SAGE THERAPEUTICS

Rethinking CNS

February 22, 2018

Q4 and Full Year 2017 Financial Results

Agenda – Today's Speakers

- **Paul Cox**, Senior Director, Investor Relations
- **Jeff Jonas**, M.D., Chief Executive Officer
- **Steve Kanes**, M.D., Ph.D., Chief Medical Officer
- **Kimi Iguchi**, Chief Financial Officer
- **Q&A Session** (joined by Mike Cloonan, Chief Business Officer and Jim Doherty, Ph.D., Chief Research Officer)

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 anticipated regulatory and development activities, milestones and results, including expected timing; the potential safety, pharmacological effect and efficacy of our product candidates; the estimated number of patients with certain disorders or diseases; expectations regarding potential commercialization of our products, if successfully developed; the potential for expedited review for brexanolone in PPD as a result of the breakthough therapy or PRIME designation; our belief in the sufficiency of the Phase 3 clinical trials of brexanolone for approval; potential future indications for our product candidates; other planned activities; our strategy and business outlook; and our expectations with respect to cash needs. 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:

- Regulatory authorities may, despite prior advice, decide that the clinical and nonclinical data from our brexanolone development program in postpartum depression are not sufficient to support a filing for regulatory approval or do not support the grant of regulatory approval, and regulatory authorities may require additional trials, analyses or data;
- Issues may arise during inspections by regulatory authorities of our facilities, data and systems or those of our contract research organization, contract manufacturer or clinical sites that could delay or prevent us from gaining approval of brexanolone;
- Success in SAGE’s pre-clinical studies or in early stage clinical trials may not be repeated or observed in ongoing or future studies involving the same compound or other product candidates, and future pre-clinical and clinical results for SAGE’s product candidates may not support further development of the product candidate or regulatory approval;
- Decisions or actions of regulatory agencies may affect the initiation, timing and progress of clinical trials, or our ability to obtain marketing approval for its product candidates;
- We may not achieve expedited development or review of SAGE-217 as a result of the Breakthrough Therapy designation;
- 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 issues, delays or unexpected challenges in launching or commercializing brexanolone IV, if approved, and we may not be successful in our commercialization efforts;
- 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, in either case which may result in the need for additional funding to support its business activities earlier than anticipated;
- 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 whom we are, or will need to be, dependent for development or manufacture of products or for future marketing, sales and distribution of products, if we are successful in our development efforts;
- We may encounter technical and other unexpected hurdles in the manufacture and development of its products.

For additional disclosure regarding these and other risks SAGE faces, see the disclosure contained in the "Risk Factors" section of SAGE’s our most recent Annual Report on Form 10-K, and in SAGE’s 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 its 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™

OUR COMMITMENT

Building a global CNS company based on novel science, innovative approaches, and differentiated medicines with a clear focus on maximizing patient benefit.

Sage Accomplishments in 6 Years

Successfully Established a Robust Pipeline Focused on Unmet Need in CNS

1

NDA-Ready Product Candidate

2

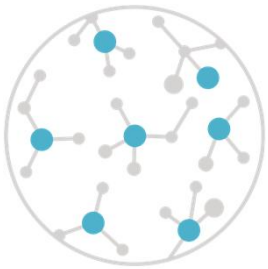
Breakthrough Designated Product Candidates

7

Development Candidates

35

Months from 1st PPD Patient to Positive Phase 3



>3,000

Diverse Compounds in Chemical Library

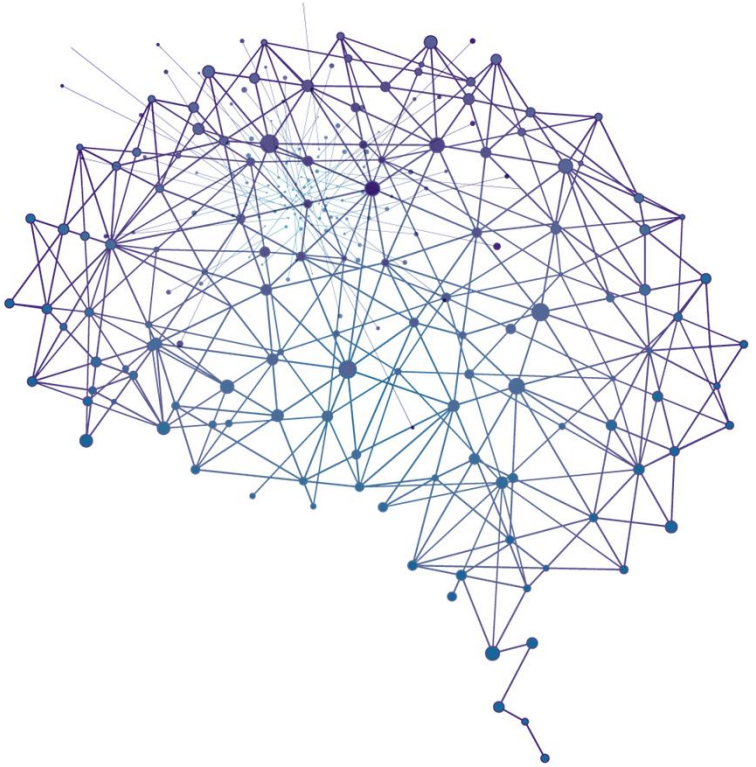
>300M

Estimated Worldwide Patients Impacted by Pipeline Indications[1,2]

