Sage Therapeutics™

J.P. Morgan Healthcare Conference

January 13, 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; the potential timing of revenue momentum; the potential for favorable reimbursement of ZULRESSO; our development and regulatory plans, goals and strategy and the potential timing and results of our efforts; the estimated prevalence of the disorders our products or product candidates may treat; the unmet need for new treatment options in areas we have pursuing; our belief in the potential of our product candidates in various indications; our belief in the leading nature and goal of our innovation; 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.
  - Regulatory authorities may delay scheduled meetings with us, may not agree with our proposals or may not give us the guidance that we seek. At any stage, regulatory authorities may ask for additional clinical trials, nonclinical studies or other data in order for us to proceed further in development or to obtain regulatory approval, and we may not be successful in these efforts.
  - 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 and the safety and tolerability profile may change at higher doses or as we treat more patients or in commercial use.
  - 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 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.

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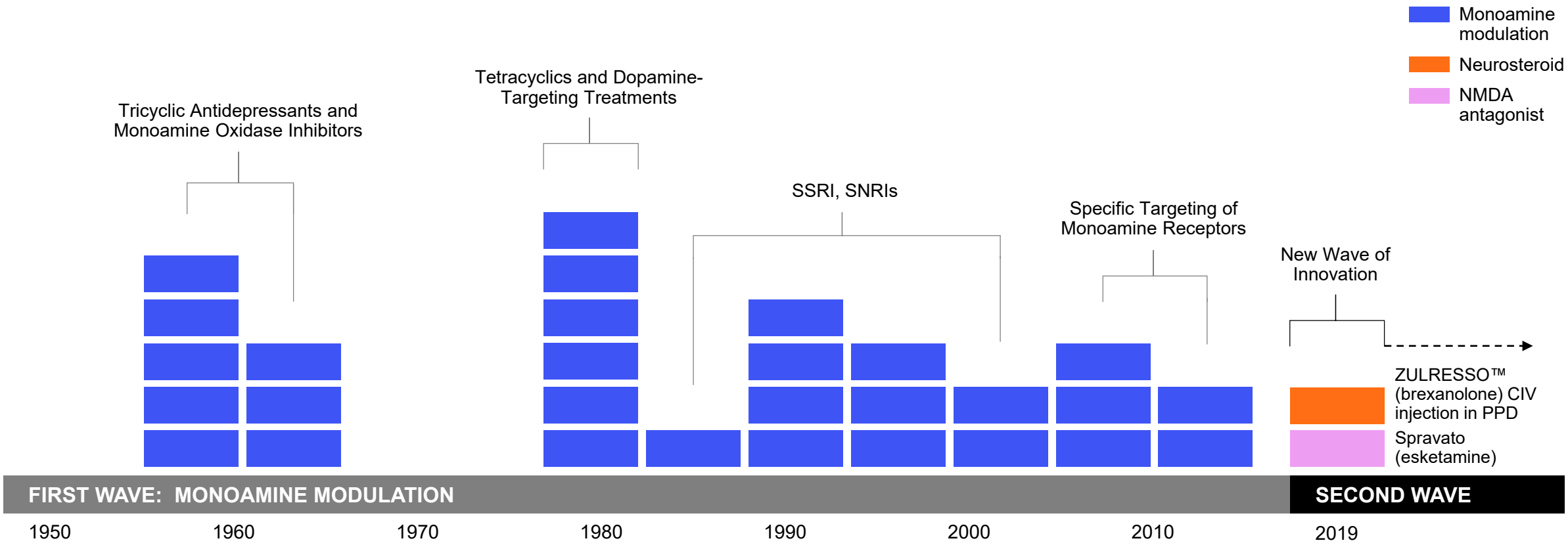
Sage Leading Second Wave of Neuropsych Innovation

