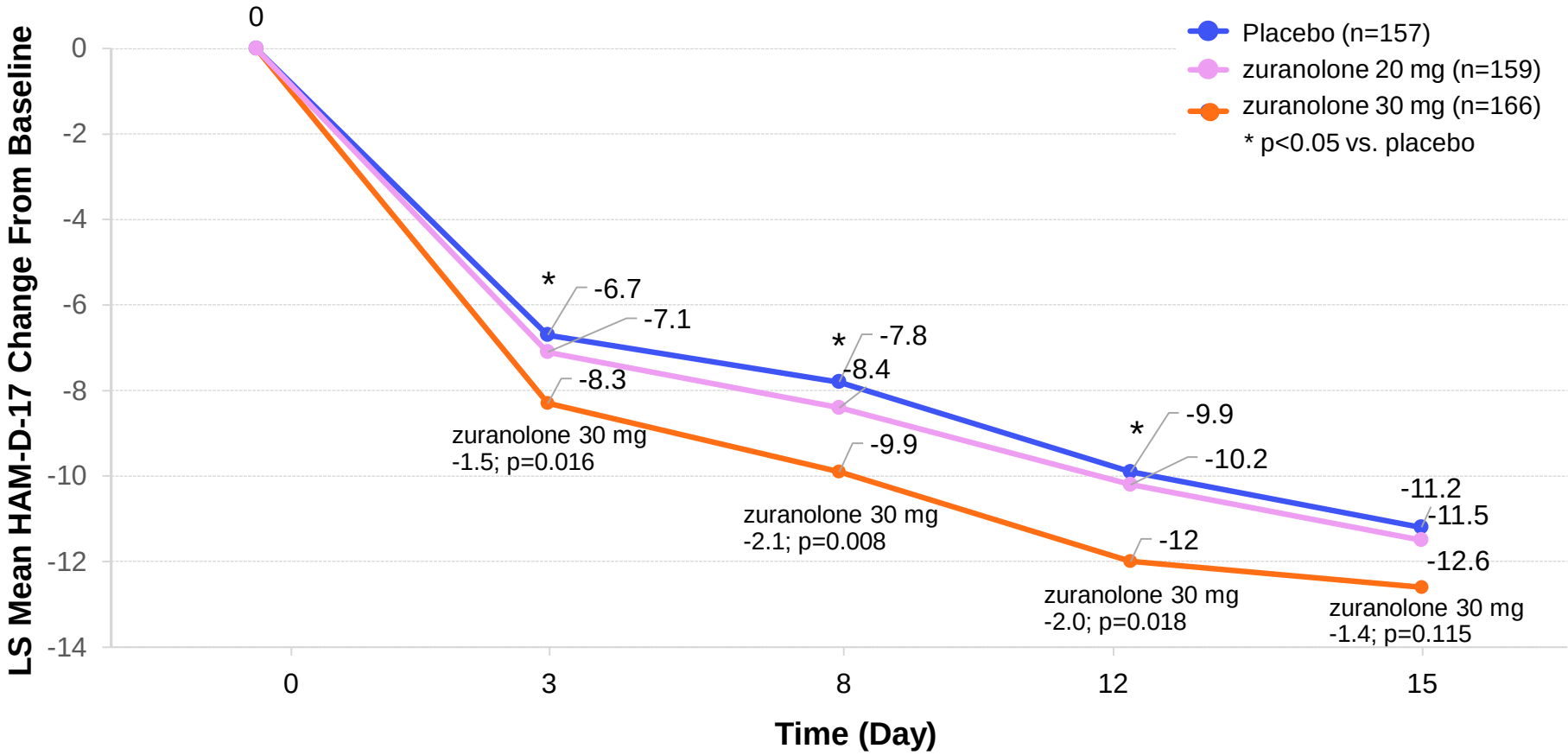
The most common AEs (≥5%) in the PPD-201 study included somnolence, headache, dizziness, upper respiratory tract infection, diarrhea, and sedation

