SAGE THERAPEUTICS™

February 23, 2017

Q4 and Year-End 2016 Financial Results

SAGE THERAPEUTICS™

RETHINKING CNS

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Agenda – Today's Speakers

- **Paul Cox**, Senior Director, Investor Relations
- **Jeff Jonas**, M.D., Chief Executive Officer
- **Jim Doherty**, Ph.D., Chief Research Officer
- **Kimi Iguchi**, Chief Financial Officer
- **Q&A Session**

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Forward-Looking Statements

The slides presented today and the accompanying oral presentation 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: the potential safety, pharmacological effect and efficacy of SAGE’s product candidates; anticipated development activities, milestones and results, including expected timing; the estimated number of patients with certain disorders or diseases; expectations regarding potential commercialization of our products, if successfully developed; the potential for expedited development and review for SAGE-547 in PPD as a result of the breakthough therapy designation; SAGE’s belief in the sufficiency of the current Phase 3 trial, if succcessful, for approval in the E.U.; potential future indications for SAGE’s product candidates; other planned activities; SAGE’s strategy and business outlook; and SAGE’s 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 SAGE’s control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risk that:

- SAGE may not be able to successfully demonstrate the efficacy and safety of its product candidates at each stage of development;
- success in SAGE’s pre-clinical studies or in earlier 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 SAGE’s ability to obtain marketing approval for its product candidates, and a regulatory authority may ultimately decide that the design or results of our clinical trials are not sufficient for regulatory approval despite earlier guidance;
- we may continue to experience slower than expected enrollment in the STATUS trial or may encounter other delays or problems, including in analyzing data or requiring the need for additional analysis, data or patients, and we may experience these types of enrollment issues and other delays and problems in our other trials, and such issues with any trial could cause delay in completion of the trial, availability of results and timing of future activities;
- even if SAGE’s 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 SAGE’s current estimates;
- SAGE 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 its patent portfolio against challenges from third parties;
- SAGE may face competition from others developing products for similar uses as those for which SAGE’s products are being developed;
- SAGE’s operating expenses may be higher than forecasted and SAGE 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;
- SAGE may not be able to establish and maintain key business relationships with third parties on whom SAGE is, or will need to be, dependent for development or manufacture of products or for future marketing, sales and distribution of products, if SAGE is successful in its development efforts;
- SAGE 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 Quarterly Report on Form 10-Q, 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 SAGE's views only as of today, and should not be relied upon as representing its views as of any subsequent date. SAGE undertakes 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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Multi-Compound Neuropsych Portfolio

Program	Compound	Indication	Preclinical	Phase 1	Phase 2	Phase 3
GABA	Brexanolone (SAGE-547)	Super-Refractory Status Epilepticus				
		Postpartum Depression				
	SAGE-217	Postpartum Depression				
		Major Depressive Disorder				
		Essential Tremor				
		Parkinson's Disease				
	SAGE-689	Status Epilepticus/Undisclosed				
	SAGE-105	Orphan Epilepsies				
	SAGE-324	GABA Hypofunction				
NMDA	SAGE-718	Cerebrosterol Deficit Disorders				
		Anti-NMDA Receptor Encephalitis				
		NMDA Hypofunction				