First new MOA in 60 years



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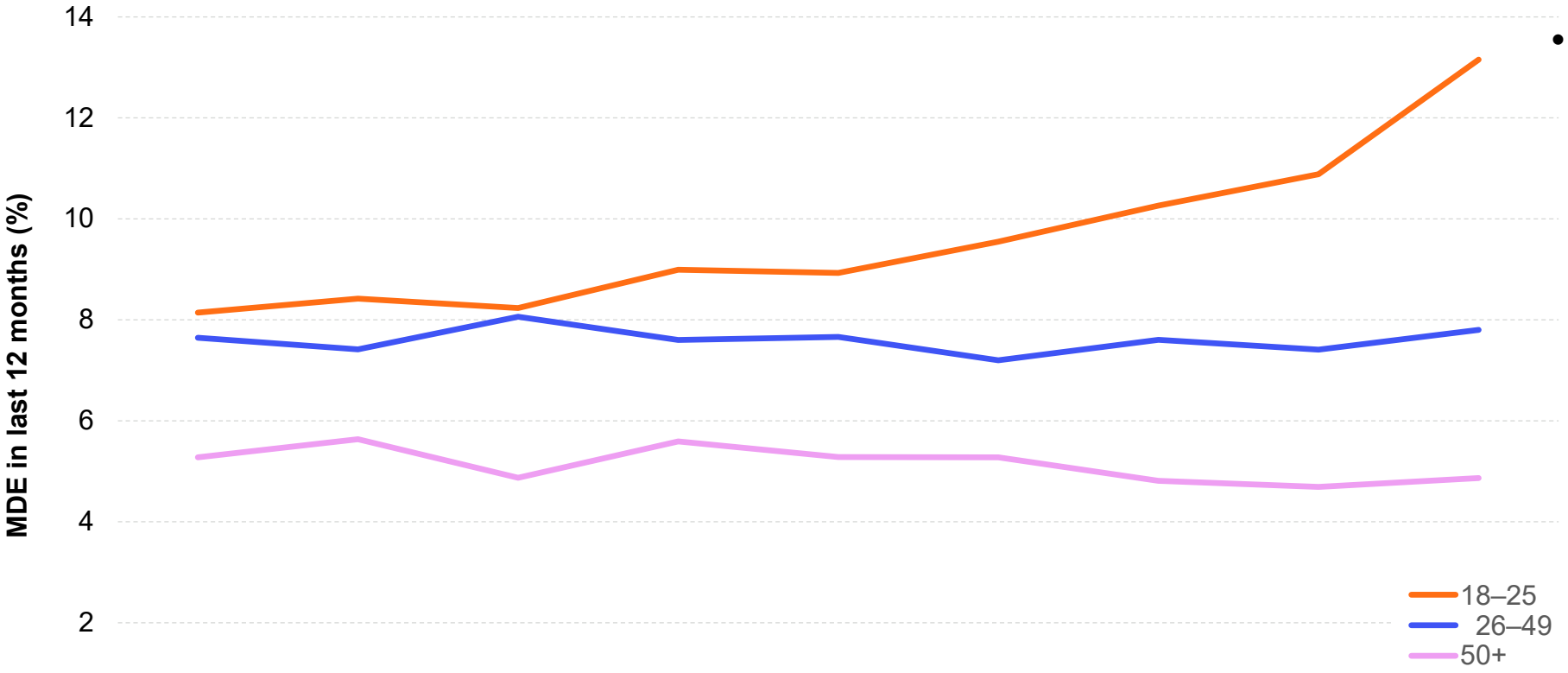
Source: Thomas, D., & Wessel, C. (2017). The State of Innovation in Highly Prevalent Chronic Diseases: Volume I: Depression Therapeutics. BIO.

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 by 63%** from 2009 to 2017

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

2009 2017 2019

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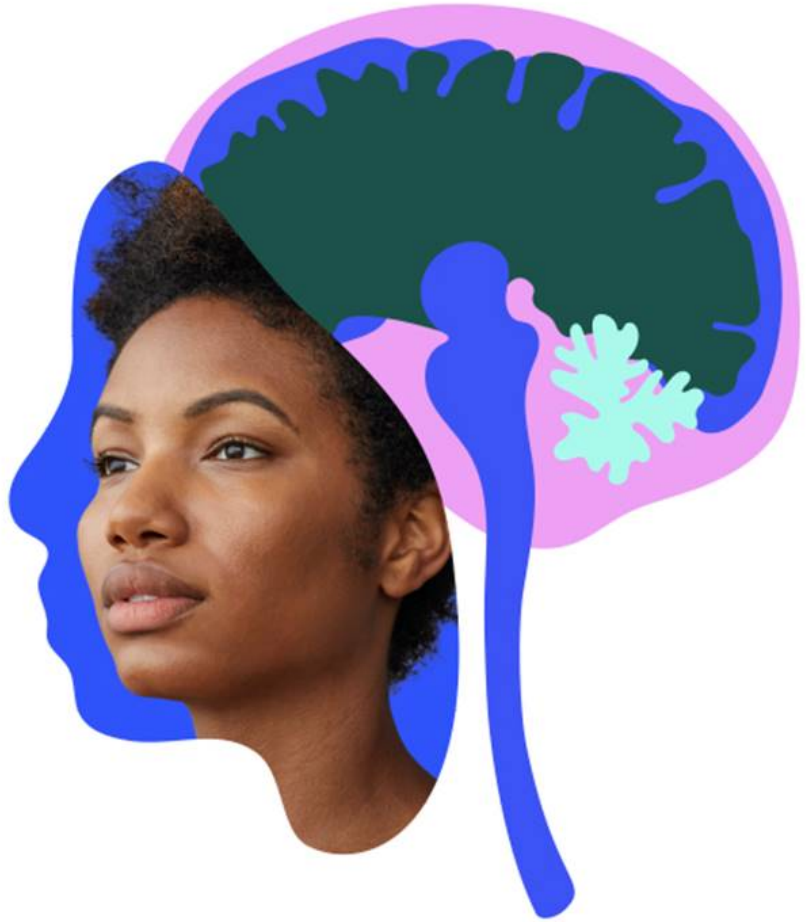
Sources: J Abnorm Psychol. 2019 Apr;128(3):185-199. doi: 10.1037/abn0000410. Epub 2019 Mar 14.