1. World Health Organization, http://apps.who.int/iris/bitstream/10665/254610/1/WHO-MSD-MER-2017.2-eng.pdf. 2. All estimates represent management's assessment of total number of patients based on relevant literature. Other estimates exist in the literature or using claims analysis which are smaller than our estimates. We attribute differences to differences in methodologies and other factors. As a result, more in-depth studies are needed to better understand prevalence in each case.

Sage Today

- Building a leading CNS biotech company
- Positioned on the cusp of potential product commercialization
- Advancing a robust development pipeline of new classes of CNS therapeutics
- Executing through a strong financial position



Advancing a Leading CNS Clinical Portfolio

GABA

COMPOUND	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	REGISTRATION
Brexanolone	Postpartum Depression					
SAGE-217	Major Depressive Disorder					
	Postpartum Depression					
	Parkinson's Disease					
	Bipolar Depression					
	Insomnia					
SAGE-324	Essential Tremor					
	Epileptiform Disorders					

NMDA

COMPOUND	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	REGISTRATION
SAGE-718	NMDA Hypofunction					

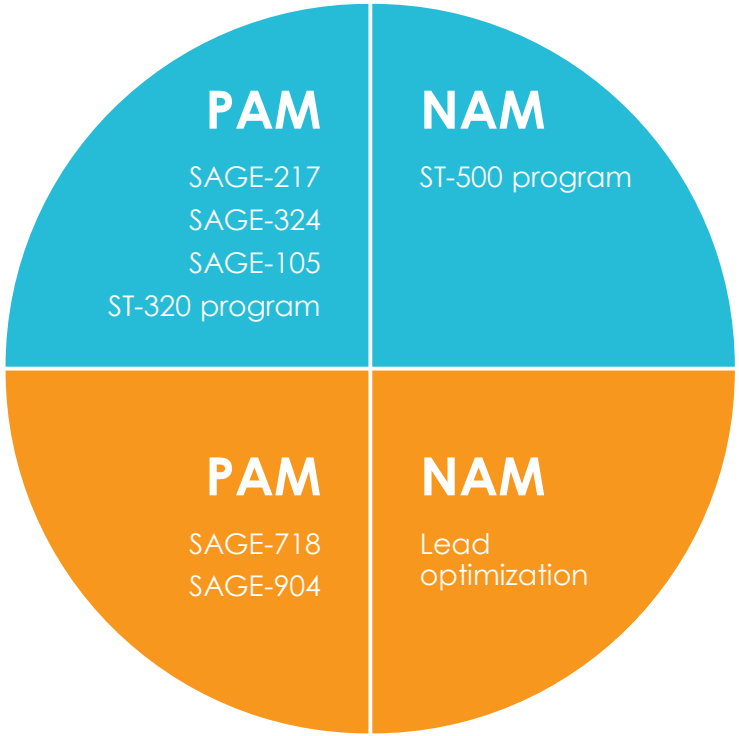
Sage's Discovery Engine

GABA

- Clinical programs
- IND-enabling programs
- ST-320 program
- Issued patents (SAGE-217)
- Large portfolio of filed patent applications

NMDA

- SAGE-718 in Phase 1
- SAGE-904 in IND-enabling
- Large portfolio of filed patent applications



GABA

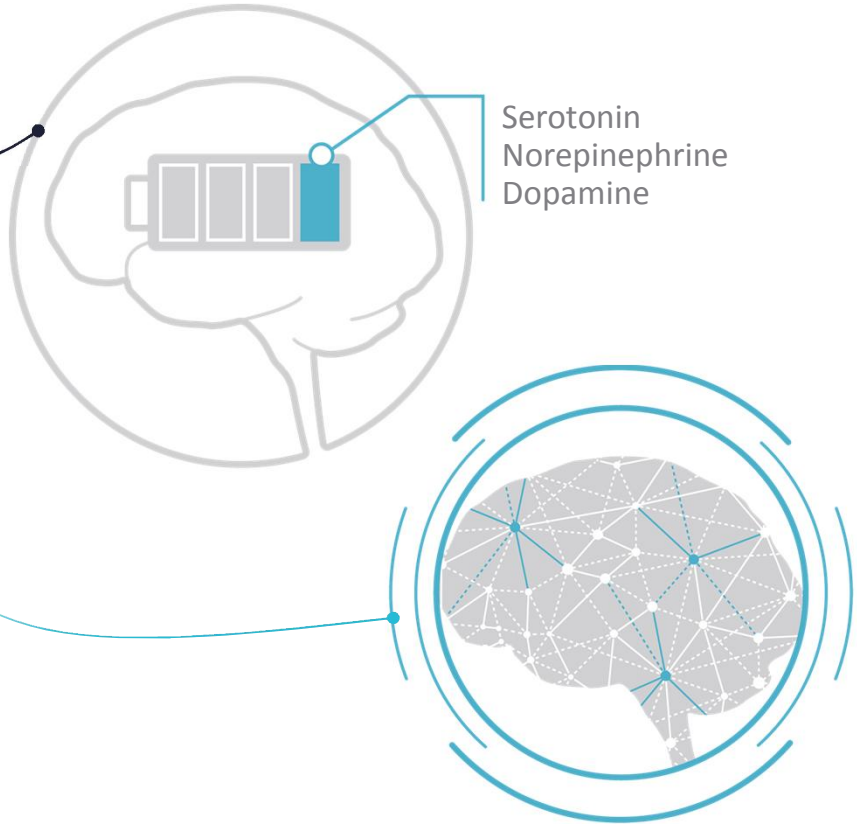
- Few examples known in literature
- ST-500 program
- Exploratory Discovery

