



Investor Presentation

February 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 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 or an increase in the number of treated patients at existing sites; the potential timing of revenue growth; the potential for favorable reimbursement of ZULRESSO; our development plans, goals and strategy and the potential timing and results of our development efforts; our plans to determine next steps with respect to the development and regulatory path forward for zuranolone and the Landscape Program, including any potential amendments to our clinical trials of zuranolone; our belief in the potential of our product candidates in various indications; the potential profile and benefit of our product candidates; and 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 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 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 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, including, for our product candidates, as a result of an increase in dosing in clinical trials.
 - 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.
 - 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 annual 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.

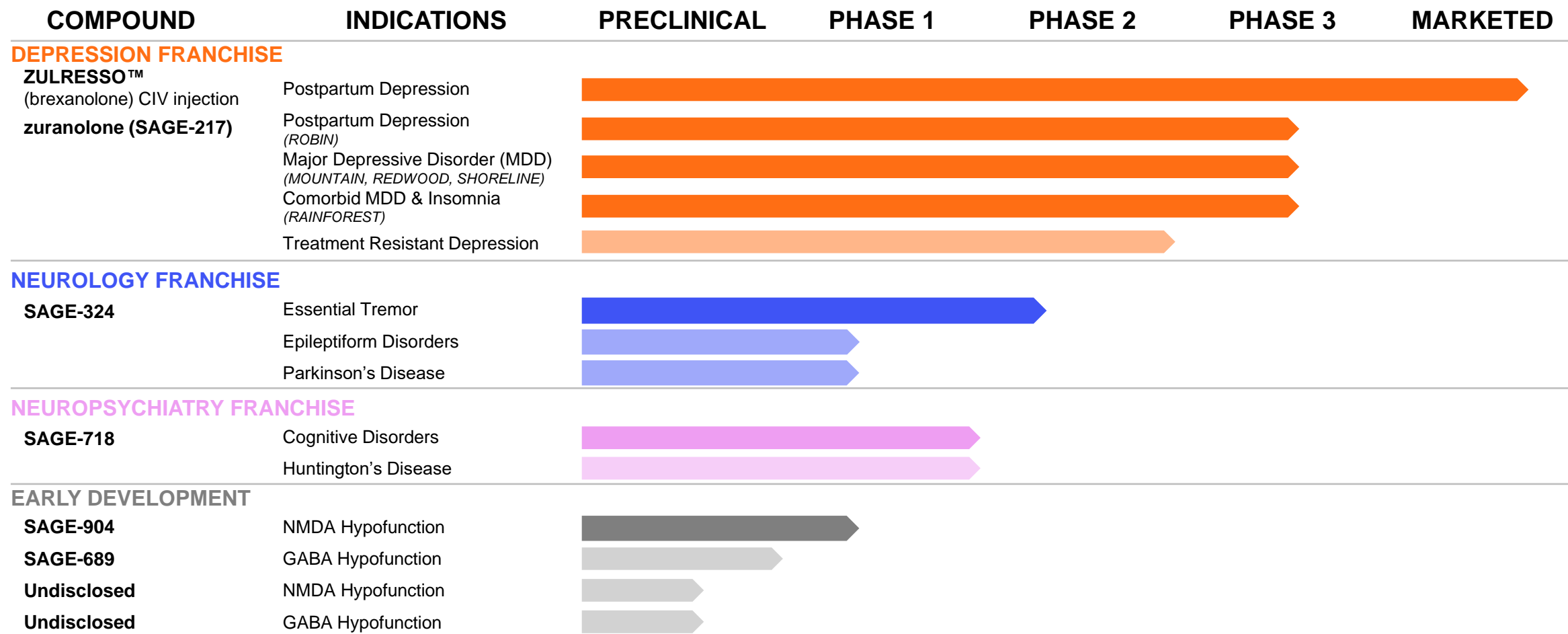
Who We Are: Sage Therapeutics

- 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** approved product for postpartum depression
 - **5** NCE clinical candidates across **8** indications
 - In-house library of **>6K** proprietary compounds
 - **\$1B** cash-on-hand