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

The Boston Globe
TOP PLACES TO WORK



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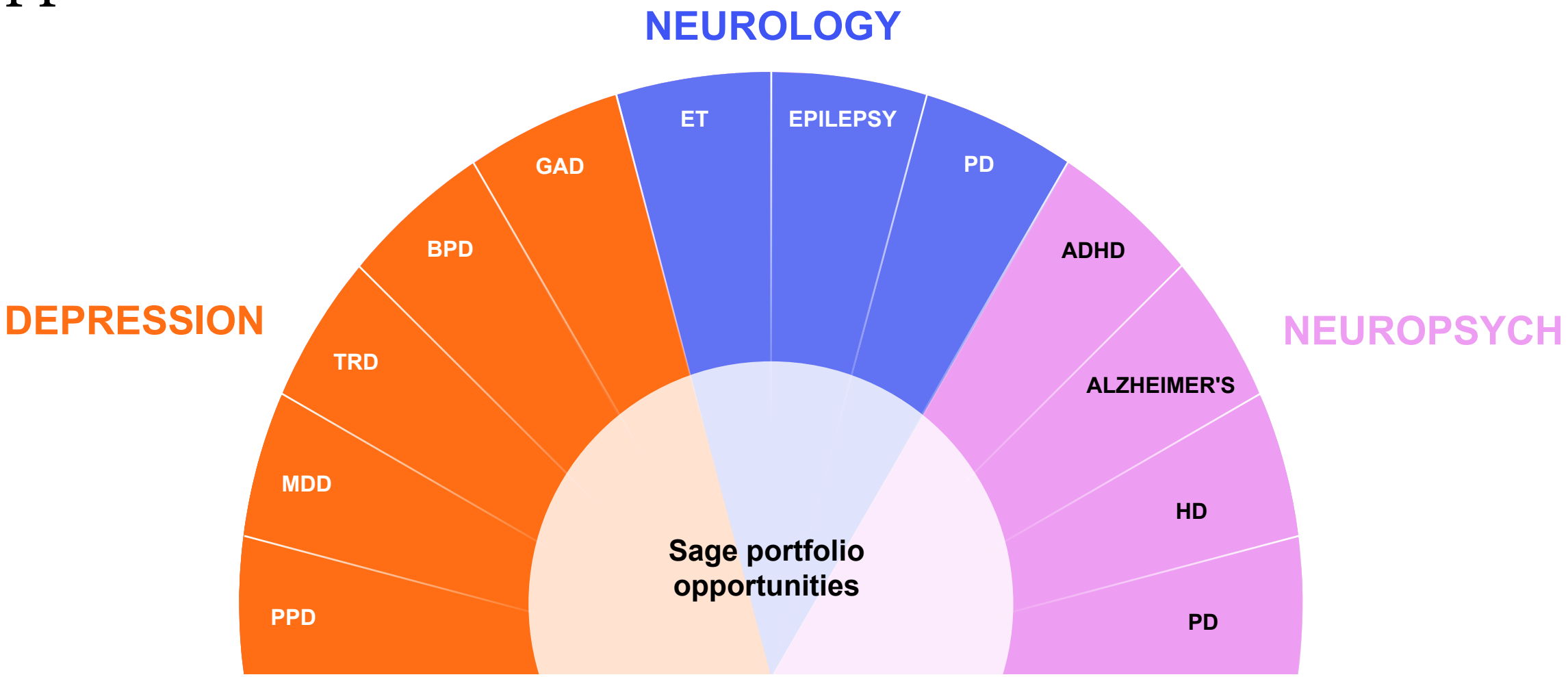
Abbreviations: NCE = new chemical entity

Multi-Franchise Company with Near, Mid- and Long-term Opportunities



Abbreviations: PPD = postpartum depression, MDD = major depressive disorder, TRD = treatment-resistant depression, BPD = bipolar disorder, GAD = generalized anxiety disorder, ET = essential tremor, PD = Parkinson's Disease, HD = Huntington's Disease, ADHD = attention deficit hyperactivity disorder

Depression Franchise

Making Psychiatry 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

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ZULRESSO™ (brexanolone) CIV Injection

First of a new generation of antidepressants

ENABLE PATHWAYS TO CARE

- Support healthcare facilities in advancing through key actions required to become treatment-ready
- Typically 6-9 months, or more, for sites to be treatment-ready

SUPPORT ACCESS AND REIMBURSEMENT

- Driven strong payer coverage (>75%*) enabling access for women with postpartum depression (PPD) and satisfactory reimbursement from payers

FOCUS ON PATIENT EXPERIENCE

- Sage Central supports women with PPD by providing customized case management services

SAGE CENTRAL™
PATIENT SUPPORT

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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

* Payer coverage as of September 30, 2019

Zuranolone's (SAGE-217) Potential to Reshape Depression Landscape

Novel NCE with strong path forward and anchor asset for Depression Franchise

STUDY	MDD-201	PPD-201	MDD-301	MDD-302	MDD-303	MDD-304
		ROBIN STUDY	MOUNTAIN STUDY	REDWOOD STUDY	SHORELINE STUDY	RAINFOREST STUDY
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	Effectiveness (polysomnography) on insomnia symptoms
Status	Complete	Complete	Complete	Evaluating Potential Amendments	Enrollment Complete	Evaluating Potential Amendments