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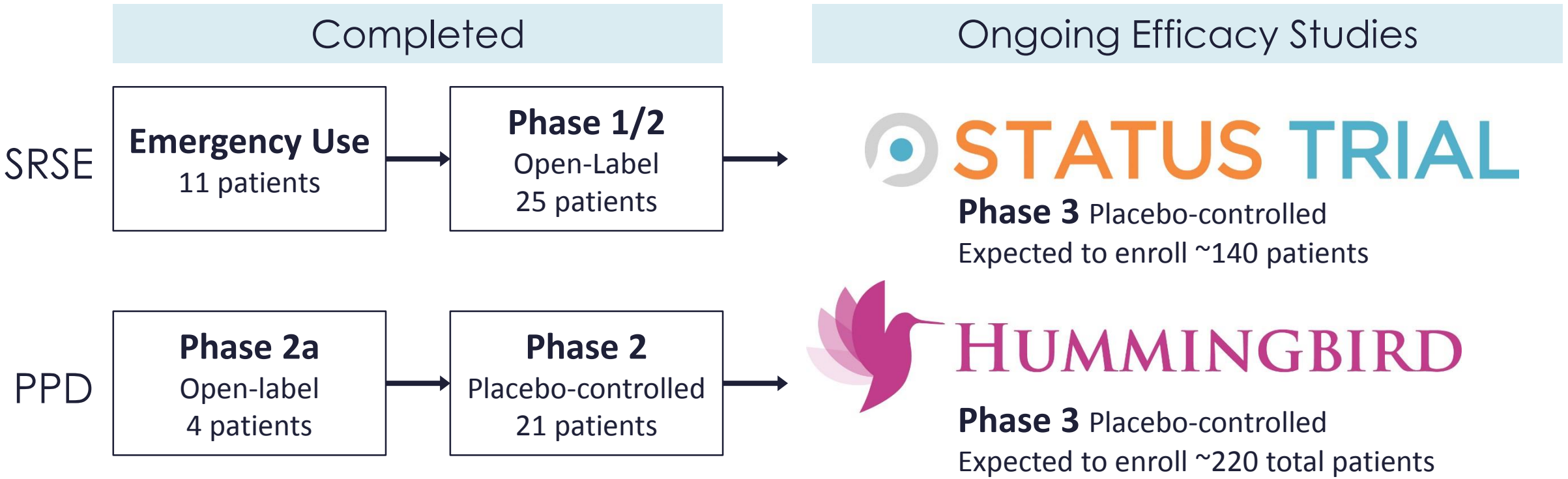
Brexanolone (SAGE-547) Dual Phase 3 Development Path



Abbreviation: SRSE, super-refractory status epilepticus; PPD, postpartum depression.

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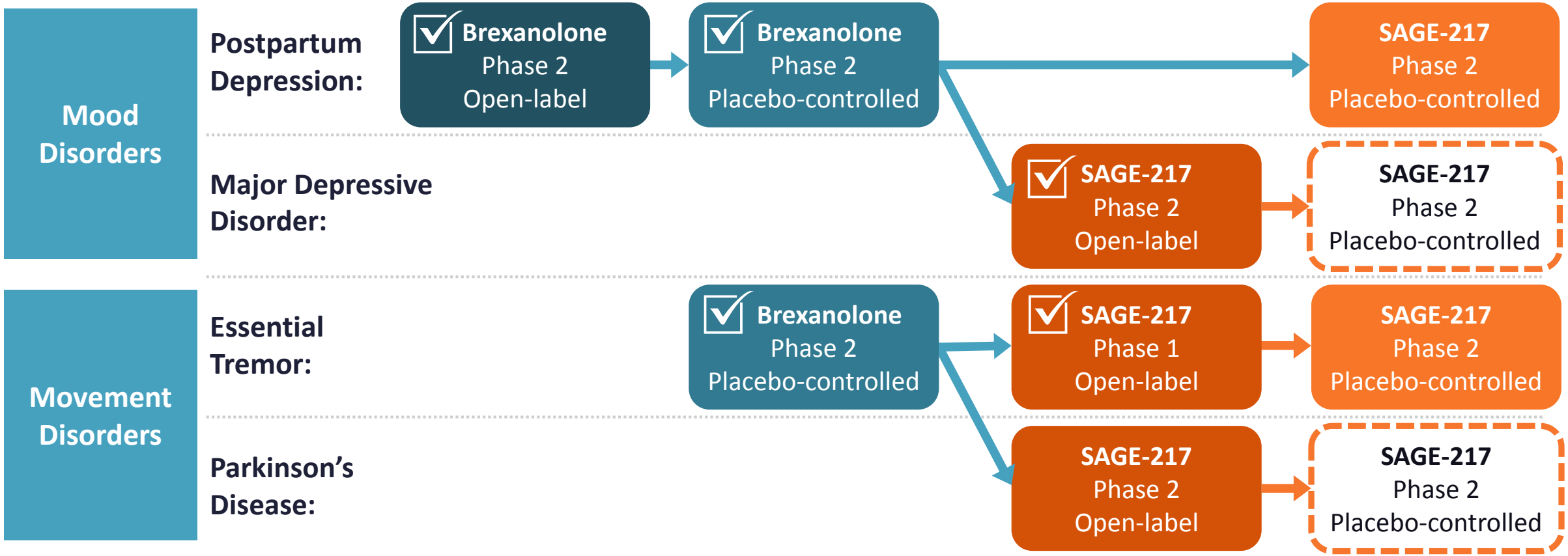
SAGE-217 Clinical Development Strategy