Sage Therapeutics™

Abbreviations: AEs = adverse events

MOUNTAIN (MDD-301) Study

Displays rapid, robust onset similar to prior pivotal studies



Zuranolone was generally well-tolerated in the study

The most common AEs (≥5%) included headache dizziness, somnolence, fatigue, diarrhea, sedation and nausea

Rapid onset of effect for zuranolone 30 mg was seen beginning at Day 3 with maintenance of effect through Day 15; statistical separation from placebo observed Days 3 – 12

Sage Therapeutics™

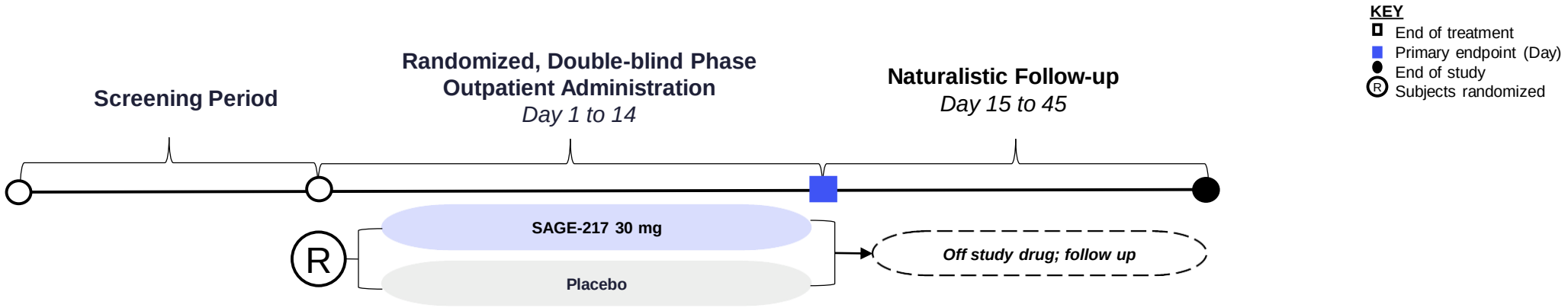
Abbreviations: AEs: = adverse events

Study Design:

Completed Studies

Completed SAGE-217 Studies

Pivotal Ph. 2 in PPD (ROBIN; PPD-201)



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*

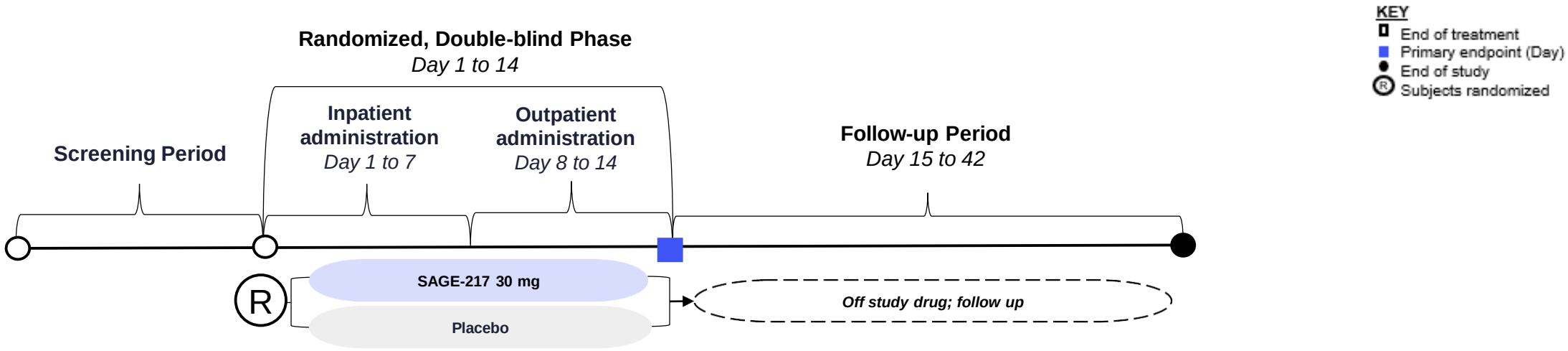
Dosing Regimen	2-week, once-nightly	**Key Exclusion Criteria**	• Active psychosis
			• Attempted suicide associated with current episode of PPD (Note, suicidal ideation is not an exclusion; other protocol-defined inclusion/exclusion criteria may apply)
			• Medical history of seizures, bipolar disorder, 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**

