



November 2, 2017

## Q3 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**

# 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 may include statements regarding: the potential safety, pharmacological effect and efficacy of SAGE’s product candidates; anticipated development and regulatory 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 brexanolone in PPD as a result of the breakthrough therapy designation; SAGE’s belief in the sufficiency of the current Phase 3 trials, if successful, for filing and potential 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 encounter delays in enrollment or other delays or problems in the conduct and completion of our clinical trials, including in analyzing data or requiring the need for additional

analysis, data or patients, and such issues with any trial could cause a 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.

# Multi-Compound CNS Portfolio

| Program  | Compound                            | Indication                      | Preclinical   | Phase 1 | Phase 2 | Phase 3 |
|----------|-------------------------------------|---------------------------------|---|---------|---------|---------|
| GABA     | Brexanolone IV                      | Postpartum Depression           | [Progress bar spanning Preclinical, Phase 1, and Phase 2] |         |         |         |
|          | SAGE-217                            | Postpartum Depression           | [Progress bar spanning Preclinical, Phase 1, and Phase 2] |         |         |         |
|          |                                     | Major Depressive Disorder       | [Progress bar spanning Preclinical, Phase 1, and Phase 2] |         |         |         |
|          |                                     | Essential Tremor                | [Progress bar spanning Preclinical, Phase 1, and Phase 2] |         |         |         |
|          |                                     | Parkinson's Disease             | [Progress bar spanning Preclinical, Phase 1, and Phase 2] |         |         |         |
|          | SAGE-324                            |                                 | [Progress bar in Preclinical phase]                       |         |         |         |
|          | SAGE-689                            | GABA Hypofunction               | [Progress bar in Preclinical phase]                       |         |         |         |
| SAGE-105 | [Progress bar in Preclinical phase] |                                 |   |         |         |         |
| NMDA     | SAGE-718                            | Cerebrosterol Deficit Disorders | [Progress bar in Preclinical phase]                       |         |         |         |
|          |                                     | Anti-NMDA Receptor Encephalitis | [Progress bar in Preclinical phase]                       |         |         |         |
|          |                                     | NMDA Hypofunction               | [Progress bar in Preclinical phase]                       |         |         |         |

# Brexanolone as a Treatment for PPD

## Phase 3 Hummingbird Program



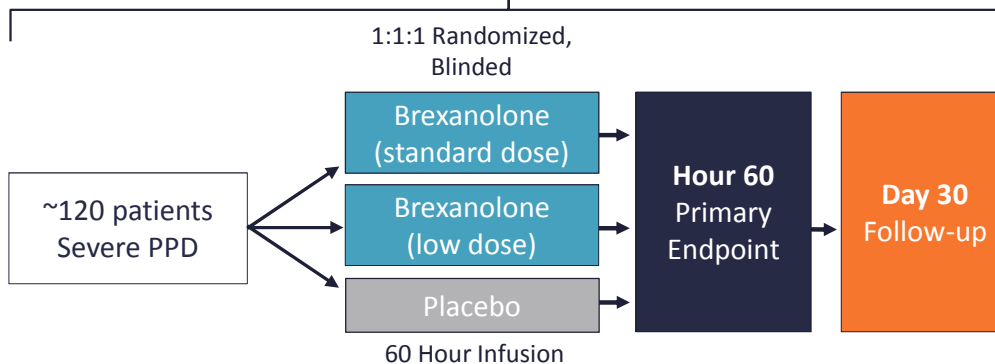
### Study Population

- Placebo-controlled, double-blind 1:1 randomization
- Major depressive episode in 3<sup>rd</sup> trimester or within 4 weeks post-birth
- HAM-D  $\geq 26$  (202B); HAM-D  $\geq 20$  and  $\leq 25$  (202C)

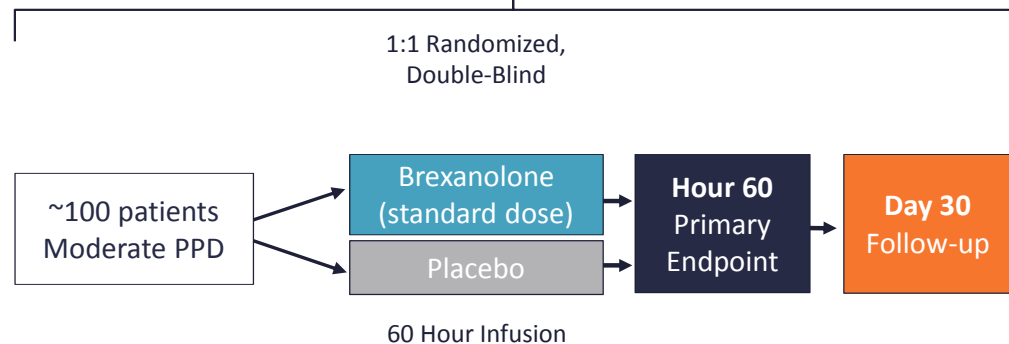
### Key Endpoints

- Change from baseline in HAM-D total score at 60 hours compared to placebo
- Safety, tolerability and pharmacokinetics

