SAGE THERAPEUTICS

DISCOVER
DEVELOP
DELIVER

Novel Medicines for Life-Altering CNS Disorders

Q3 2016 Financial Results
November 3, 2016

Agenda

- **Introduction:** Paul Cox, Senior Director, Investor Relations
- **Business Update:** Jeff Jonas, M.D., Chief Executive Officer
- **Clinical Overview:** Steve Kanes, M.D., Ph.D., Chief Medical Officer
- **Financial Results:** Kimi Iguchi, Chief Financial Officer
- **Q&A Session**

Forward-Looking Statements

These slides 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,” “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 milestones and results, including expected timing; the estimated number of patients with certain disorders or diseases, including SRSE and PPD; expectations regarding potential commercialization of SAGE-547, 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 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 SAGE’s ability to obtain marketing approval for its product candidates;
- we may continue to experience slower than expected enrollment in the STATUS trial, and we may experience, or may encounter delays or problems in analyzing data or the need for additional analysis, data or patients, and we may experience these issues in other trials.
- 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.

Developing a Multi-Product CNS Portfolio

Compound	Indication		Preclinical	Phase 1	Phase 2	Phase 3
GABA Programs						
SAGE-547	Super-Refractory Status Epilepticus				STATUS TRIAL	
	Postpartum Depression				HUMMINGBIRD STUDY	NEST PROGRAM
SAGE-217	Mood Disorders	Postpartum Depression				NEST PROGRAM
		Major Depressive Disorder				
	Movement Disorders	Essential Tremor				
		Parkinson's Disease				
SAGE-689	Status Epilepticus					
SAGE-105/ SAGE-324	Orphan Epilepsies					
NMDA Programs						
SAGE-718	Cerebrosterol Deficit Disorders					
	Anti-NMDA Receptor Encephalitis					

Recent and Expected Near-Term Clinical Milestones

Compound	Indication	2H 2016	1H 2017	2H 2017
GABA Programs				
SAGE-547	Super-Refractory Status Epilepticus		○ **Phase 3 top-line data**	
	Postpartum Depression	✓ **202A top-line data** ✓ 202B initiation ✓ 202C initiation		○ **202B top-line data** ○ **202C top-line data**
SAGE-217	Postpartum Depression	○ Phase 2 initiation		○ **Phase 2 top-line data**
	Major Depressive Disorder	○ Phase 2 PoC initiation	○ **Phase 2 PoC data**	
	Essential Tremor	○ Phase 2 initiation		○ **Phase 2 top-line data**
	Parkinson's Disease	○ Phase 2 PoC initiation	○ **Phase 2 PoC data**	
SAGE-105/ SAGE-324	Orphan Epilepsies	○ Initiate IND-enabling studies		
NMDA Programs				
SAGE-718	Cerebrosterol Deficit Disorders		○ Phase 1 initiation	○ **Phase 1 SAD data**
	Anti-NMDA Receptor Encephalitis			