Positive Data Drive Incremental De-Risking



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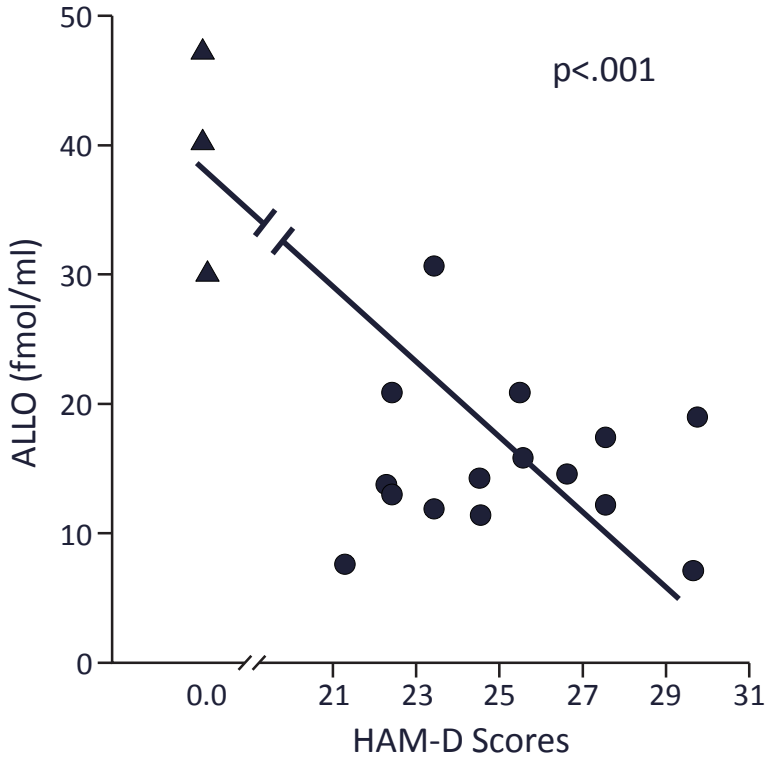
Why Major Depressive Disorder?

Low Allopregnanolone Levels have Been Observed in MDD Patients

Allo CSF Levels Decrease with Severity[1]



Disease Overview

- Majority of patients may not adequately respond to initial antidepressant therapy[2,3]
- Antidepressants are widely used, but large scale studies have demonstrated the need for additional therapies[2,3]

Pathophysiology

- Preclinical and clinical evidence suggest the role of GABAergic dysfunction in depression
- Low GABA and allopregnanolone levels have been found in the brain, CSF and plasma of depressed patients[4]
- Antidepressant therapy can restore allopregnanolone levels in animal models of depression[5]

1. Uzunova et al., *PNAS*, 1998; 2. Trivedi et al, *Am J Psychiatry,* 2006; 3. Rush et al, *Am J Psychiatry,* 2006; 4. Luscher et al, *Molecular Psychiatry*, 2011; 5. Schule et al, *Progress in Neurobiology*, 2014.

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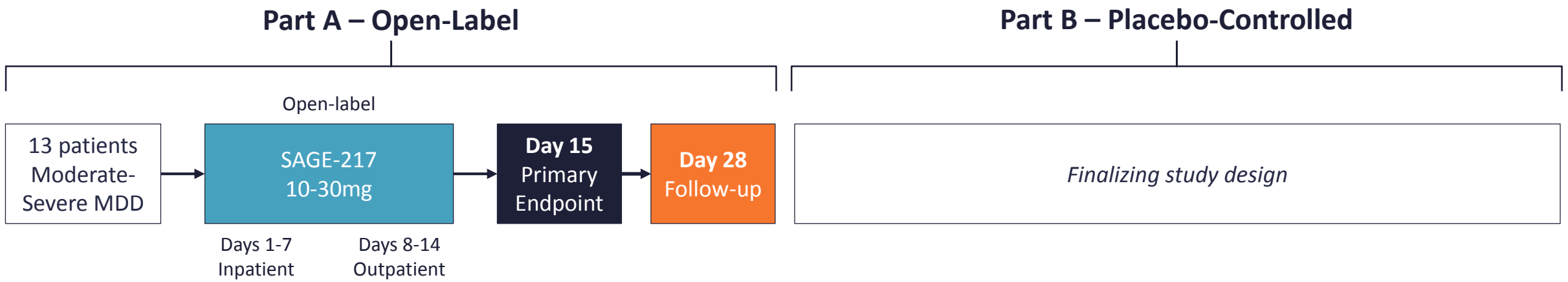
SAGE-217 in MDD