NMDA

- Exploring two distinct series
- Lead Op program underway
- Patents filed

Rethinking Our Understanding of Depression

- Depression theories have been heavily influenced by the **monoamine hypothesis**
- Slow onset of traditional antidepressants has led to multiple hypotheses to explain efficacy following chronic treatment
- Newer theories are reframing depression as an episodic state, involving the promotion of negative states triggered by **hyperactive brain networks**
- Potential for development of antidepressants to rapidly disrupt hyperactive brain networks



Building A Depressive Disorder Franchise

First ever successful PPD clinical development program

SAGE-217 Phase 2 in MDD establishes potential for **broad footprint** in depressive disorders

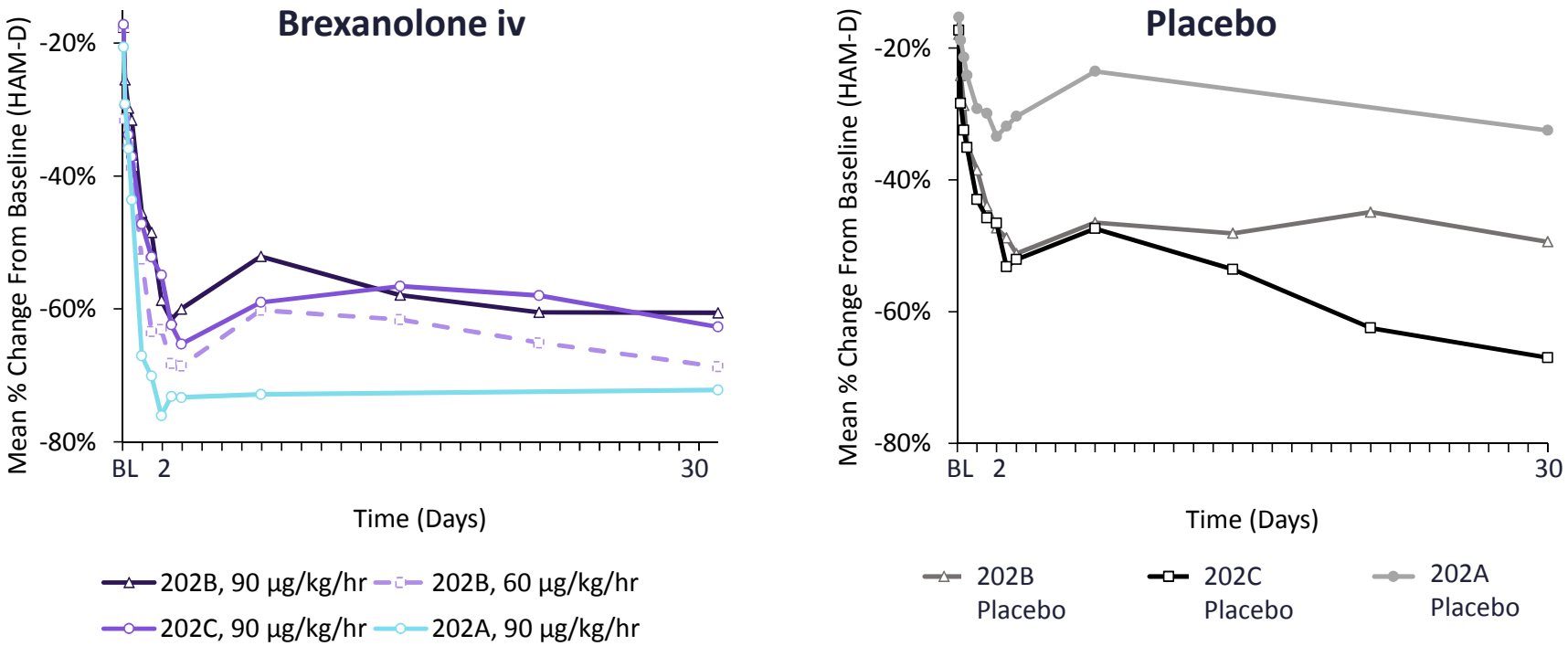
Potential for **groundbreaking approach** to mood disorders