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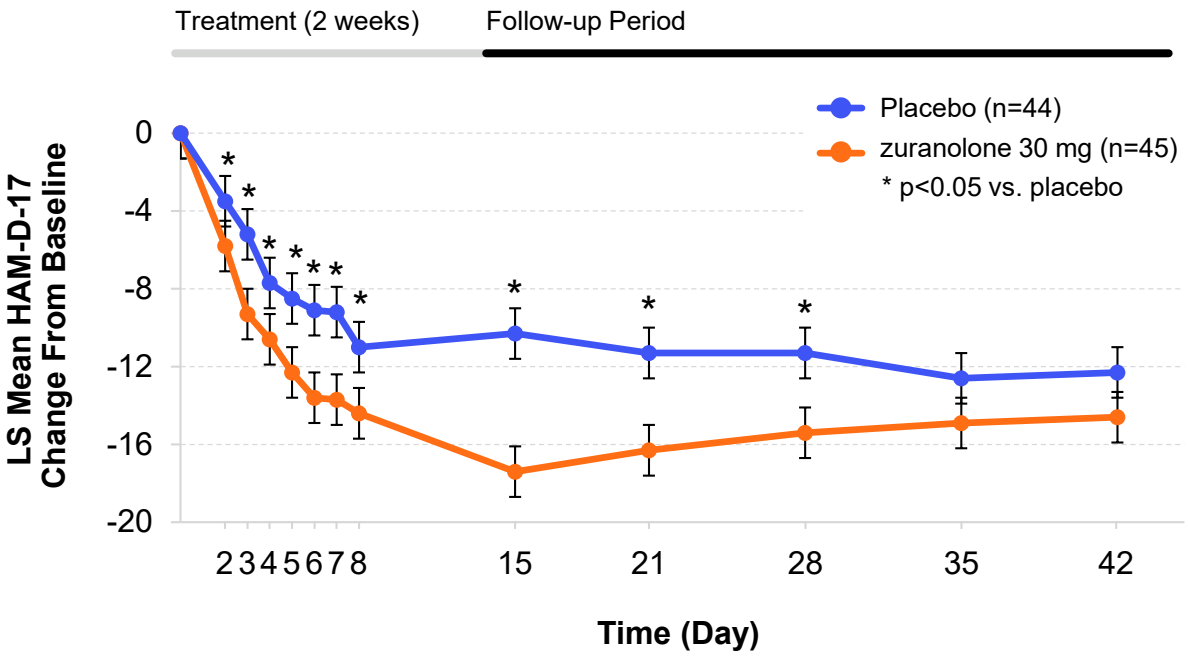
Abbreviations: PPD = postpartum depression, MDD = major depressive disorder, NCE = new chemical entity