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

NCT02978326. Available from: clinicaltrials.gov [accessed November 2019]

Completed SAGE-217 Studies

Pivotal Ph. 2 in MDD (MDD-201)



STUDY OVERVIEW

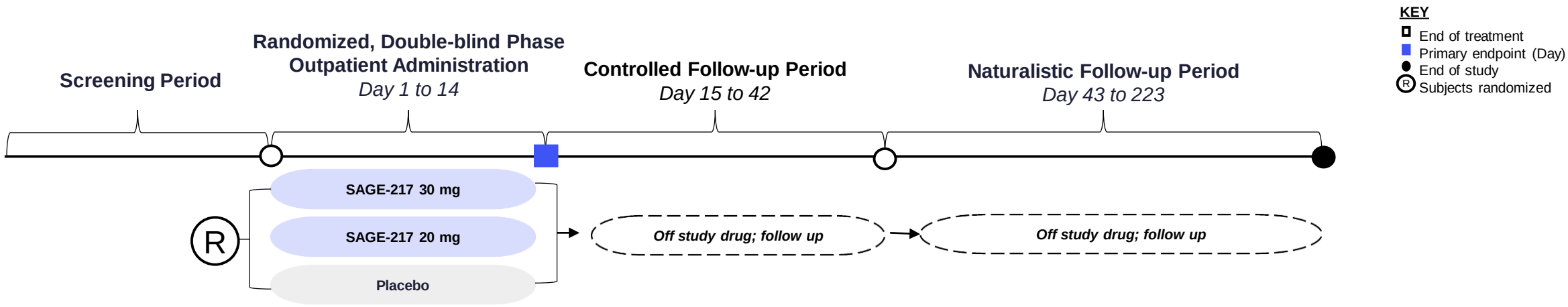
Arms	Randomization: 1:1 • SAGE-217 30 mg • Placebo	**Inclusion Criteria**	• Diagnosis of MDD with symptoms that have been present for at least a 4-week period	**Primary Endpoint**	• Change from baseline in HAM-D*
Dosing Regimen	2-week, once-nightly	**Exclusion Criteria**	• History of suicide attempt • 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	**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**

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

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

Completed SAGE-217 Studies

Phase 3 MOUNTAIN (MDD-301)



STUDY OVERVIEW

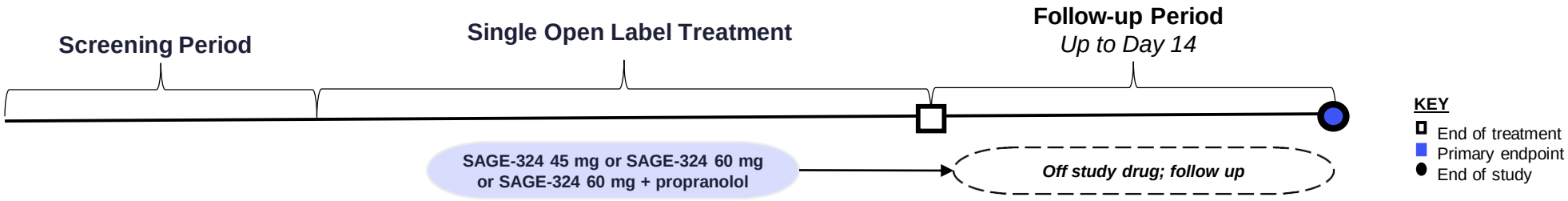
Status	Complete	**Inclusion Criteria**	• Diagnosis of MDD with symptoms that have been present for at least a 4-week period • MADRS total score ≥32 and HAM-D total score ≥22 at screening and Day 1 (prior to dosing)
Indication	MDD		
Phase	Phase 3	**Exclusion Criteria**	• Active psychosis • Attempted suicide associated with the current episode of MDD • Medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder
Start/End Date* *topline data announced	Sep. 2018; Dec. 2019		
Arms	Double-blind, randomized: 1:1:1 • SAGE-217 20 mg, SAGE-217 30 mg, placebo	**Primary Endpoint**	• Change from baseline in HAM-D total score*
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**