Unmet Need

- Rapidly-acting
- Profound
- Durable
- Well-tolerated

Brexanolone in PPD

Consistent Rapid Antidepressant Effect in Three Placebo-Controlled Trials



Brexanolone was generally well tolerated in all three studies. One patient experienced two SAEs in each Phase 3 PPD trial; neither required hospitalization and both SAEs in one subject (in 202B) were deemed by the investigator not to be study-drug related. Most common AEs were headache, dizziness, and somnolence.

SAGE THERAPEUTICS™

By **thinking differently**, we can discover new things from R&D to commercial to patient care

Potential to Create New Treatment Pathway in Indication that May Affect Over 400,000 U.S. Women Each Year

Today's PPD Experience

- Lack of clear pathways to care
- Inconsistent screening and diagnosis
- Limited empowerment for patient and HCPs
- Current treatments can take 6-8 weeks for efficacy
- Feelings of fear, isolation and stigma

Targeted PPD Experience with Brexanolone

- Potential 1st approved therapy for PPD
- Increased disease awareness and urgency to treat
- HCPs feel more accountable for diagnosis and care
- Rapid onset and potential for resolution in days
- No patient falls through the cracks

Annual PPD Population (estimated)

>400,000

Women experience PPD each year in the US

~70-80% of patients are **moderate to severe**

1. CDC, https://www.cdc.gov/mmwr/volumes/66/wr/mm6606a1.htm, 2017. 2. Bonthapally, ISPOR Annual International meeting, 2017. 3. PACT, The Lancet, 2015. 4. All estimates represent management's assessment of total number of patients in U.S. based on relevant literature. Other estimates exist in the literature or using claims analysis which are smaller than our estimates. We attribute differences to differences in methodologies and other factors. As a result, more in-depth studies are needed to better understand prevalence in each case.

Goals for Brexanolone Launch and Rethinking How Care is Delivered

Taking on the stigma of PPD ►	• Establishing knowledge base of PPD as a medical complication of pregnancy
Establishing clear pathways to care ►	• OB/GYN and Psychiatrist engagement, ACOG leadership
Ensuring strong access and supply ►	• Payer engagement strategy, value story, supply chain readiness
Delivering family-centric support model ►	• Multiple site of care options, home infusion, patient support model
Expanding the footprint ►	• Potential EU expansion, disciplined evaluation of other markets
Growing the team ►	• Field teams, increased depth in core functions, patient/family centric culture

Brexanolone Supply Chain Readiness

On Track for Potential Commercial Launch

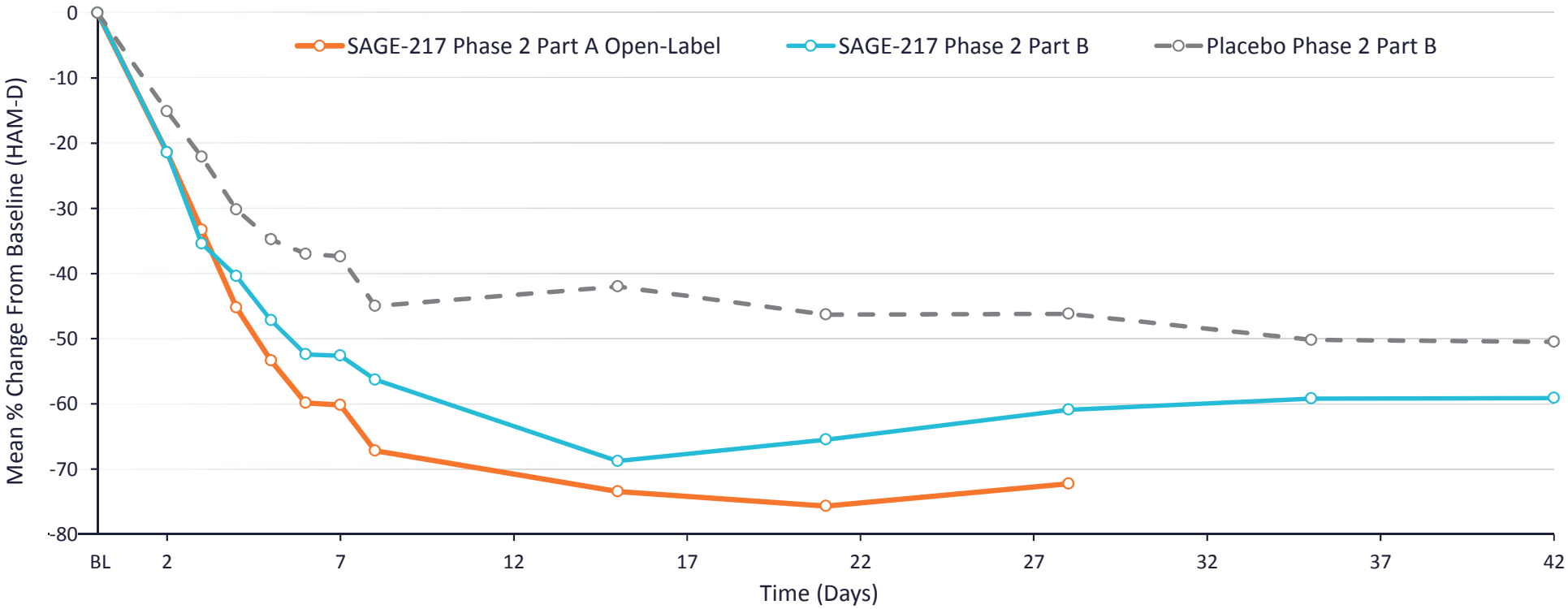
- Brexanolone supply chain readiness on track for commercial launch timeline
- Clinical supply chain active, clinical safety stock in place
- Technical Operations and Quality teams in place
- Commercial manufacturing process developed and scale-up completed
- Registration batches completed, 2+ years shelf life refrigerated