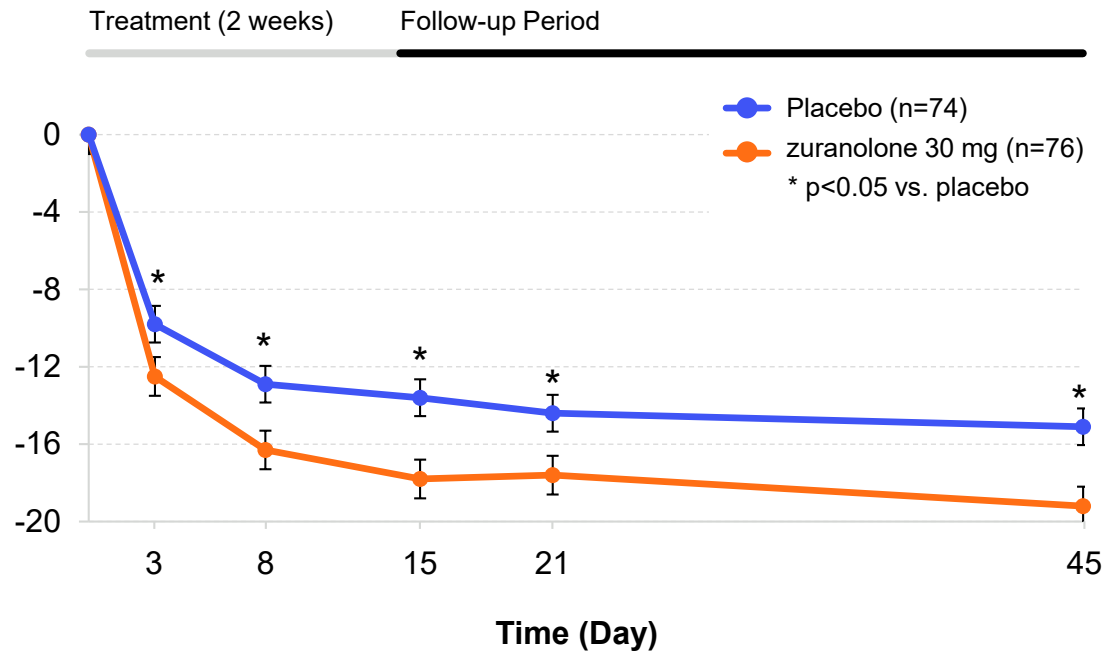
MDD-201 & ROBIN Studies

Replication of 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

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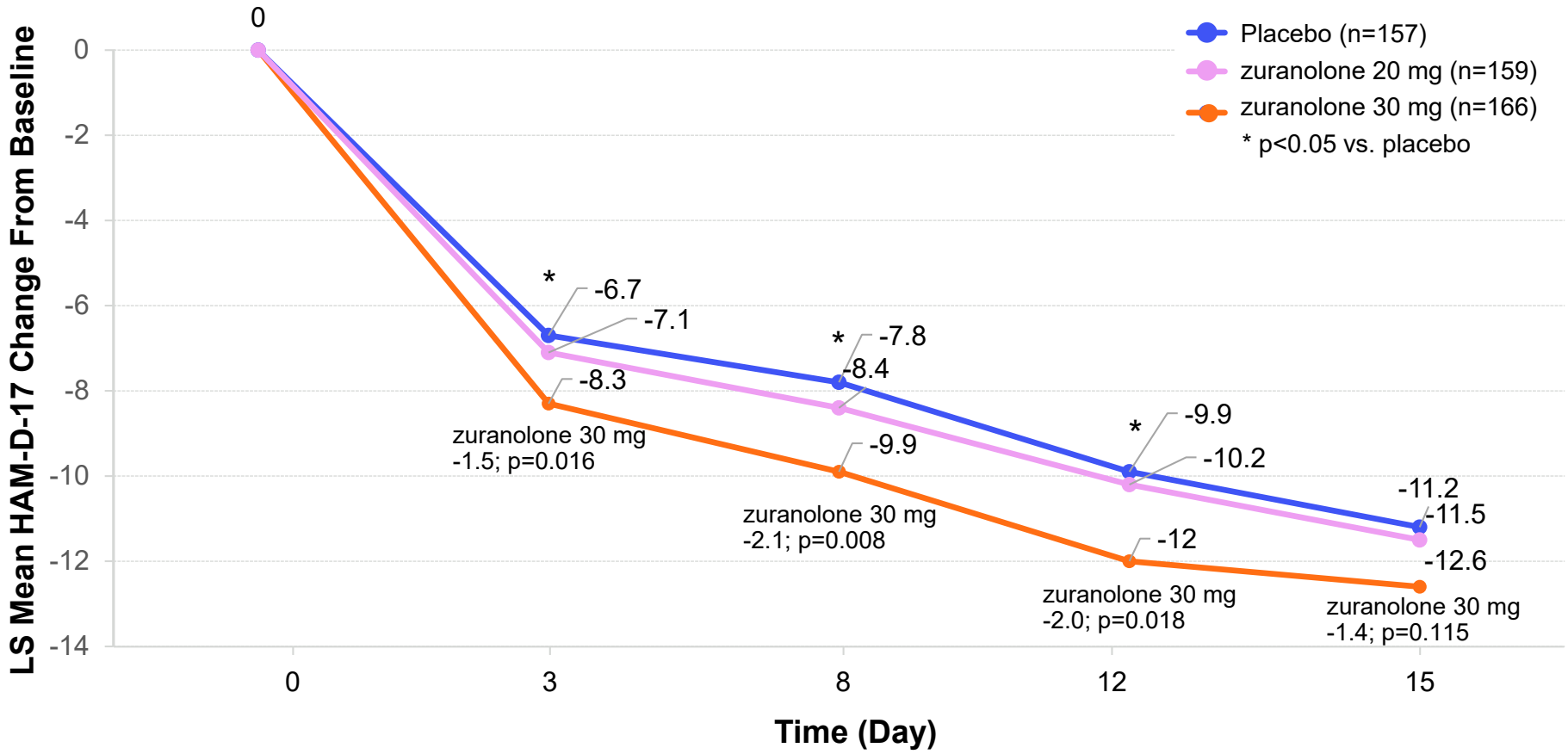
Abbreviations: AEs = adverse events

MOUNTAIN Study

Continues to display activity with rapid onset



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

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Abbreviations: AEs: = adverse events

Actionable Insights for the Landscape Program

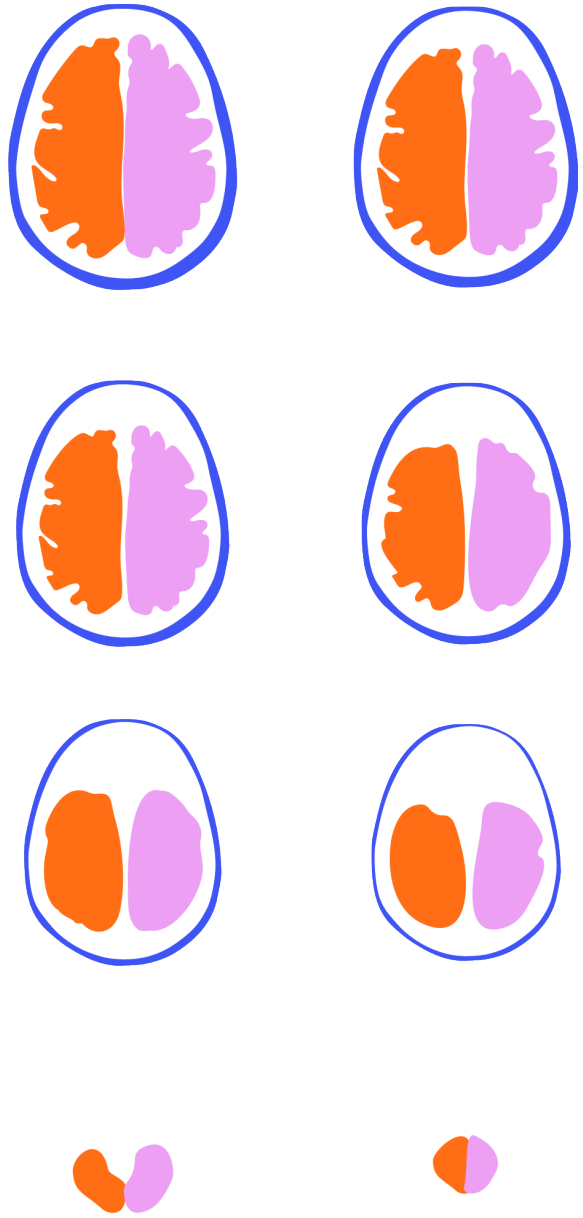
- **Learnings from completed studies inform path forward**:
  - Observed consistent activity and tolerability profile
  - Will evaluate potential to achieve higher exposure to maximize activity
  - Data continue to support paradigm shift to treatment-free intervals