The Boston Globe
TOP PLACES TO WORK



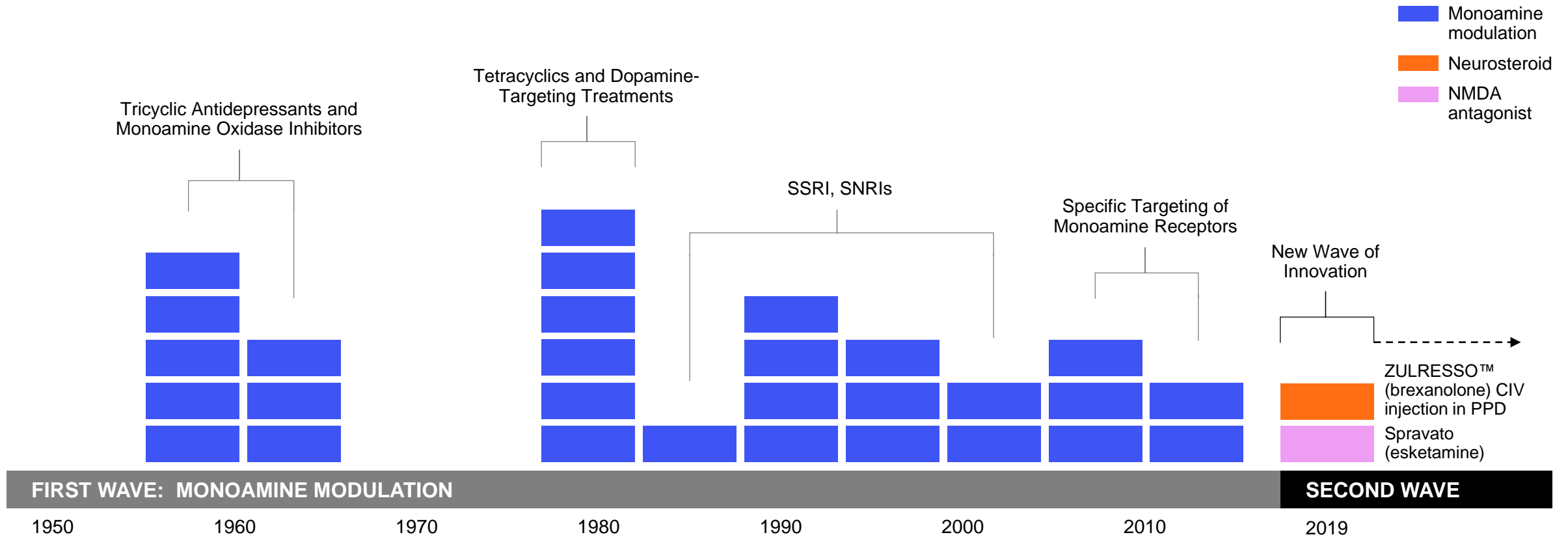
A Leading Brain Health Portfolio



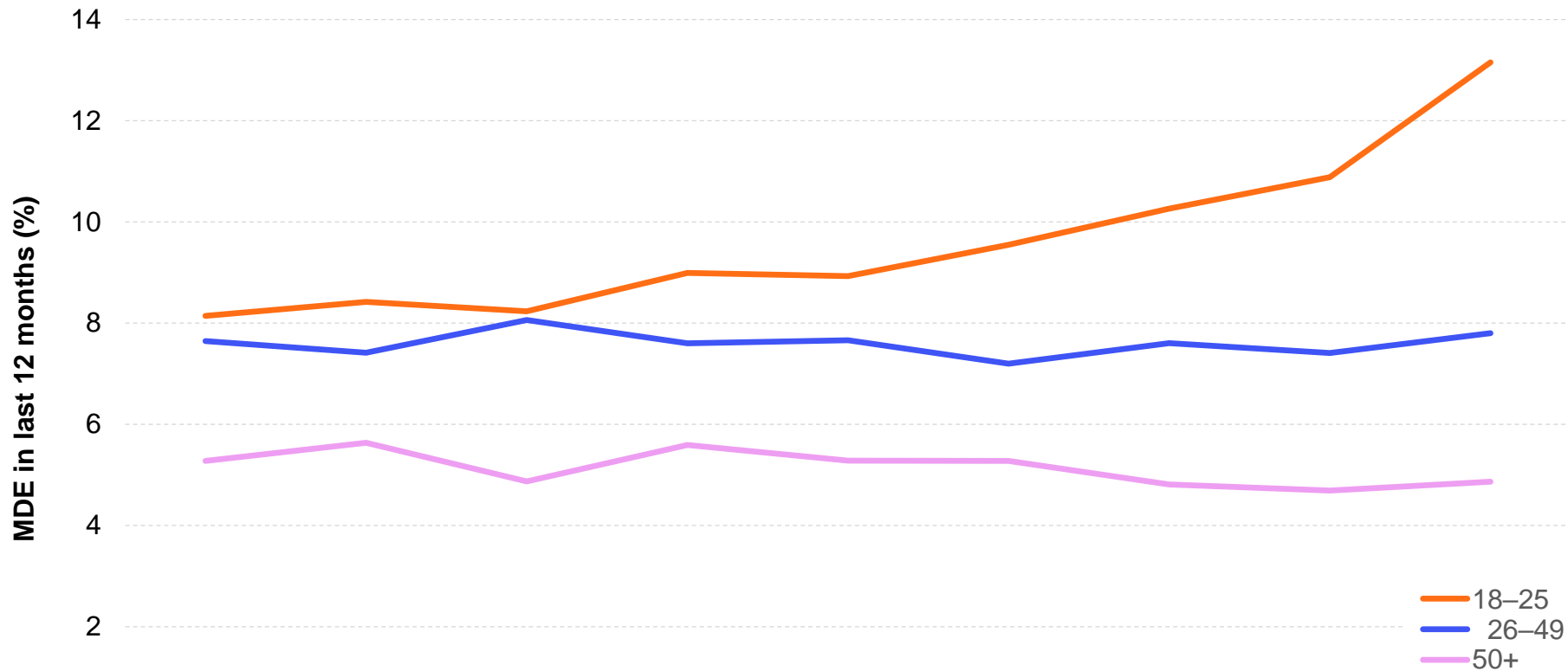
Light shades indicate trials in the planning or evaluation stage