Expanding SAGE-217 Clinical Potential with Unifying Focus on Related Symptoms

INDICATION	Sleep disruption	Mood disruption	Potential for episodic treatment	Potential for chronic treatment	Motor disruption
Major Depressive Disorder	✓	✓	✓	✓	
Postpartum Depression	✓	✓	✓	✓	
Bipolar Depression	✓	✓	✓	✓	
Parkinson's Disease	✓	✓		✓	✓
Insomnia	✓		✓		

SAGE-217: Potential 1st Line Treatment for MDD

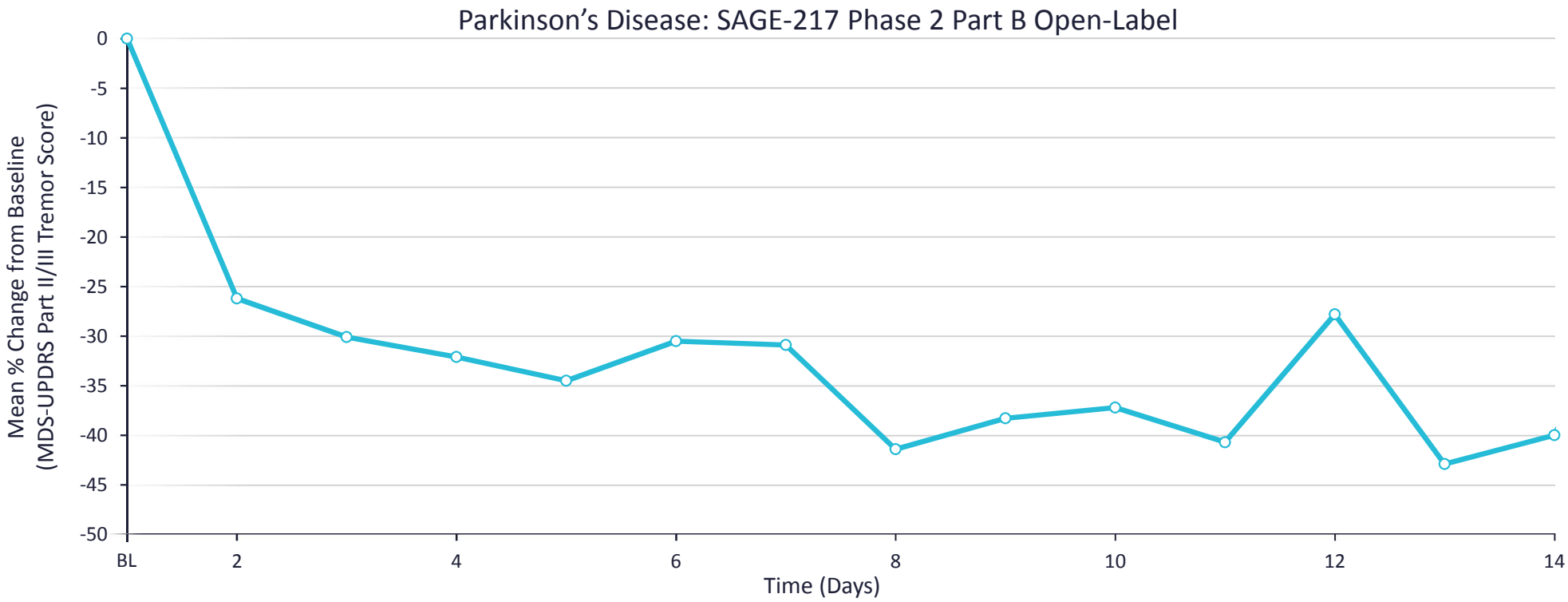
Positive Placebo-Controlled Phase 2 Results Demonstrate Potential in Depressive Disorders



SAGE-217 was generally well-tolerated in both studies. The most common adverse events in both trials included headache, dizziness, nausea and somnolence, and in Part A, also included myalgia.