### Phase 3 Study 202B

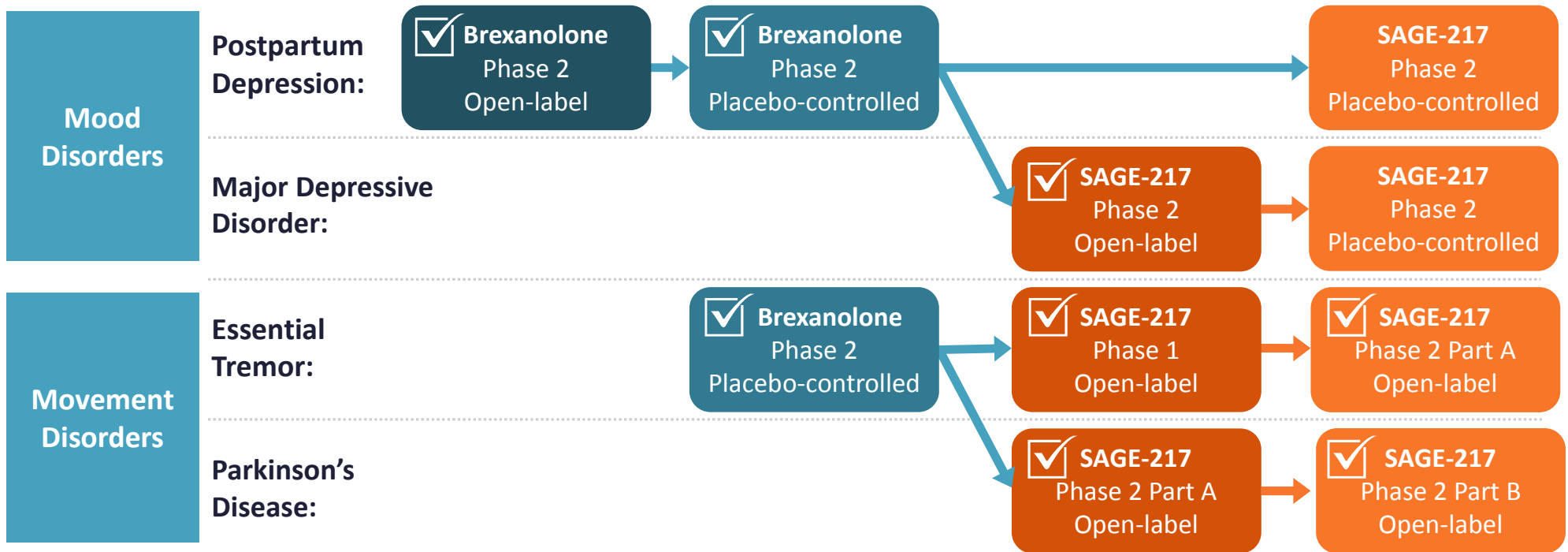


### Phase 3 Study 202C



# SAGE-217 Clinical Development Strategy

Positive Data Drive Incremental De-Risking



# SAGE-217 in Parkinson's Disease

## Top-Line Results from Open-Label Part B of Phase 2 Clinical Program

### Top-Line Results Summary

- Part B evaluated SAGE-217 as an adjunctive treatment for 7 days in 14 tremor-predominant Parkinson's disease patients who were on stable doses of anti-Parkinsonian agents
- Improved tremor symptoms, as assessed by the MDS-UPDRS - Part II/III tremor score, by a mean change of 7.7 points (40.0%) by Day 8 from a mean baseline score of 19.1 points (primary efficacy endpoint)
- Additional secondary efficacy endpoints were consistent with the primary efficacy endpoint:
  - Improved overall Parkinson's disease motor symptoms, as assessed by the MDS-UPDRS Part III motor score, by a mean change of 18.6 points (36.3%) by Day 8 from a mean baseline score of 52.4 points
  - Improved symptoms of sleep dysfunction in 5 patients with clear sleep dysfunction at baseline, as assessed by the Parkinson's Disease Sleep Scale (PDSS-2) score, by a mean change of 12.2 points (41.2%) by Day 8 from a mean baseline score of 29.8 points