Use of antidepressants, antianxiety or insomnia medications restricted during controlled follow-up period; however, these medications may be used during the naturalistic follow up period as indicated by clinical judgement of the Investigators

*During double-blind phase; **During double-blind and follow-up periods; NCT03672175. Available from: clinicaltrials.gov [accessed January 2020]

Completed SAGE-324 Study

Open-label essential tremor study (324-CLP-101E)



STUDY OVERVIEW

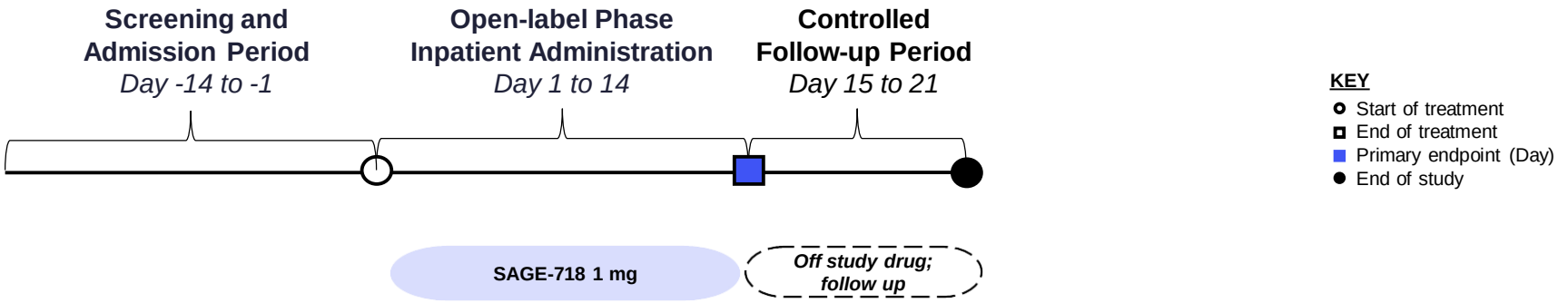
Status	Completed	**Inclusion Criteria**	• Diagnosis of ET consisting of
			  • bilateral upper limb action tremor
			  • at least 3 years duration
			  • with or without tremor in other locations
			  • absence of other neurological signs
			• Combined TETRAS upper limb total score of ≥ 8 on the performance subscale part 4

Indication	Essential Tremor (ET)		
Phase	Phase 1	**Exclusion Criteria**	• History or evidence of clinically relevant medical disorders (with exception of ET) • Current or recent exposure to tremorgenic drugs or drug withdrawal state • Previous surgery for the treatment of ET
Start/End Date	Aug. 2018 / Dec. 2019		
Cohorts	Open-label study: • SAGE-324 45 mg • SAGE-324 60 mg • SAGE-324 60 mg + propranolol	**Primary Endpoint**	• Safety and tolerability as assessed by frequency and severity of AE/SAE
Dosing Regimen	Single dose	**Secondary Endpoints**	• PK profile of SAGE-324
		Exploratory Endpoint	• Change from baseline over time in TETRAS performance subscale and Kinesia™ accelerometer scores

Sage Therapeutics™

Completed SAGE-718 Study

Open-label Cohort of Patients with Huntington's Disease (CLP-102 Part B)



STUDY OVERVIEW

Status	Completed
Indication	Huntington's Disease Cognitive Impairment
Phase	Phase 1
Start/End Date* *topline data announced	Jan. 2019 / Dec. 2019
Arms	Open-label SAGE-718 1 mg oral solution
Dosing Regimen	2-week, once daily