Sage Leading Second Wave of Neuropsych Innovation

First new MOA in 60 years



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

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



Opportunity to Take on Stigma of Postpartum Depression

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

- PPD is one of the most common medical complications during and after pregnancy¹⁻⁷
- PPD can lead to devastating consequences for a woman⁸⁻¹² and for her family¹³⁻¹⁵
- Suicide is a leading cause of pregnancy related mortality¹⁶⁻¹⁸

Estimated
400k women experience PPD each year in the US^{1,16}

~50%
of patients are currently diagnosed¹⁷

20–30%
are severe^{18-20, a}

ZULRESSO™ (brexanolone) CIV Injection

Full Year 2019 update



ENABLE PATHWAYS TO CARE

- Support healthcare facilities in advancing through key actions required to become treatment-ready
 - **175+** ZULRESSO REMS-certified sites of care across **75 of the top 140** Metropolitan Statistical Areas in the U.S.
 - **29** sites of care completed the steps required to be treatment-ready and infused patients with ZULRESSO
- Estimate the majority of sites will take **9+ months** to become treatment-ready
 - Anticipate that large hospitals and healthcare systems will take **12 months or longer**

SUPPORT ACCESS AND REIMBURSEMENT

- Favorable payor coverage with satisfactory reimbursement
 - **80%** of aggregated lives have coverage with **light to no restrictions** across plans
 - Sites must often negotiate the reimbursement amount for each payor under commercial coverage
- Focus on enabling access to treatment through Medicaid reimbursement
 - **HCPCS C-code assigned to ZULRESSO** by the Centers for Medicare & Medicaid Services in January 2020
 - Availability and sufficiency of Medicaid reimbursement varies by state and often depends on whether the state treats the ZULRESSO infusion as an outpatient or inpatient administration

FOCUS ON PATIENT EXPERIENCE

- Strong patient demand and support from HCPs
 - **50% increase** in the number of patient start forms and a **100% increase** in HCP referrals from 3Q19 to 4Q19
 - **500+** patient start forms and **300+** referring HCPs since launch
- Provide customized case management services to women with PPD through Sage Central, Sage's national patient support center
 - **95%+** of referred patients are utilizing Sage Central's resources