### Safety and Tolerability Summary

- Administration of SAGE-217 in the evening was generally well-tolerated with no SAEs or discontinuations
- The most common AEs were dizziness, sedation, and somnolence, each occurring in 2 patients

# SAGE-217 in Essential Tremor

## Top-Line Results from Open-Label Part A of Phase 2 Clinical Program

### Top-Line Results Summary

- Part A enrolled 16 patients diagnosed with essential tremor, defined as visible and persistent bilateral postural tremor and kinetic tremor, involving hands and forearms, with a duration greater than 5 years prior to screening
- SAGE-217 improved tremor symptoms, as assessed by the TETRAS upper limb combined kinetic score, by at least 30% on Day 7 in 8/12 patients (67%) who received SAGE-217 oral capsule in the study for 7 days
- Sage is currently conducting Part C of an exploratory Phase 2 clinical trial of SAGE-217 in essential tremor
  - Part C is an open-label clinical trial that was initiated to study higher doses and extended evening dosing of SAGE-217
  - As a result of the change in design, enrollment in Parts A and B of the trial was discontinued prior to completion

### Safety and Tolerability Summary

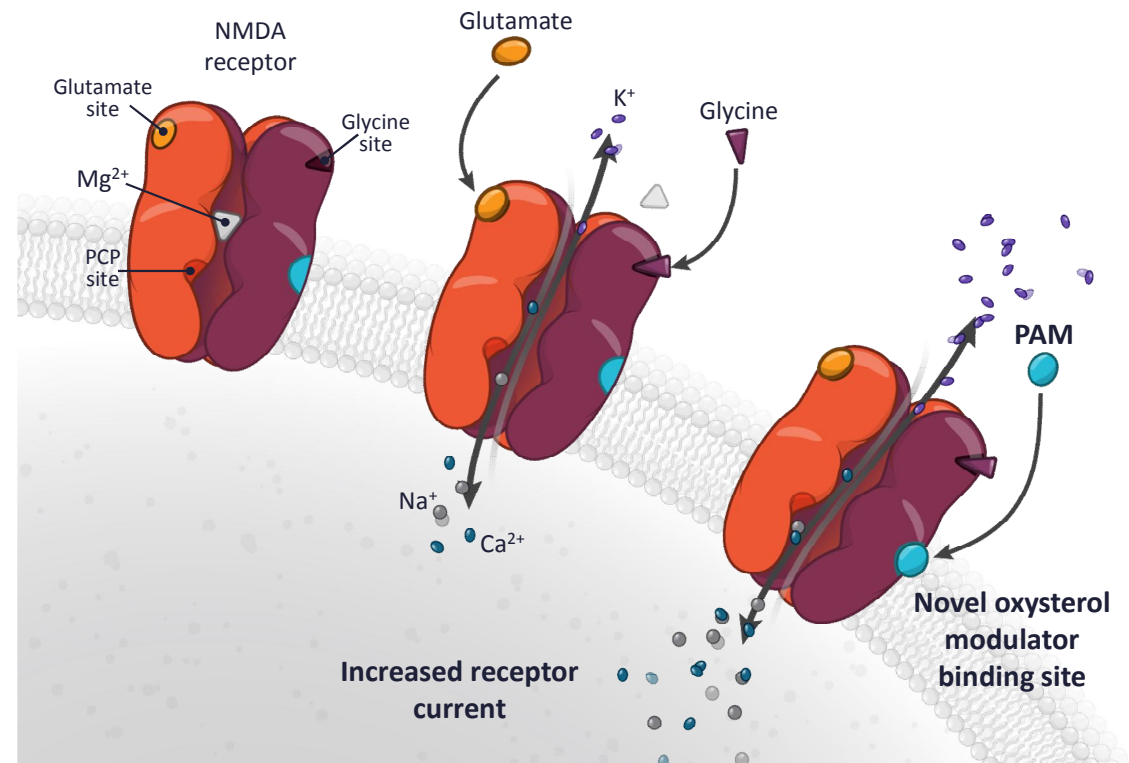
- Administration of SAGE-217 in the morning was generally well-tolerated
- The most common AEs were somnolence, dizziness, and sedation
- There were no SAEs reported in the 14 patients receiving SAGE-217 oral capsule
- There was one SAE(confusion) reported in 1 of the 2 patients who received oral solution



# SAGE-718: First-in-Class NMDA Receptor Modulator

## Currently in Phase 1 Clinical Development

- SAGE-718 is a novel, oral, first-in-class, oxysterol-based positive allosteric modulator (PAM) of the NMDA receptor
- SAGE-718 was well-tolerated with no SAEs reported in Phase 1 single ascending dose study
- NMDA receptor system plays a critical role in brain network balance and plasticity
- Loss of NMDA function may have significant impact on neuropsych disorders