Parkinson's Disease: Developing a Novel Mechanism

Extending Exploratory Methodology Studies into Clinical Development Programs



- SAGE-217 was generally well tolerated.
- Most common AEs were dizziness, sedation, and somnolence.

Positive Phase 1/2 Results for SAGE-217 in Insomnia Model

Primary Endpoint and Multiple Secondary Endpoints Met

Efficacy Summary:

- SAGE-217 met primary endpoint of improved Sleep Efficiency and demonstrated improvements in maintaining sleep compared to placebo
- Secondary endpoint measures demonstrated dose response with statistical significance in Total Sleep Time and time spent awake after sleep onset, though there was not a significant impact on Latency to Persistent Sleep
- Data support further development of SAGE-217 in disorders associated with disruption of normal sleep

Safety and Tolerability Summary:

- SAGE-217 was generally well tolerated
- Adverse event (AE) rates were low across all dose groups and all AEs were mild
- No serious AEs or AEs leading to discontinuation

Top-line Efficacy Results*

	Primary Endpoint	Secondary Endpoints		
	Sleep Efficiency	Wake After Sleep Onset	Total Sleep Time	Latency to Persistent Sleep
SAGE-217 30 mg	84.64% (p<0.0001)	55.0 mins (p<0.0001)	406.25 mins (p<0.0001)	SAGE-217 did not have a significant impact (p=0.7049) with either dose
SAGE-217 45 mg	87.55% (p<0.0001)	42.5 mins (p<0.0001)	420.25 mins (p<0.0001)	
Placebo	72.92%	113 mins	350.0 mins	

**All data presented are median values*

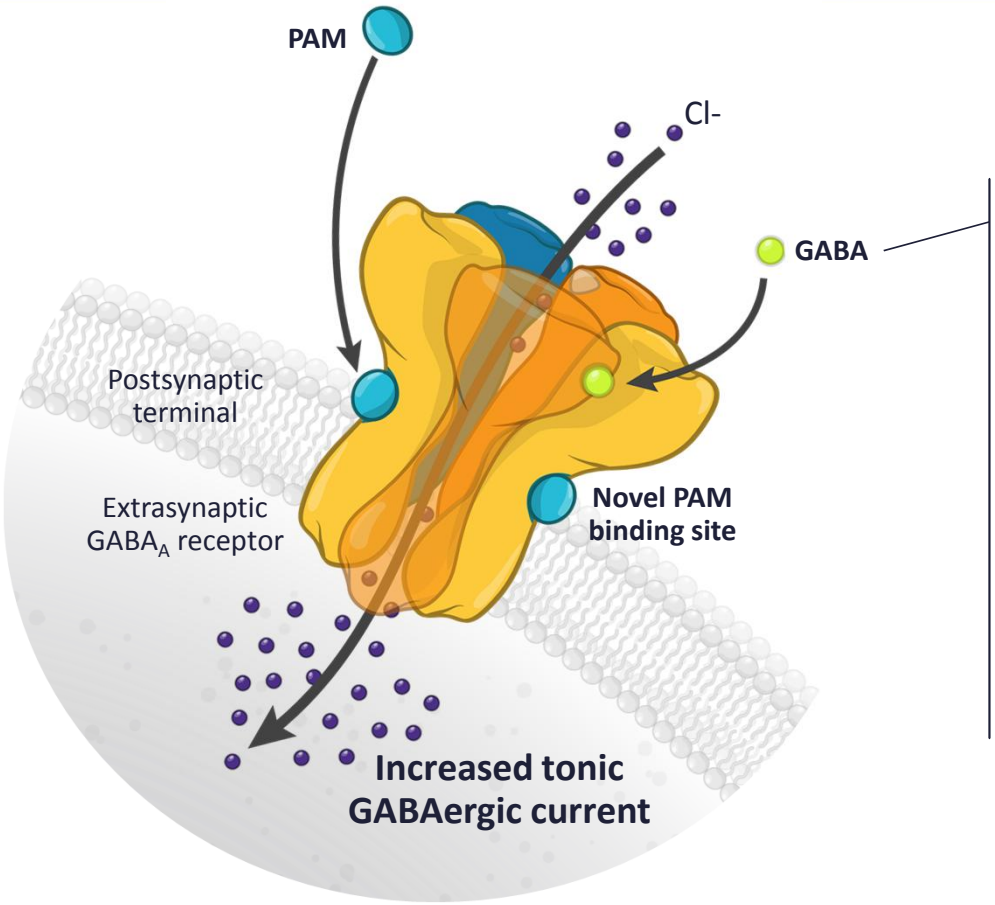
SAGE-217: Well Positioned for Development in Broad Market CNS Indications