Inclusion Criteria	• Positive for mutant *HTT* (documented CAG repeats ≥ 36 units) • Total Functional Capacity (TFC) score > 6 • Score 28 or less on the MoCA at Screening
Exclusion Criteria	• Unstable co-morbid medical conditions
Primary Endpoint	• Incidence of adverse events and serious adverse events, and changes from baseline in vital signs, safety EEGs, ECGs, laboratory parameters, and Columbia-Suicide Severity Rating Scale (C-SSRS).
Secondary and Other Endpoints	• PK profile of SAGE-718 following administration of multiple doses of SAGE-718 oral solution • Change from baseline on a computerized cognitive battery

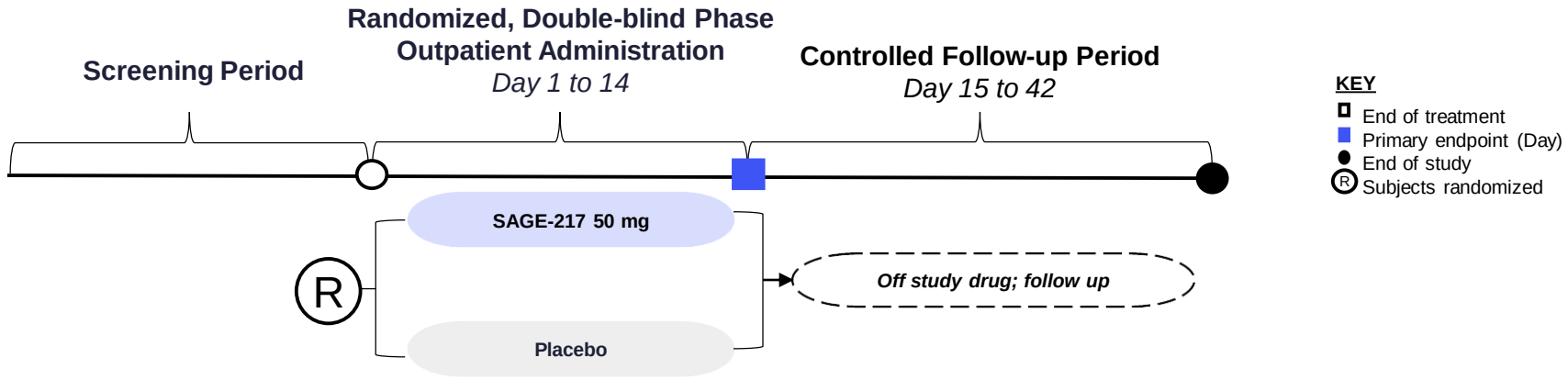
Sage Therapeutics™

Study Design:

Planned / Ongoing Studies

Zuranolone (SAGE-217) - 50 mg

*New placebo-controlled **MDD** study (MDD-301B)*



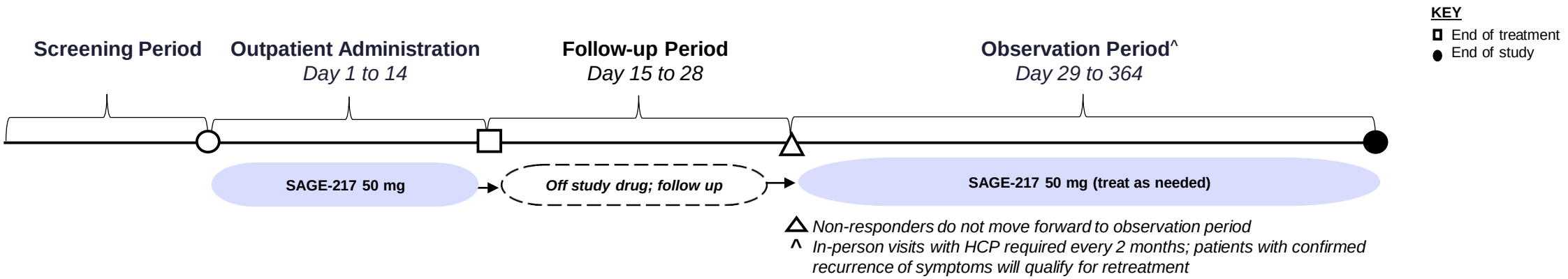
STUDY OVERVIEW

Status	Planned 2020 Initiation	**Inclusion Criteria**	• Diagnosis of MDD with symptoms that have been present for at least a 4-week period • HAM-D total score ≥24 at screening and Day 1 (prior to dosing)
Indication	MDD		
Phase	Phase 3	**Exclusion Criteria**	• Active psychosis • Attempted suicide associated with the current episode of MDD • Medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder
Start/End Date	May 2020 / TBA		
Arms	Double-blind, randomized: 1:1 • SAGE-217 50 mg, placebo	**Primary Endpoint**	• Change from baseline in HAM-D total score at Day 15
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