# Solid Financial Position to Advance Programs

## Q3 2017 Financial Results (as of 9/30/2017)

|                                | Q3 '17   | Q4 '16   |
|--------------------------------|----------|----------|
| Cash and Marketable Securities | \$243.5M | \$397.5M |

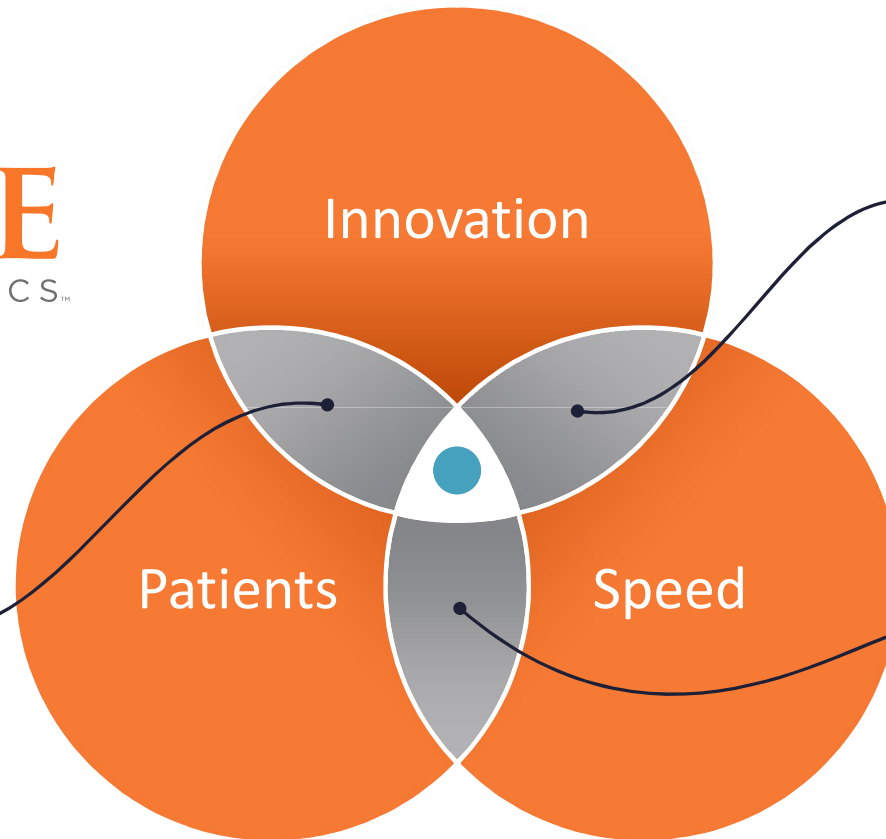
  

|                          | Q3 '17  | Q3 '16  |
|--------------------------|---------|---------|
| Research & Development   | \$58.3M | \$29.1M |
| General & Administrative | \$16.1M | \$9.0M  |
| Net Loss                 | \$73.7M | \$37.8M |

# Recent and Expected Milestones

| Program | Compound            | Indication   | 2H 2017   | 1H 2018                         |
|---------|---------------------|--|---|---------------------------------|
| GABA    | Brexanolone         | Postpartum Depression  | <ul style="list-style-type: none"> <li>✓ EMA scientific advice</li> <li>○ Phase 3 top-line results                             <ul style="list-style-type: none"> <li>○ 202B - Severe</li> <li>○ 202C - Moderate</li> </ul> </li> </ul> |                                 |
|         | SAGE-217            | Postpartum Depression  |   | ○ Phase 2 top-line results (1Q) |
|         |                     | Major Depressive Disorder  | ○ Phase 2 Part B top-line results   |                                 |
|         |                     | Essential Tremor   | <ul style="list-style-type: none"> <li>✓ Phase 2 Part A open-label results</li> <li>○ Phase 2 Part C open-label results</li> </ul>  |                                 |
|         | Parkinson's Disease | <ul style="list-style-type: none"> <li>✓ Phase 2 Part B initiation</li> <li>✓ Phase 2 Part B open-label results</li> </ul> |   |                                 |
| NMDA    | SAGE-718            | Cerebrosterol Deficit Disorders  | ✓ Phase 1 SAD results   | ○ Phase 1 MAD initiation        |
|         |                     | Anti-NMDA Receptor Encephalitis  |   |                                 |
|         |                     | NMDA Hypofunction  |   |                                 |

# Positioned for Leadership in CNS



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

Tackling the **innovation** gap in CNS

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



*RETHINKING CNS*