- **Meeting scheduled with FDA in 1Q 2020 to evaluate proposed 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



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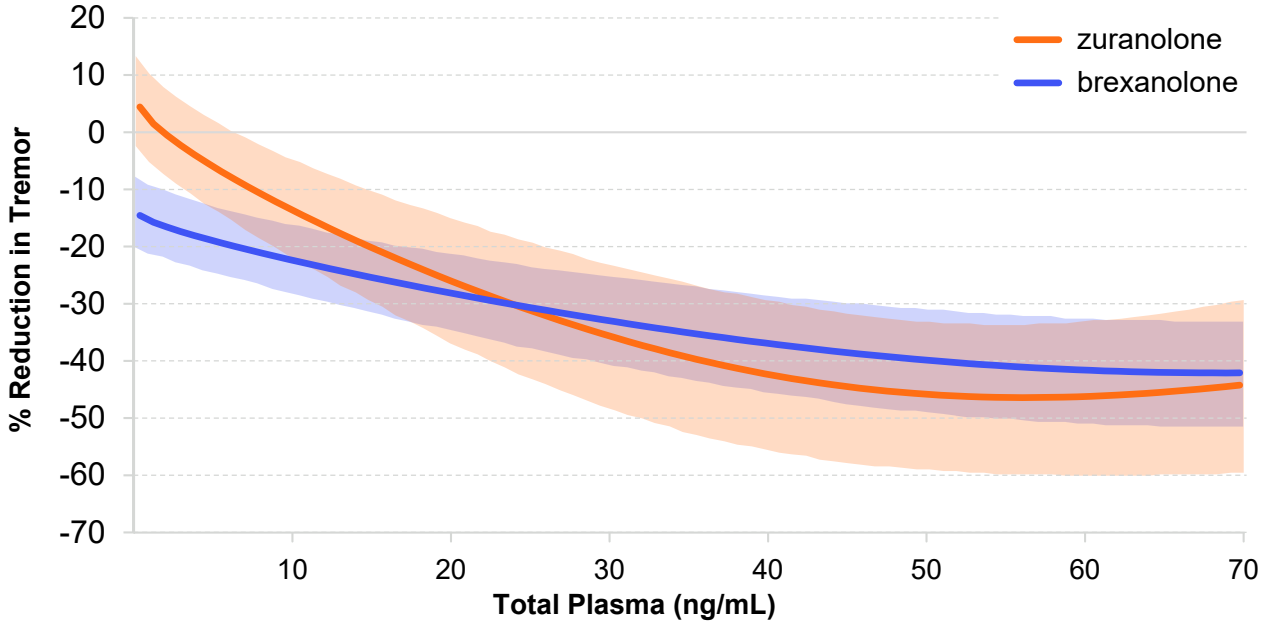
On Track to Initiate Phase 2 Study in Essential Tremor

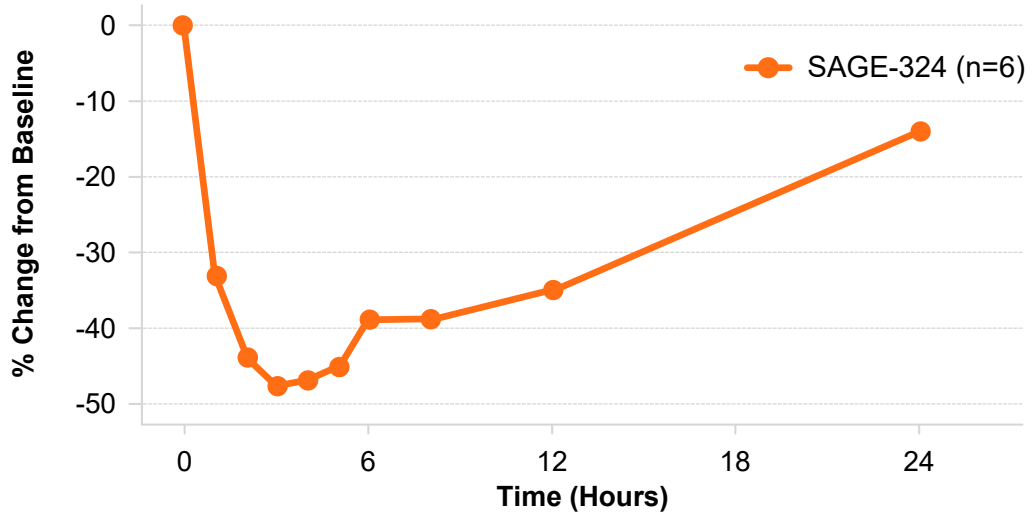
- **Essential tremor (ET)** is the most prevalent movement disorder, estimated to affect more than **6M** people in the U.S.; up to 1M seek treatment
- **High unmet need**; 50% of treated patients do not respond or have sub-optimal response to standard of care[1]