Use of antidepressants, antianxiety or insomnia medications restricted during controlled follow-up period

Zuranolone (SAGE-217) - 50 mg

*SHORELINE (**MDD**-303; 50 mg cohort)*



50 mg will be examined in subjects having already received 30 mg, as well as enrollment of a new cohort of 50 mg only subjects

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	TBA	**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 50 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*

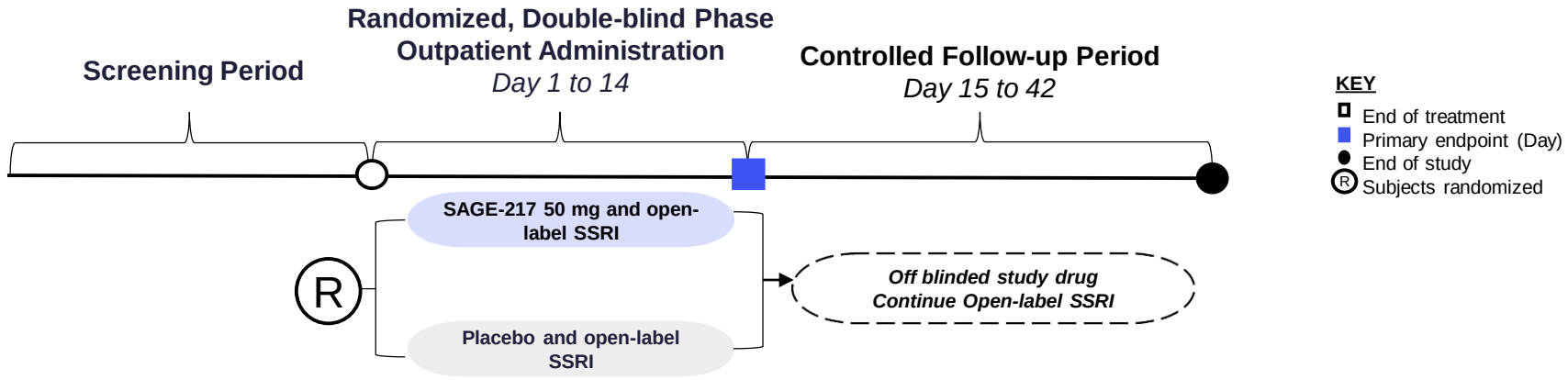
*During double-blind and follow-up periods