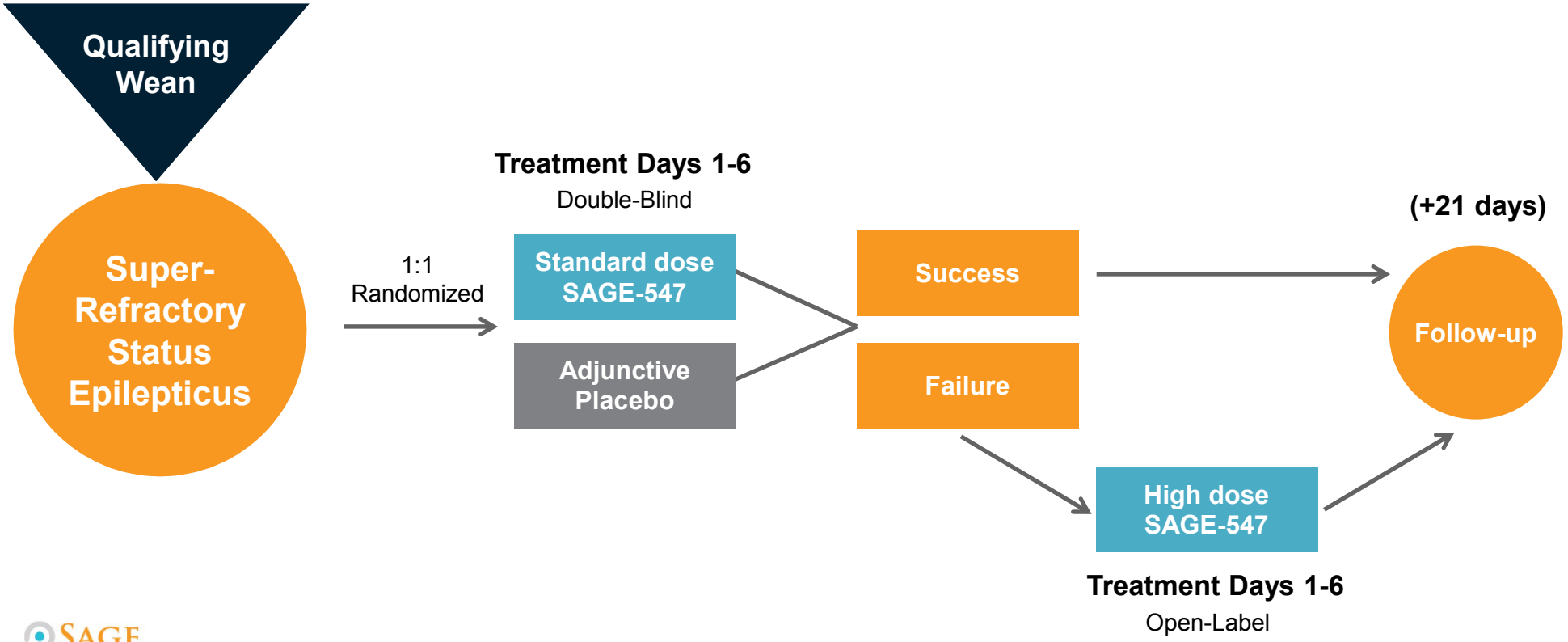
SAGE-547: Potential Near-Term Commercial Opportunities to Treat SRSE and PPD

	Super-Refractory Status Epilepticus	Postpartum Depression
Regulatory Designations:	• Fast Track (U.S.) • Orphan Drug (U.S.)	• Breakthrough Therapy (U.S.)
Estimated U.S. Patient Population:	• 25,000 – 41,000 per year[1]	• 500,000 - 750,000 pear year[2,3] • Up to 80% moderate-severe[4]
Expected Treatment Setting:	• ICU, Neuro-ICU	• Facilities where IV administration is possible, such as a hospital, holding unit, or psych facility
Preliminary Pricing Assumptions:	• $25,000 - $75,000 per patient	• Per patient pricing of up to 25% as a proportion of SRSE pricing, based on expected lower dosing and shorter duration for PPD

[1] Beg et al. Burden of illness for super-refractory status epilepticus patients. *Journal of Medical Economics,* 2016, Aug 11:1-9. doi: 10.1080/13696998.2016.1223680.
[2] Hamilton et al. Births: Final data for 2014. *National Vital Statistics Reports*. National Center for Health Statistics, 2015, 64, 12.
[3] O'Hara MW & McCabe JE. Postpartum depression: Current status and future directions. *The Annual Review of Clinical Psychology,* 2013, 9, 379-407. doi: 10.1146/annurev-clinpsy-050212-185612.
[4] PACT. Lancet Psychiatry. 2015;2(1):59. Bobo. Mayo Clin Proc. 2014;89(6):835.