Phase 2 Proof-of-Concept Program

Study Population	Key Endpoints
• Patients with MDD present for 4-week period • HAM-D ≥22 • 13 patients (Part A)	• Safety, tolerability and pharmacokinetics • Change from baseline in HAM-D total score



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SAGE-217 in MDD

Open-Label Part A of Phase 2: Top-Line Results

Safety and Tolerability (Primary Endpoint)

- SAGE-217 was generally well tolerated in Part A of the study
- There were no deaths, serious adverse events or discontinuations
- The most common adverse events were sedation/somnolence, headache, dizziness, and myalgia

Effect on Depressive Symptoms at Day 15

- SAGE-217 reduced depressive symptoms as assessed by the HAM-D total score, with patients experiencing a 19.9 mean reduction in their HAM-D total score at Day 15, a decrease from a mean total score of 27.2 at baseline to 7.3 at Day 15
- At least a 50% reduction in HAM-D total score was demonstrated in 11 of 13 patients (85%)
- Remission from depression, as determined by a HAM-D total score less than or equal to 7, was seen in 8 of 13 patients (62%)

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		NMDA Hypofunction				

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2017 Key Objectives

1. Complete Phase 3 development of brexanolone in both SRSE and PPD, and, if successful, expeditiously file for regulatory approval

2. Prepare for potential commercial launch of brexanolone in both SRSE and PPD

3. Advance Phase 2 development of next-generation oral compound, SAGE-217, in mood and movement disorders

4. Advance lead NMDA modulator, SAGE-718, into Phase 1 clinical development

5. Continue discovery and development of other novel compounds, including IND-enabling studies for GABA development candidates SAGE-105 and SAGE-324

6. Grow translational science expertise to better enhance the probability of future development success

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Jim Doherty, Ph.D., Chief Research Officer

Jim Doherty, PhD

Chief Research Officer

Dr. Doherty joined Sage in 2012 and most recently served as Senior Vice President of Research. Before SAGE, he served as Director and Head of the Neuroscience Department for the CNS and Pain Innovative Medicine Unit of AstraZeneca Pharmaceuticals in Sodertalje, Sweden, and prior to that, he was Director and Head of the Neuroscience Department at AstraZeneca Pharmaceuticals in Wilmington, Delaware. He has experience with discovery, translational science and early development in several areas of neuroscience research, including psychiatry, neurology, cognition, epilepsy and analgesia. He has authored more than 30 peer-reviewed research and review articles. Dr. Doherty holds a B.A. in biology from the University of Delaware and a Ph.D. in neuroscience from Georgetown University. He was a postdoctoral fellow at Emory University Medical School.

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Experimental Medicine

Key Objectives

1. Identify functional biomarkers in animals that respond to target engagement and can be deployed in human clinical trials
2. Identify genetic and biochemical criteria to identify patient populations to increase the technical chances of success of a clinical trial
3. Translate insights between compounds and indications for better odds of success across the pipeline
4. Oversee small, exploratory human studies in new disease areas

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Strong Financial Position to Advance Programs

Q4 and Year-End 2016 Financial Results (as of 12/31/2016)

	FY '16	FY '15
Cash and Marketable Securities	$397.5M	$186.8M

	Q4 '16	Q4 '15	FY '16	FY '15
Research & Development	$42.0M	$20.4M	$120.8M	$69.4M
General & Administrative	$14.4M	$8.2M	$39.4M	$25.3M
Net Loss	$55.9M	$24.0M	$159.0M	$94.5M

Guidance:

- Based on current operating plans, expect existing cash balance will be sufficient to fund operations into Q2 2018

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Recent and Expected Milestones

Program	Compound	Indication	2H 2016	1H 2017	2H 2017
GABA	SAGE-547	Super-Refractory Status Epilepticus	✓ EMA Scientific Advice	○ Ph 3 top-line data	
		Postpartum Depression	✓ Ph 2 top-line data ✓ FDA BTD Meeting ✓ EMA PRIME ✓ Ph 3 initiation	○ EMA Scientific Advice	○ Ph 3 top-line data ▪ 202B - Severe ▪ 202C - Moderate
	SAGE-217	Postpartum Depression	✓ Ph 2 initiation		○ Ph 2 top-line data
		Major Depressive Disorder	✓ Ph 2 initiation	✓ Ph 2 open-label data ○ Initiate Ph 2 Part B	
		Essential Tremor	✓ Ph 2 initiation		○ Ph 2 top-line data
		Parkinson's Disease	✓ Ph 2 initiation	○ Ph 2 open-label data	
	SAGE-105, SAGE-324	Orphan Epilepsies, GABA Hypofunction	✓ Initiate IND-enabling studies		
NMDA	SAGE-718	Cerebrosterol Deficit Disorders		○ Ph 1 initiation	○ Ph 1 SAD data
		Anti-NMDA Receptor Encephalitis			
		NMDA Hypofunction			