Zuranolone's (SAGE-217) Landscape Program

Potential to reshape the depression landscape



MOUNTAIN
STUDY



REDWOOD
STUDY



SHORELINE
STUDY

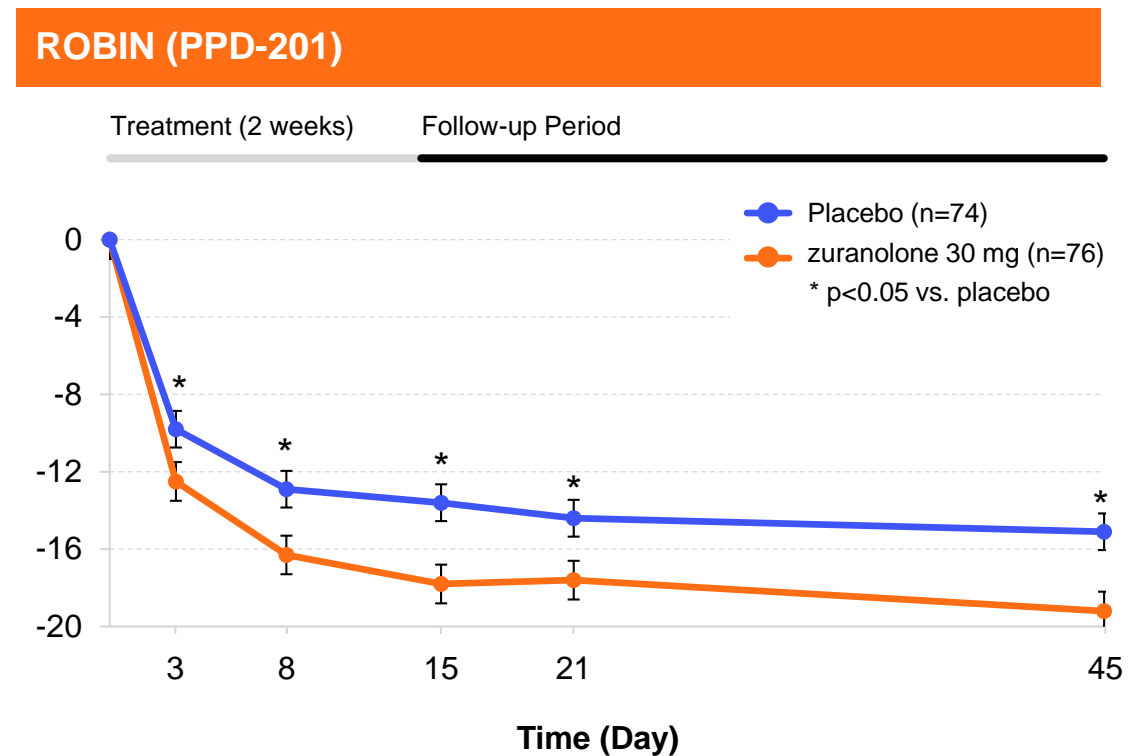
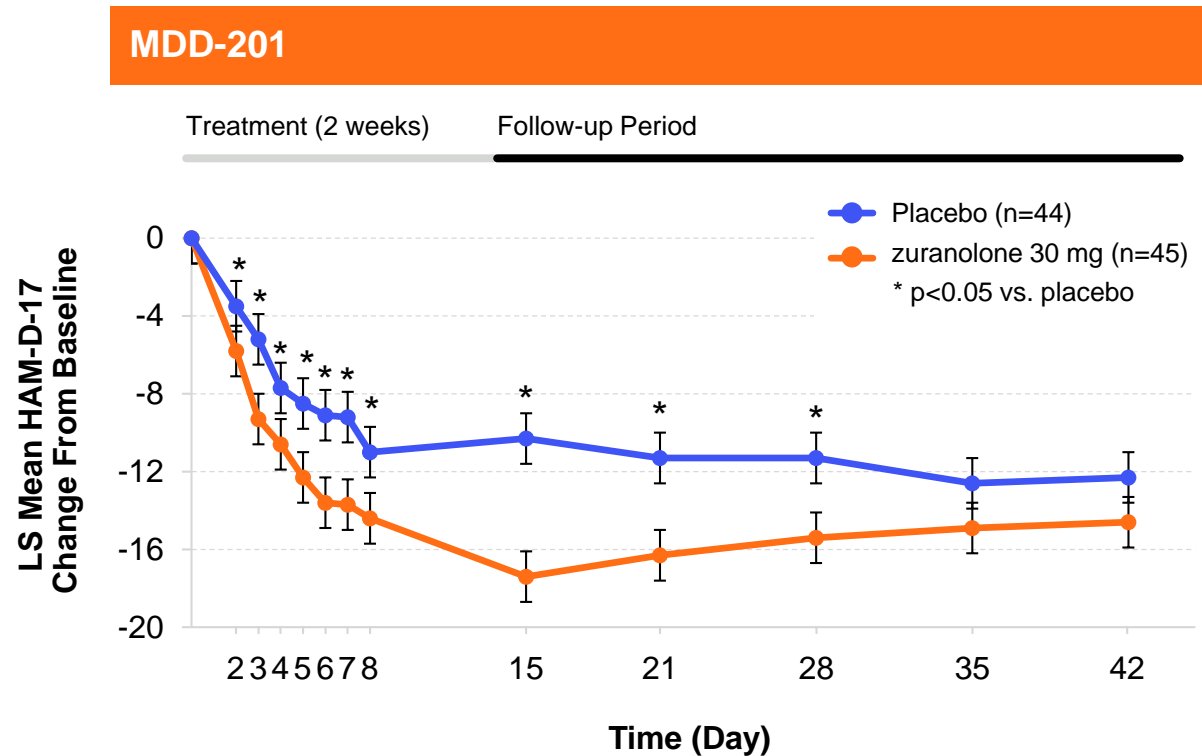


RAINFORREST
STUDY

STUDY	MDD-201	PPD-201	MDD-301	MDD-302	MDD-303	MDD-304
Indication	MDD	PPD	MDD	MDD	MDD	Co-morbid MDD and Insomnia
Phase	Pivotal Ph. 2	Pivotal Ph. 2	Pivotal Ph. 3	Pivotal Ph. 3	Pivotal Ph. 3	Pivotal Ph. 3
Objectives	Efficacy in the treatment of MDD compared to placebo	Efficacy in the treatment of PPD 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 re-treatment(s) over a 1-year period	Efficacy in the treatment of sleep efficiency
Status	Complete	Complete	Complete	Potential Amendments	Enrollment Complete (30 mg); Potential Amendments	Potential Amendments