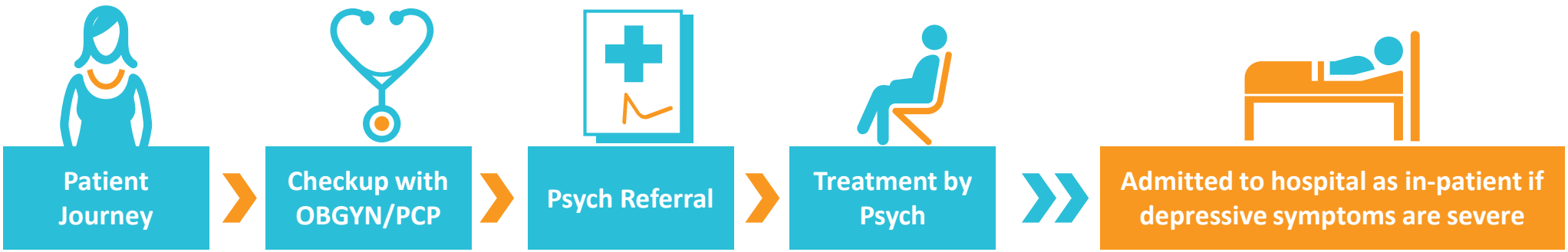
Global Phase 3 STATUS Trial of SAGE-547 in SRSE

- STATUS Trial: First randomized, double-blind, placebo-controlled trial of SRSE, being conducted with FDA Special Protocol Assessment
- Expect up to 140 patients enrolled to get 126 evaluable patients
- Primary Efficacy Endpoint: Continued resolution of SE for 24 hours following wean of all 3rd-line agents and SAGE-547/placebo
- Top-line results anticipated in 1H 2017 based on expected enrollment



PPD is a Serious Mental Health Disorder

- BTD underscores significant unmet need; no approved therapies specifically for PPD
- Estimated PPD prevalence of 500k-750k mothers per year in US[1,2]
- Up to 80% of PPD patients may be moderate-severe, per market research[3]
- Hospitalization may be needed for some PPD patients
- Onset of symptoms within 4 weeks after birth and initial treatment can extend for a minimum of 6 months
- PPD carries an increased risk for suicide, which is the leading cause of maternal death following childbirth[4]



[1] Hamilton et al. Births: Final data for 2014. *National Vital Statistics Reports*. National Center for Health Statistics, 2015, 64, 12.
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[3] PACT. Lancet Psychiatry. 2015;2(1):59. Bobo. Mayo Clin Proc. 2014;89(6):835.
[4] Savitz et al, *Ann Epidemiol*. 2011 Jun;21(6):399-406; DSM-5

SAGE-547 PPD Clinical Program

- BTD for SAGE-547 in PPD provides opportunity to potentially accelerate program
- FDA Breakthrough Meeting expected to provide program guidance by year end

Positive Completed Studies

Positive PPD Probe Study
- Open-label, single center
- n=4 severe PPD patients

Positive SAGE-547 Phase 2 Trial (202A)
- Double-blind, placebo-controlled, multi-center
- n=21 severe PPD patients

Ongoing Studies

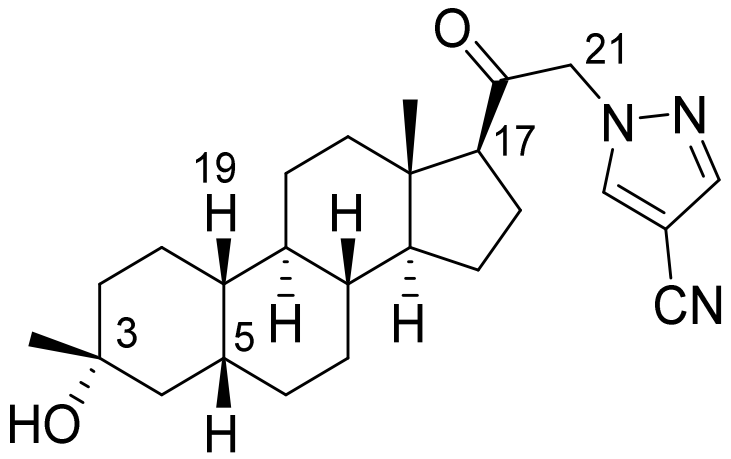
SAGE-547 Phase 2 Expansion

Severe PPD (202B)
- Double-blind, placebo-controlled
- 50 sites
- n=approx. 60 severe patients
- Dose-ranging