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Commitment to Neuroscience Leadership

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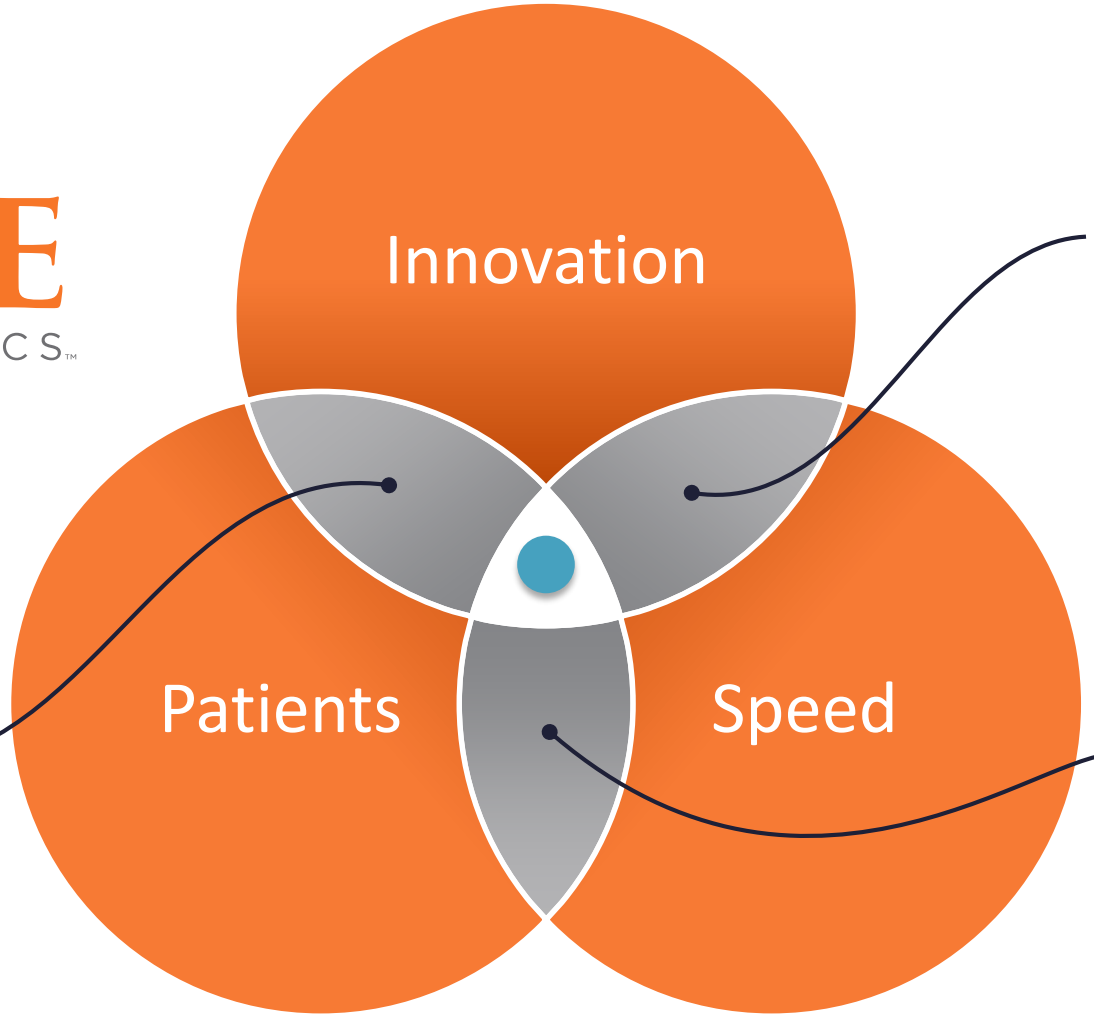

Advancing novel medicines through deliberate, stepwise and data-driven development

Tackling the **innovation** gap in CNS

Responsibly pursuing **expedited pathways** to deliver new treatments

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