MDD-201 & ROBIN Studies

Rapid onset of activity with generally well-tolerated safety profile



Zuranolone was generally well-tolerated in both studies

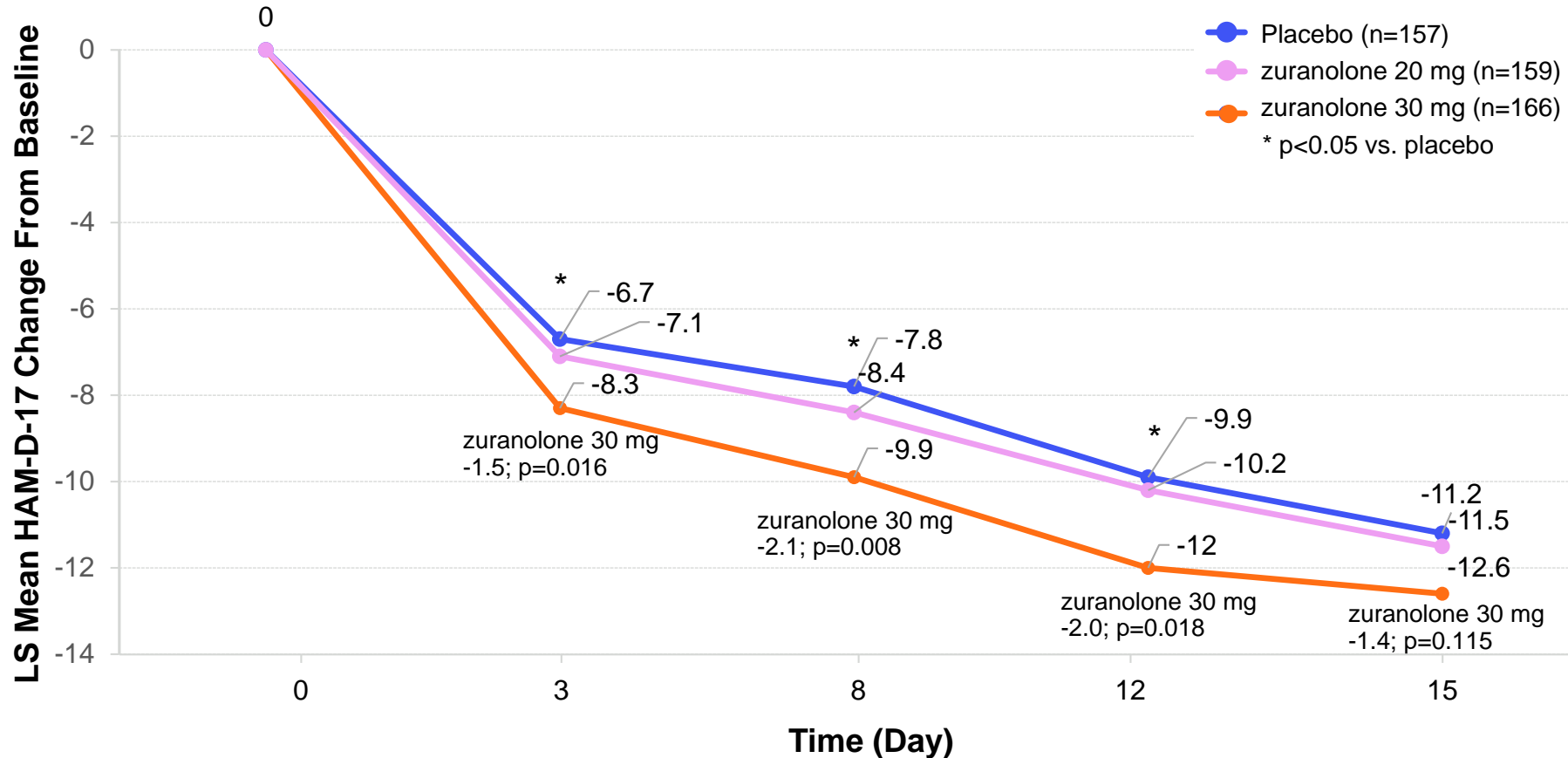
The most common AEs ($\geq 5\%$) in the MDD-201 study included headache, dizziness, nausea, and somnolence

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



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 ($\geq 5\%$) 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

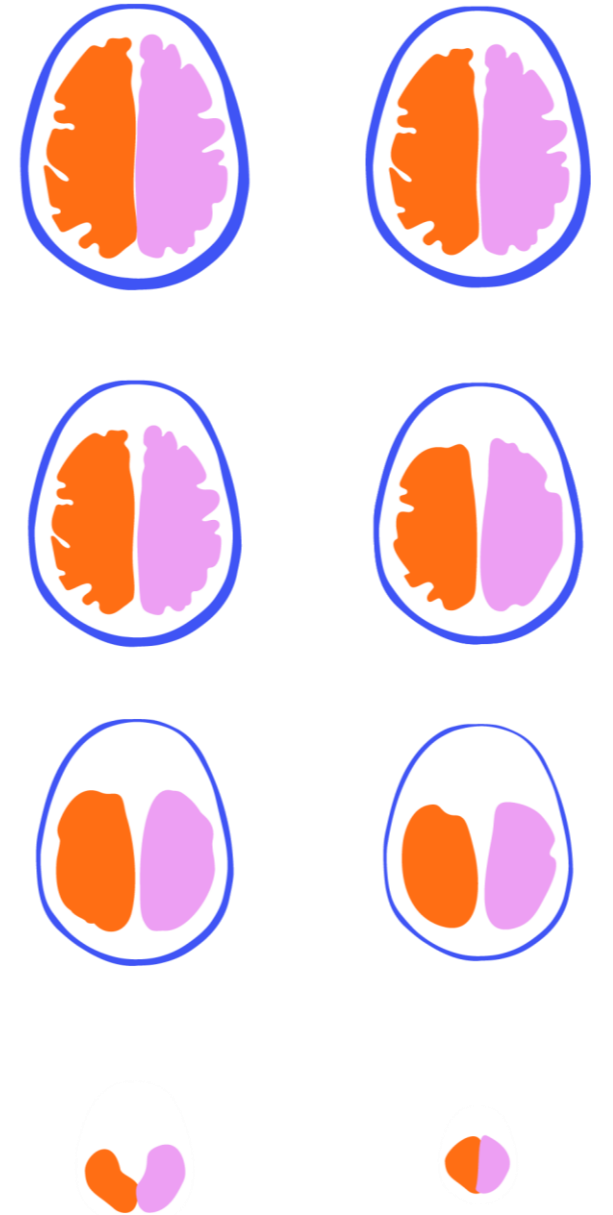
Actionable Insights for the Landscape Program