	Estimated Total U.S. Patient Population
Major Depressive Disorder	• ~16.6 million adults reported at least one major depressive episode in the past year[1,8]
Postpartum Depression	• >400,0000 new mothers are identified with PPD each year[2,3,8] • ~70-80% of patients have moderate to severe PPD[4,8]
Bipolar Depression	• ~3.5-4.0 million adults had bipolar (I-II) disorder in the past year[5,8]
Parkinson's Disease:	• ~700,000 total patients[6,8] • ~60,000 new diagnoses per year[7,8]

1. Kessler et al, Annual Review of Public Health, 2008; 2. CDC, https://www.cdc.gov/mmwr/volumes/66/wr/mm6606a1.htm, 2017. 3. Bonthapally, ISPOR Annual International meeting, 2017. 4. PACT, The Lancet, 2015; 5. Merikangas et al, Arch Gen Psychiatry 2007; 6. Willis et al, *Neuroepidemiology*, 2010; 7. Parkinson's Disease Foundation. 8. All estimates represent management's assessment of total number of patients in U.S. with the applicable disease based on relevant literature. Other estimates exist in the literature or using claims analysis which are smaller than our estimates. We attribute differences to differences in methodologies and other factors. More in-depth studies are needed to better understand prevalence in each case.

SAGE-324

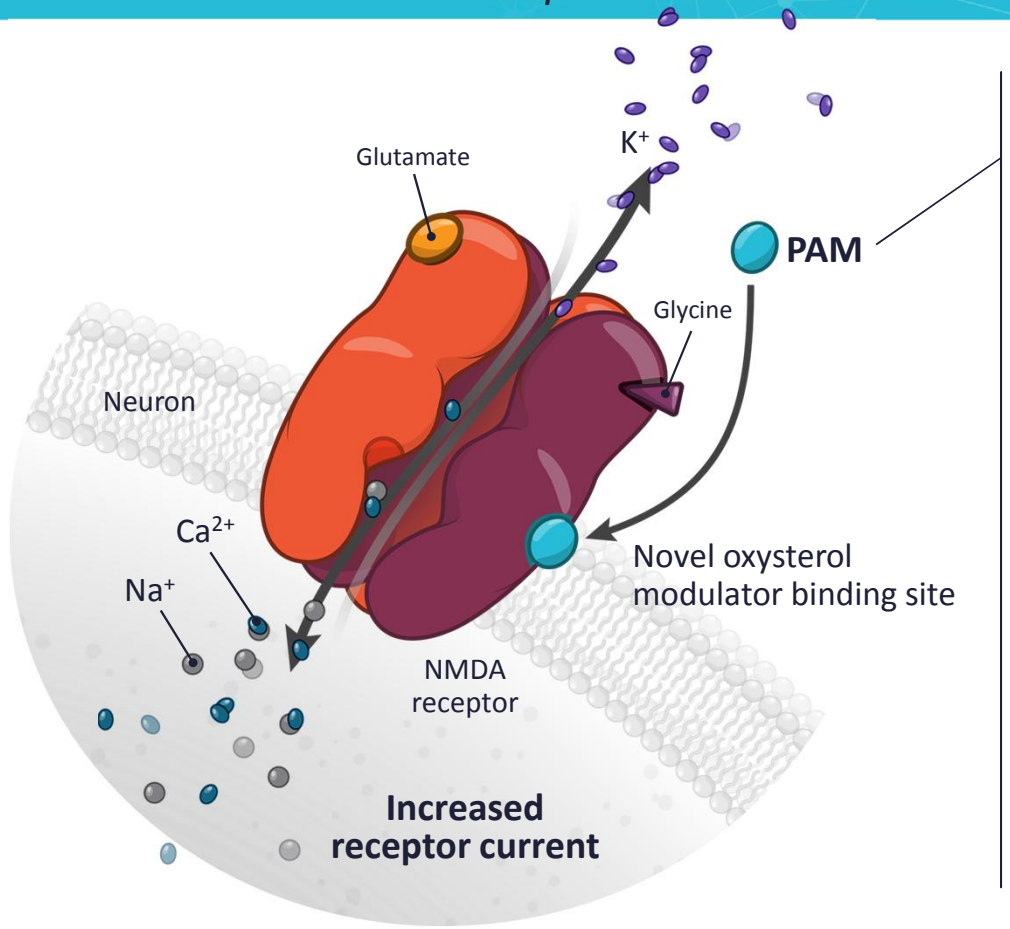
Next Generation Oral $GABA_A$ Receptor PAM



- Potent anti-seizure activity in preclinical models
- Differentiated preclinical profile (less sedative, potential for BID dosing)
- Targeted in essential tremor and epileptiform disorders
- On track to initiate Phase 1 in 2018