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

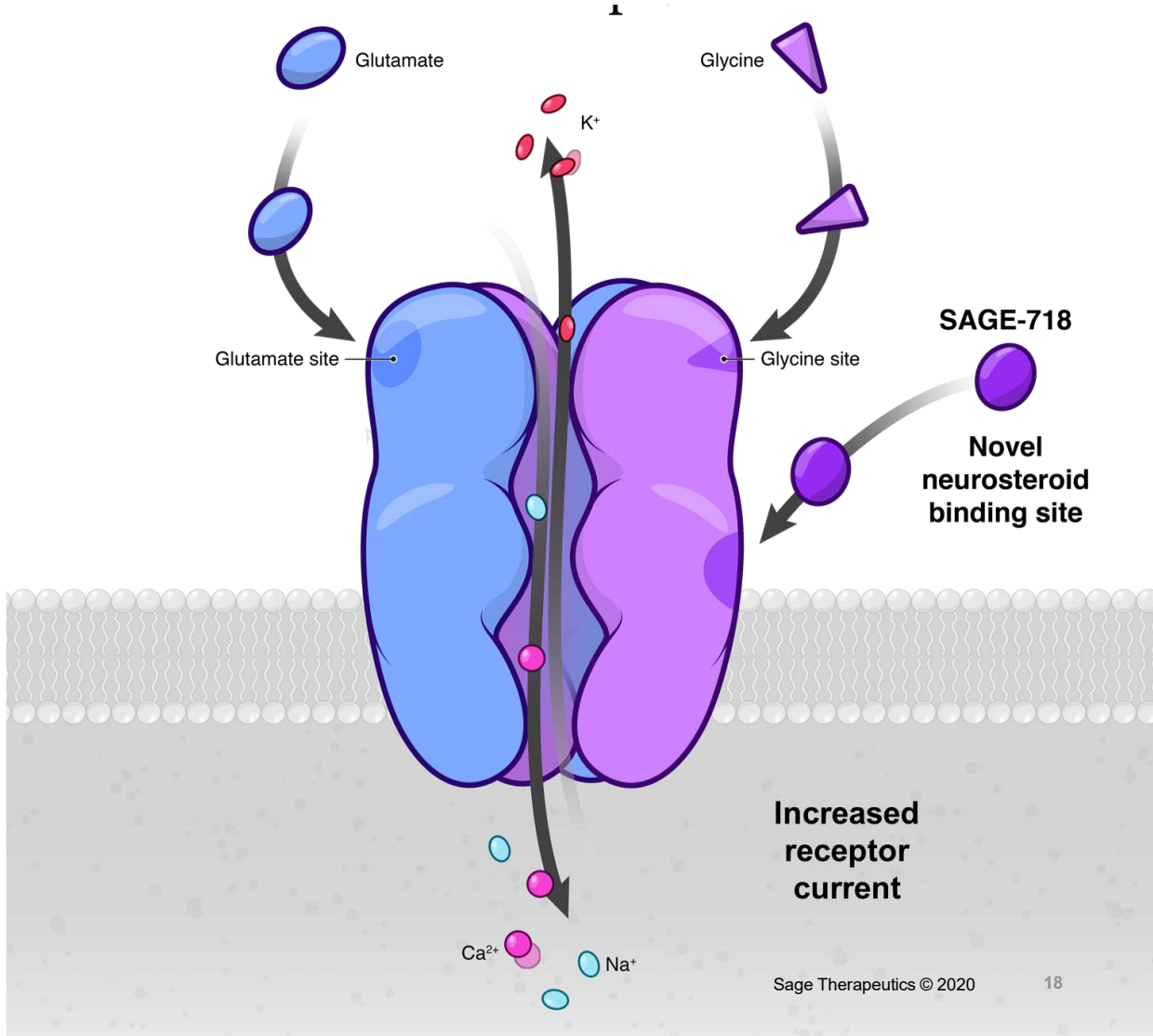
Source: [1]Louis et al.; Abbreviations: AEs = adverse events

Neuropsych 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 NMDAR (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