- Learnings from completed studies inform path forward
 - Observed consistent activity and tolerability profile
 - Will evaluate potential to achieve higher exposure to maximize activity
 - Data continue to support paradigm shift to treatment-free intervals
- Sage previously announced that a meeting with the FDA to discuss zuranolone would occur in the first quarter of 2020. The Company continues to evaluate data from the MOUNTAIN Study and will announce next steps in the Landscape Program upon completion of relevant correspondence with the FDA, including receipt of meeting minutes, and determination of the development and regulatory path forward

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-324 in Essential Tremor

On track to initiate Phase 2 placebo-controlled study in 1H 2020

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 interventions²¹
- Approximately 50% of diagnosed patients receive pharmacotherapy for ET²²

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%

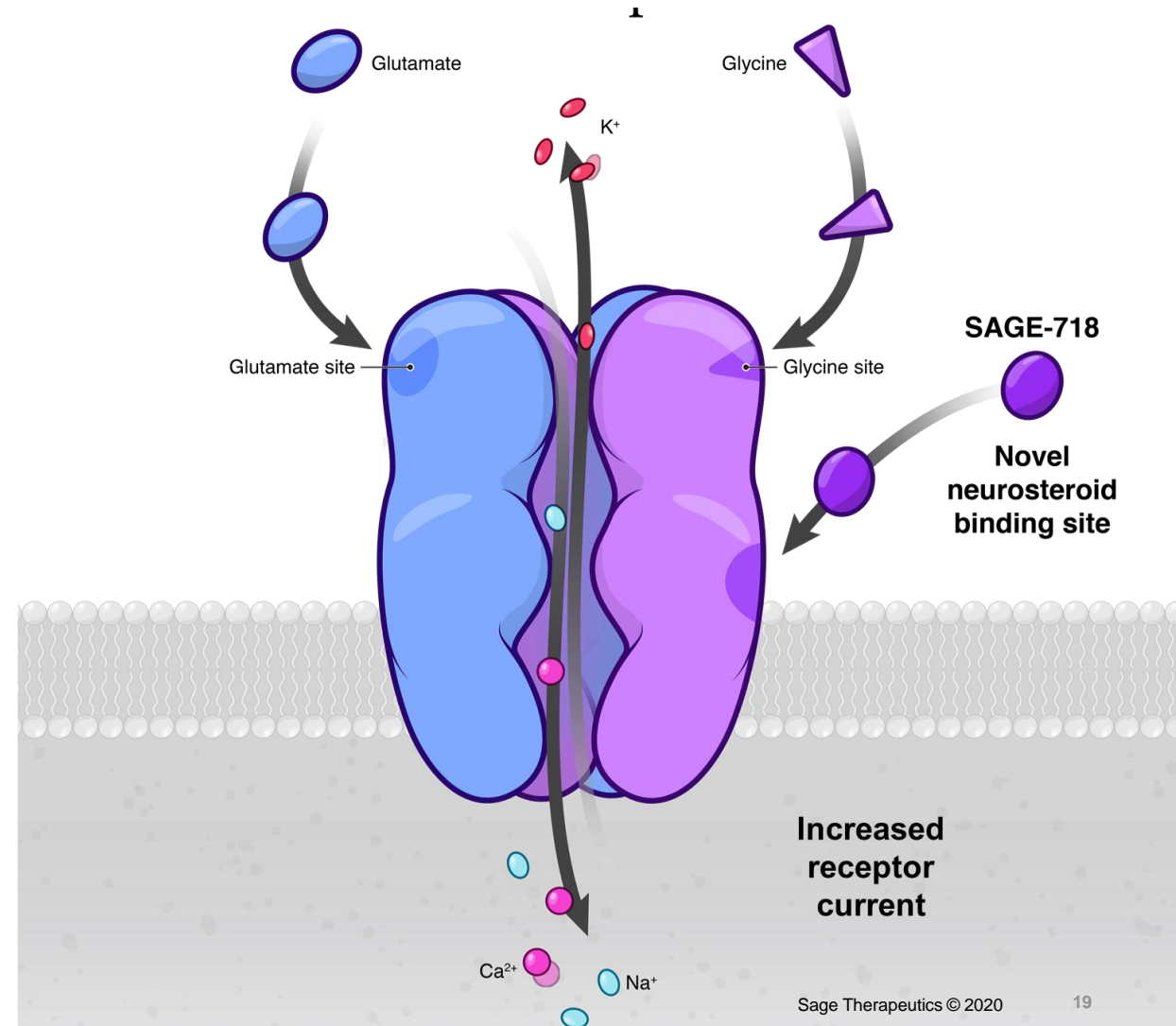
of patients seeking care do not respond or have a sub-optimal response to standard of care²³