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

35

Zuranolone (SAGE-217) - 50 mg

*New active-controlled RRT in **MDD** study (MDD-305)*



STUDY OVERVIEW

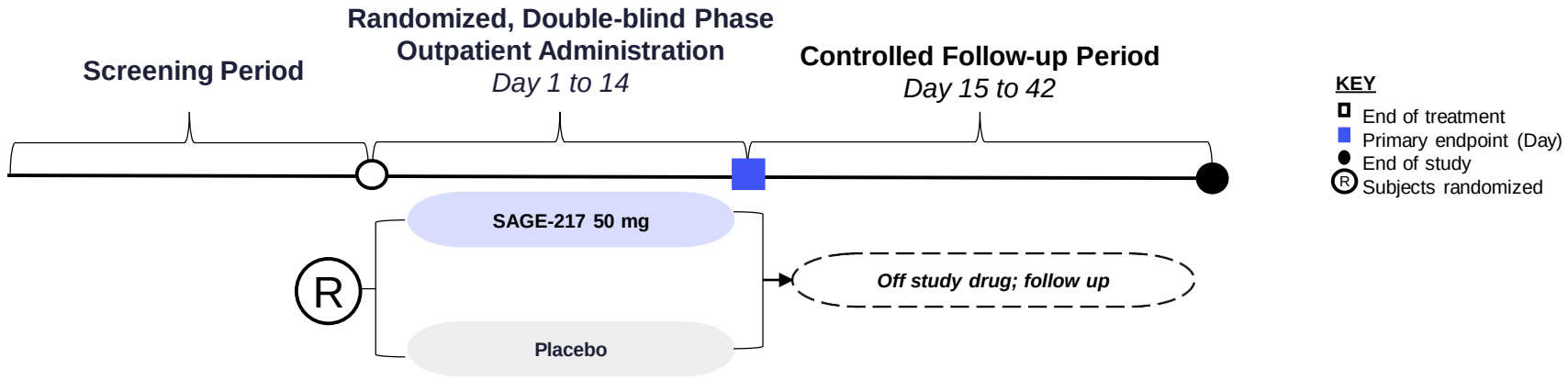
Status	Planned 2020 Initiation	**Inclusion Criteria**	• Diagnosis of MDD with symptoms that have been present for at least a 4-week period • HAM-D total score ≥24 at screening and Day 1 (prior to dosing)
Indication	MDD		
Phase	Phase 3	**Exclusion Criteria**	• Active psychosis • Attempted suicide associated with the current episode of MDD • Medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder
Start/End Date	TBA		
Arms	Double-blind, randomized: 1:1 • SAGE-217 50 mg, placebo added to open-label SSRI	**Primary Endpoint**	• Change from baseline in HAM-D total score at Day 15
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

Use of antidepressants, antianxiety or insomnia medications restricted during controlled follow-up period

RRT = rapid response therapy

Zuranolone (SAGE-217) - 50 mg

*New placebo-controlled **PPD** study (PPD-301)*

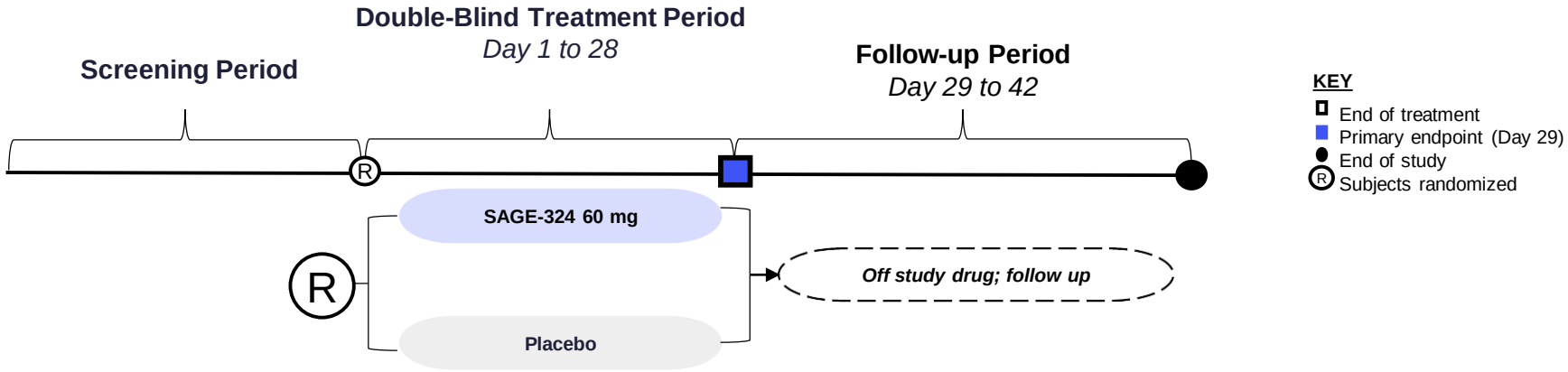


STUDY OVERVIEW

Status	Planned 2020 Initiation	**Inclusion Criteria**	• Diagnosis of MDD with symptoms that have been present for at least a 4-week period • HAM-D total score ≥26 at screening and Day 1 (prior to dosing)
Indication	PPD		
Phase	Phase 3	**Exclusion Criteria**	• Active psychosis • Attempted suicide associated with the current episode of PPD • Medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder
Start/End Date	Jun. 2020 / TBA		
Arms	Double-blind, randomized: 1:1 • SAGE-217 50 mg, placebo	**Primary Endpoint**	• Change from baseline in HAM-D total score at Day 15
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