Moderate PPD (202C)
- Double-blind, placebo-controlled
- 50 sites
- n=approx. 36 moderate patients
- 1:1 randomization

SAGE-217: Positive Phase 1 Clinical Program Results

- SAGE-217 studied in 108 healthy volunteers in Phase 1 SAD and MAD
- Plasma half-life consistent with once/day dosing (if desired)
- Generally well-tolerated with no serious adverse events reported during the treatment and follow-up periods
- EEG showed clear evidence of target engagement ($GABA_A$ receptor modulation) starting at the lowest dose tested (15 mg MAD study)
- No significant effect on psychomotor and cognitive assessments at doses likely to be used in clinic



SAGE-217: Multiple Phase 2 Programs Anticipated to Begin in 2H 2016

- Plan to advance into multiple Phase 2 clinical programs in mood and movement disorders
  - Applying validated probe approach to SAGE-217 for indication selection
  - Multiple program readouts expected in 2017 to allow data-driven portfolio decisions

Mood Disorders

Postpartum Depression

- Double-blind, placebo-controlled
- Multi-center

Major Depressive Disorder

- Part A – Open-label panel
  - Single-center
- Part B – Placebo-controlled
  - Multi-center

Movement Disorders

Essential Tremor

- Double-blind, placebo-controlled
- Randomized withdrawal design
- Multi-center

Parkinson's Disease

- Part A – Open-label panel
  - Single-center
- Part B – Placebo-controlled
  - Multi-center

SAGE-217 Strongly Positioned for Development in Broad Market CNS Indications

- Developing SAGE-217 as a first-in-class oral GABA modulator
- Exploring markets linked to GABA dysfunction with suitability for oral therapy
- Strong IP position with expected composition of matter to 2034

		Estimated U.S. Patient Population
Movement Disorders	**Essential Tremor:**	• ~6 - 7 million total patients[1]
	Parkinson's Disease:	• ~700,000 total patients[2] • 60,000 new diagnoses per year[3]
Mood Disorders	**Postpartum Depression:**	• ~500,000 - 750,000 new diagnoses per year[4,5] • Up to 80% moderate-severe[6]
	Major Depressive Disorder:	• ~16 million adults reported at least one major depressive episode in the past year[7]

[1] Louis ED, Ottman R. How many people in the USA have essential tremor? Deriving a population estimate based on epidemiological data. *Tremor Other Hyperkinet Mov.* 2014; 4. doi: 10.7916/D8TT4P4B[2] Willis et al, Neuroepidemiology.2010;34:143–151

[3] Parkinson's Disease Foundation, http://www.pdf.org/

[4] Hamilton et al. Births: Final data for 2014. *National Vital Statistics Reports*. National Center for Health Statistics, 2015, 64, 12.

[5] O'Hara MW & McCabe JE. Postpartum depression: Current status and future directions. *The Annual Review of Clinical Psychology,* 2013, 9, 379-407. doi: 10.1146/annurev-clinpsy-050212-185612.

[6] PACT. Lancet Psychiatry. 2015;2(1):59. Bobo. Mayo Clin Proc. 2014;89(6):835.

[7] National Institute of Mental Health website, 2014..

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Strong Financial Position to Advance Programs

Q3 2016 Financial Results (as of 9/30/2016)

	Q3 '16	Q4 '15
Cash and Marketable Securities	$431.3M	$186.8M

	Q3 '16	Q3 '15
Research & Development	$29.1M	$17.5M
General & Administrative	$9.0M	$6.6M
Net Loss	$37.8M	$24.0M

Guidance:

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

Upcoming Events and Conferences

- **Society for Neuroscience Annual Meeting**
  - November 12-16, 2016
  - San Diego, CA
- **Stifel Nicolaus Weisel Healthcare Conference**
  - November 16, 2016
  - New York, NY
- **American Epilepsy Society Annual Meeting**
  - December 2-6, 2016
  - Houston, TX
- **Sage 2016 R&D Day**
  - December 13, 2016
  - Boston, MA

Q&A Session