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

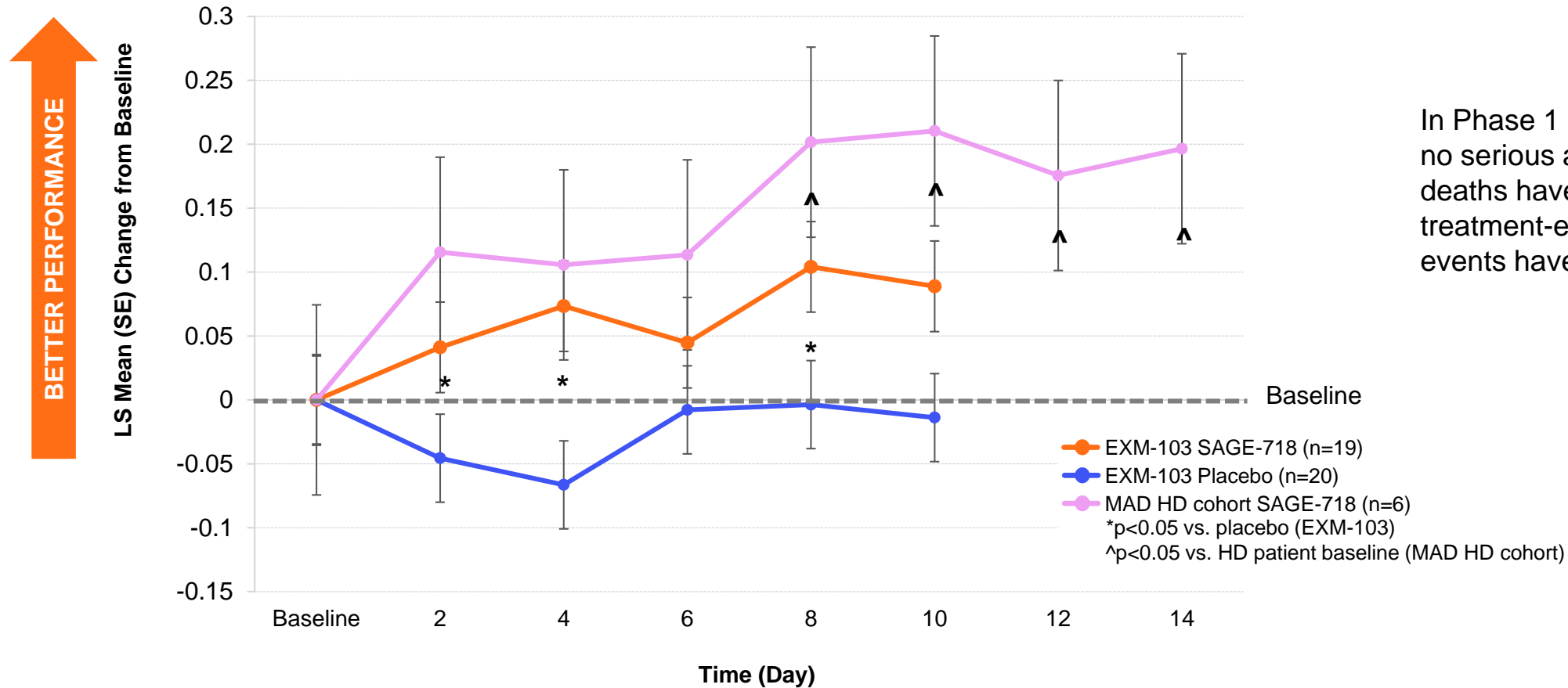
Endogenous & Exogenous Ligands at the NMDA Receptor



SAGE-718 Demonstrated Activity on Executive Function

Assessment using two-back test

SAGE-718 IN HEALTHY VOLUNTEERS AND IN PATIENTS WITH HUNTINGTON'S DISEASE



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

Fourth Quarter & Full Year 2019 Financial Results

Strong financial position with \$1B in cash

	4Q'19	4Q'18	FY'19	FY'18
Cash and Marketable Securities			\$1.0B	\$0.9B
Product Revenue	\$2.0M	–	\$4.0M	–
Collaboration Revenue	–	\$0.3M	\$2.9M	\$90.3M
Total Revenue	\$2.0M	\$0.3M	\$6.9M	\$90.3M
Operating Costs & Expenses				
Costs of Goods Sold	\$0.2M	–	\$0.4M	–
Research & Development	\$91.3M	\$88.8M	\$368.8M	\$282.1M
Selling, General & Administrative	\$85.1M	\$75.7M	\$345.8M	\$201.4M
Total Operating Costs & Expenses	\$176.6M	\$164.5M	\$715.0M	\$483.5M
Net Loss	(\$168.7M)	(\$158.4M)	(\$680.2M)	(\$372.9M)