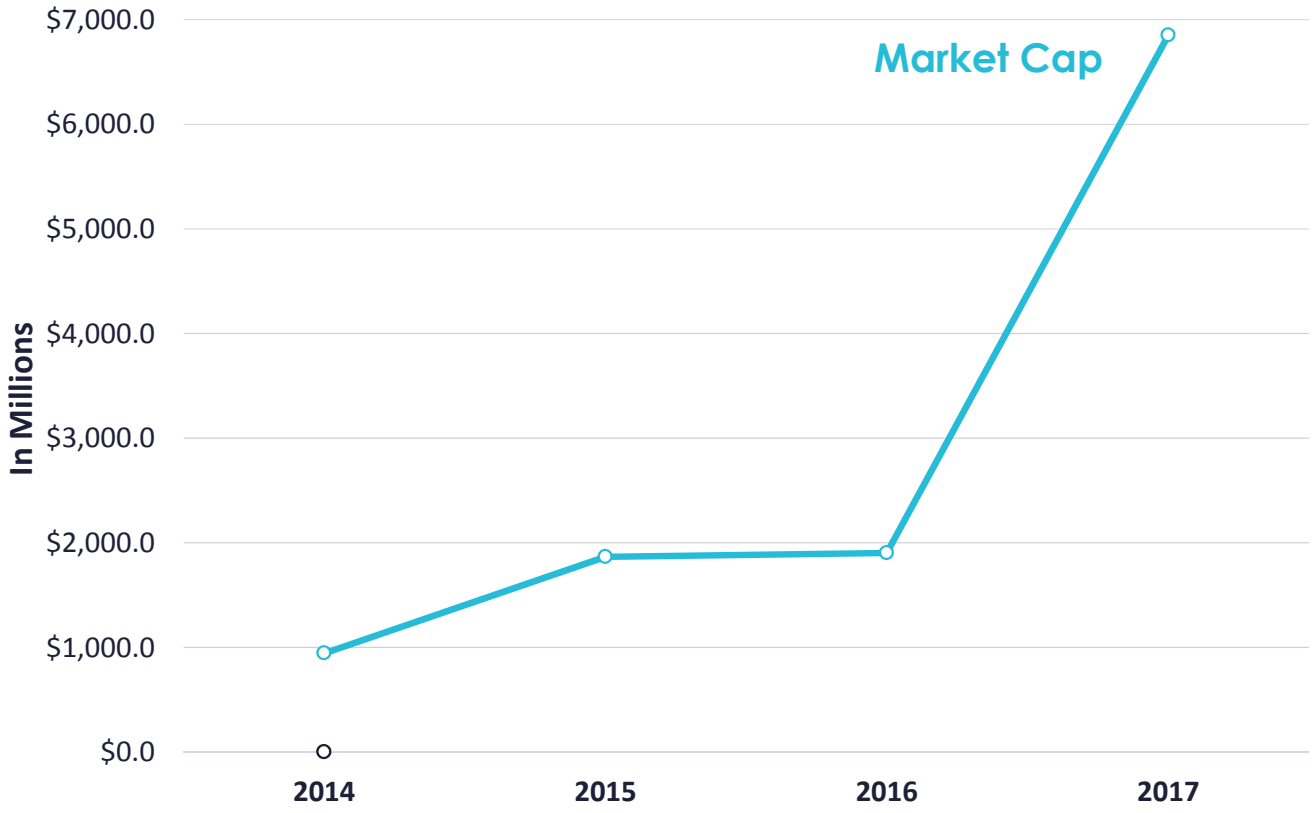
SAGE-718

First-in-Class NMDA Receptor Modulator



- Novel, proprietary, oral, first-in-class, oxysterol-based positive allosteric modulator (PAM) of the NMDA receptor
- Strong preclinical basis for role of NMDA receptor system in cognition
- Multiple disease entities associated with low NMDA function, including Huntington's, ADHD, and Alzheimer's
- Currently in Phase 1 clinical development

Significant Value Creation to Date



~$1.6 B
Cumulative cash raised

~$500 M
Cumulative cash spent

$519 M
2017 ending cash & cash equivalents (unaudited)

Continued Momentum in 2018 and Beyond

ANTICIPATED TIMELINE	EVENTS
1H 2018	• NDA filing in U.S. for brexanolone in PPD
1H 2018	• SAGE-324 initiation of Phase 1 development
1H 2018	• SAGE-718 initiation of Phase 1 multiple ascending dose program
2018	• SAGE-217 planned trial initiations in MDD, Bipolar depression, Parkinson's, sleep disorders
2H 2018	• SAGE-718 Phase 1 data from multiple ascending dose program
4Q 2018	• SAGE-217 Phase 2 data in PPD
2018-2019	• SAGE-217 results from trials in MDD, Bipolar depression, Parkinson's, sleep disorders
1H 2019	• Brexanolone commercial launch in PPD, if approved

Positioning as a Leader in CNS

What Sets Us Apart

New classes of CNS therapies

Deep pipeline, multiple indication potential

Efficient clinical development strategy

1st PPD Patient to Positive Phase 3 in 35 Months

Disciplined execution driven by a strong organization, people and culture

….and we're just getting started.

SAGE THERAPEUTICS™

RETHINKING treatment of brain disorders.
ORIGINATING differentiated medicines.
INNOVATING with a purpose for patient benefit.