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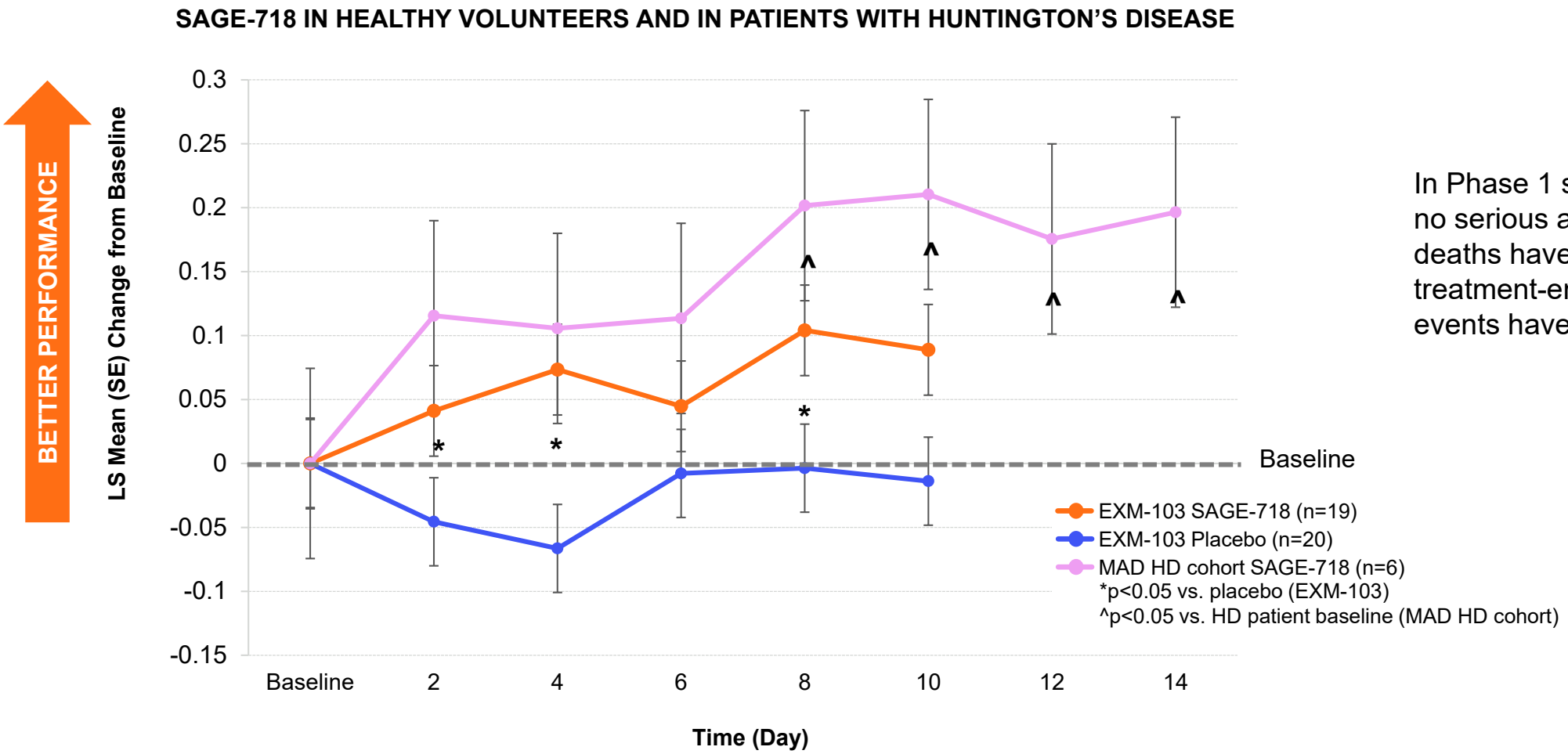
SAGE-718 Demonstrated Activity on Executive Function

Assessment using two-back test



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

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A Leading Brain Health Portfolio

COMPOUND	INDICATIONS	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	MARKETED
DEPRESSION FRANCHISE						
ZULRESSO™ (brexanolone) CIV injection	Postpartum Depression					
zuranolone (SAGE-217)	Postpartum Depression *(ROBIN)*					
	Major Depressive Disorder (MDD) *(MOUNTAIN, REDWOOD, SHORELINE)*					
	Comorbid MDD & Insomnia *(RAINFOREST)*					
	Treatment Resistant Depression					
NEUROLOGY FRANCHISE						
SAGE-324	Essential Tremor					
	Epileptiform Disorders					
	Parkinson's Disease					
NEUROPSYCH FRANCHISE						
SAGE-718	Cognitive Disorders					
	Huntington's Disease					
EARLY DEVELOPMENT						
SAGE-904	NMDA Hypofunction					
SAGE-689	GABA Hypofunction					
Undisclosed	NMDA Hypofunction					
Undisclosed	GABA Hypofunction					

Light shades indicate trials in the planning or evaluation stage

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Anticipated Milestones in 2020
Continued focus on execution

FRANCHISE	PROGRAM	ANTICIPATED MILESTONE
DEPRESSION	**ZULRESSO™ (brexanolone) CIV injection**	C-code implementation EMA discussions
	zuranolone (SAGE-217)	Meeting with the FDA to discuss path forward in Landscape Program (1Q 2020) Resume REDWOOD and RAINFOREST studies with amended protocols SHORELINE topline data
NEUROLOGY	**SAGE-324**	Initiate Ph. 2 study in essential tremor (1H 2020)
NEUROPSYCH	**SAGE-718**	Explore additional patient populations in other neuropsych indications Continue preparations for Ph. 2 study in Huntington's Disease

Seeing the brain differently *makes a world of difference*

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