Financial Guidance

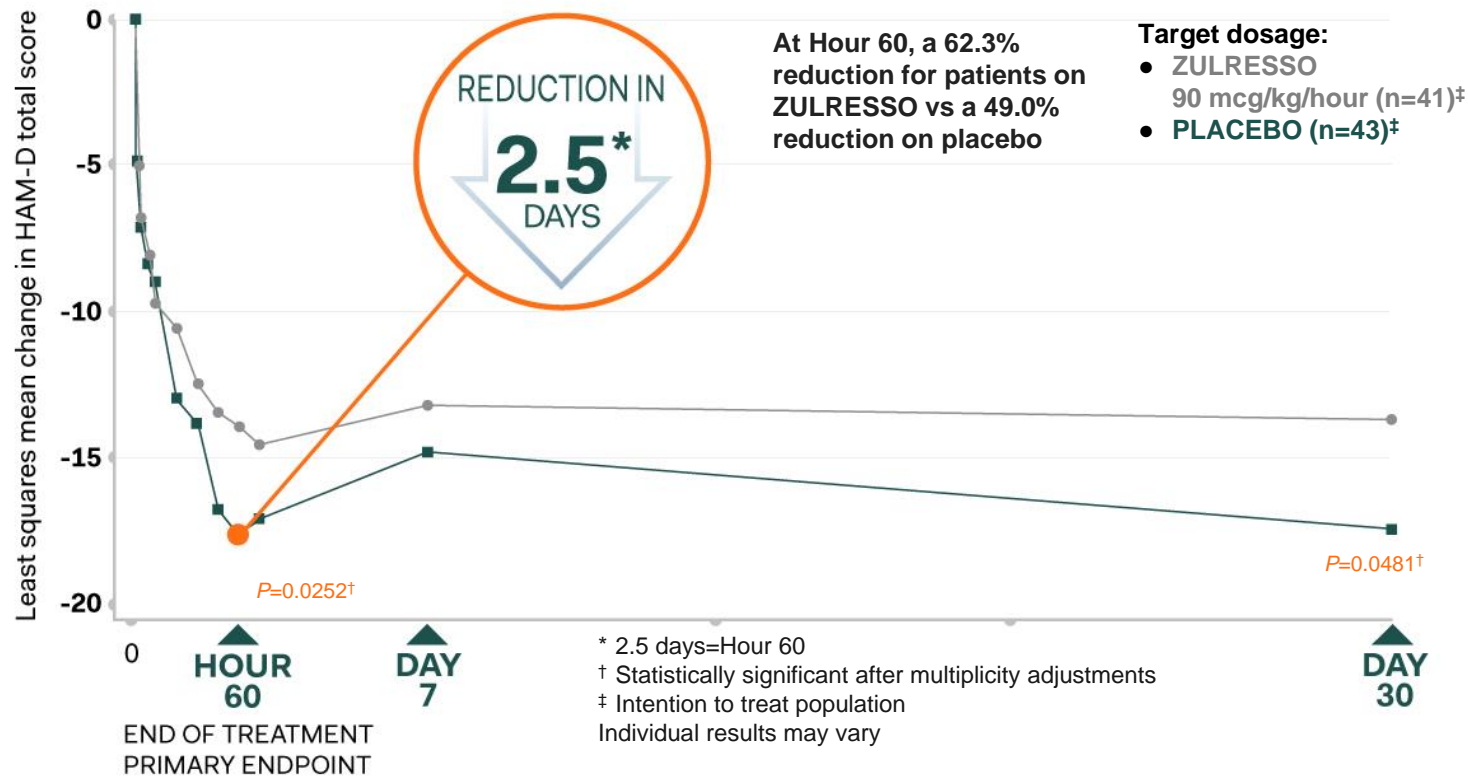
- Sage expects ZULRESSO™ (brexanolone) CIV injection revenue growth will be modest over the next couple of quarters with an increase in the rate of growth of ZULRESSO revenue anticipated in the second half of 2020, assuming an increase in the number of treatment-ready sites, including larger hospitals administering ZULRESSO to treat women with PPD, and an increase in the volume of patients treated at existing sites. To accomplish this objective, Sage is guiding large sites through the steps necessary to become treatment-ready and supporting hospital administrations' efforts to reduce the complexity of those steps

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 30ⁱ

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 placeboⁱ

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 REMSⁱⁱⁱ

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



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.

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



\$90M

Upfront payment

\$485M

Potential development & commercial milestones

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