Use of antidepressants, antianxiety or insomnia medications restricted during controlled follow-up period

SAGE-324
*Placebo-controlled **Essential Tremor** study (324-ETD-201)*



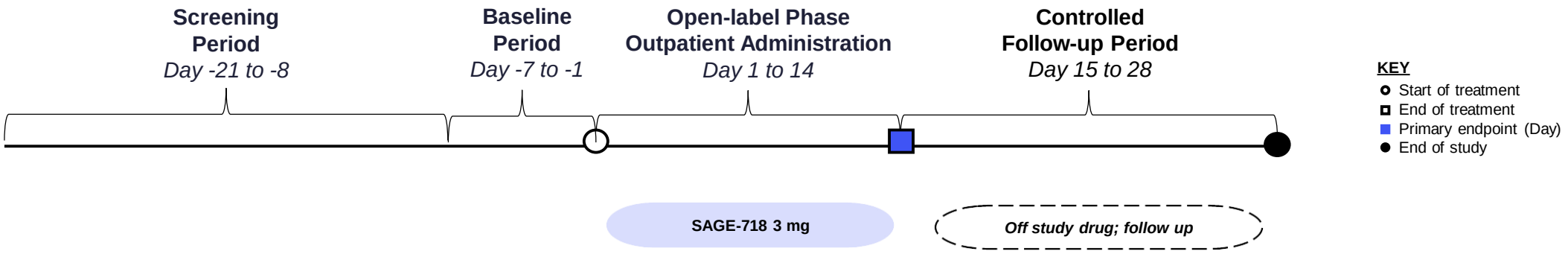
STUDY OVERVIEW

Status	Ongoing	**Inclusion Criteria**	• Diagnosis of ET consisting of
			  • bilateral upper limb action tremor
			  • at least 3 years duration
			  • with or without tremor in other locations
			  • absence of other neurological signs, sudden onset or evidence of stepwise deterioration of tremor
			• Score of at least 1.5 for each TETRAS performance subscale part 4 items with total score for the dominant upper limb of at least 5.5

Indication	Essential Tremor (ET)		
Phase	Phase 2	**Exclusion Criteria**	• Presence of known causes of enhanced physiological tremor • Recent exposure to tremorgenic drugs or presence of alcohol withdrawal state • Direct or indirect injury or trauma to the nervous system within 3 months before the onset of tremor • Previous procedure for the treatment of ET, deep brain stimulation, brain lesioning, or magnetic resonance guided procedure
Start/End Date	TBA		
Arms	Double-blind, randomized: 1:1 • SAGE-324 60 mg: placebo	**Primary Endpoint**	• Change from baseline in TETRAS performance subscale part 4 upper limb tremor score on Day 29
Dosing Regimen	28 days, once-daily	**Secondary Endpoints**	• Change from baseline in TETRAS performance subscale part 4 upper limb tremor score at all other timepoints • Change from baseline in Kinesia ONE accelerometer scores

Sage Therapeutics™

SAGE-718
*New Open-label **Mild Cognitive Impairment** Study*



STUDY OVERVIEW

Status	Start-up	**Inclusion Criteria**	TBA
Indication	Cognitive impairment		
Phase	Phase 2	**Exclusion Criteria**	TBA
Start/End Date	TBA		
Arms	Open-label SAGE-718 3 mg oral tablet	**Primary Endpoint**	• Incidence of treatment-emergent adverse events (TEAEs)
Dosing Regimen	2-week, once daily	**Secondary and Other Endpoints**	• Change from baseline in vital signs, clinical laboratory analytes, electrocardiograms, and responses on the Columbia–Suicide Severity Rating Scale (C-SSRS) • Change from baseline on comprehensive neurocognitive and neuropsychiatric batteries

Sage Therapeutics™