SAGE THERAPEUTICS™

May 9, 2017

Q1 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 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 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 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.

SAGE THERAPEUTICS™

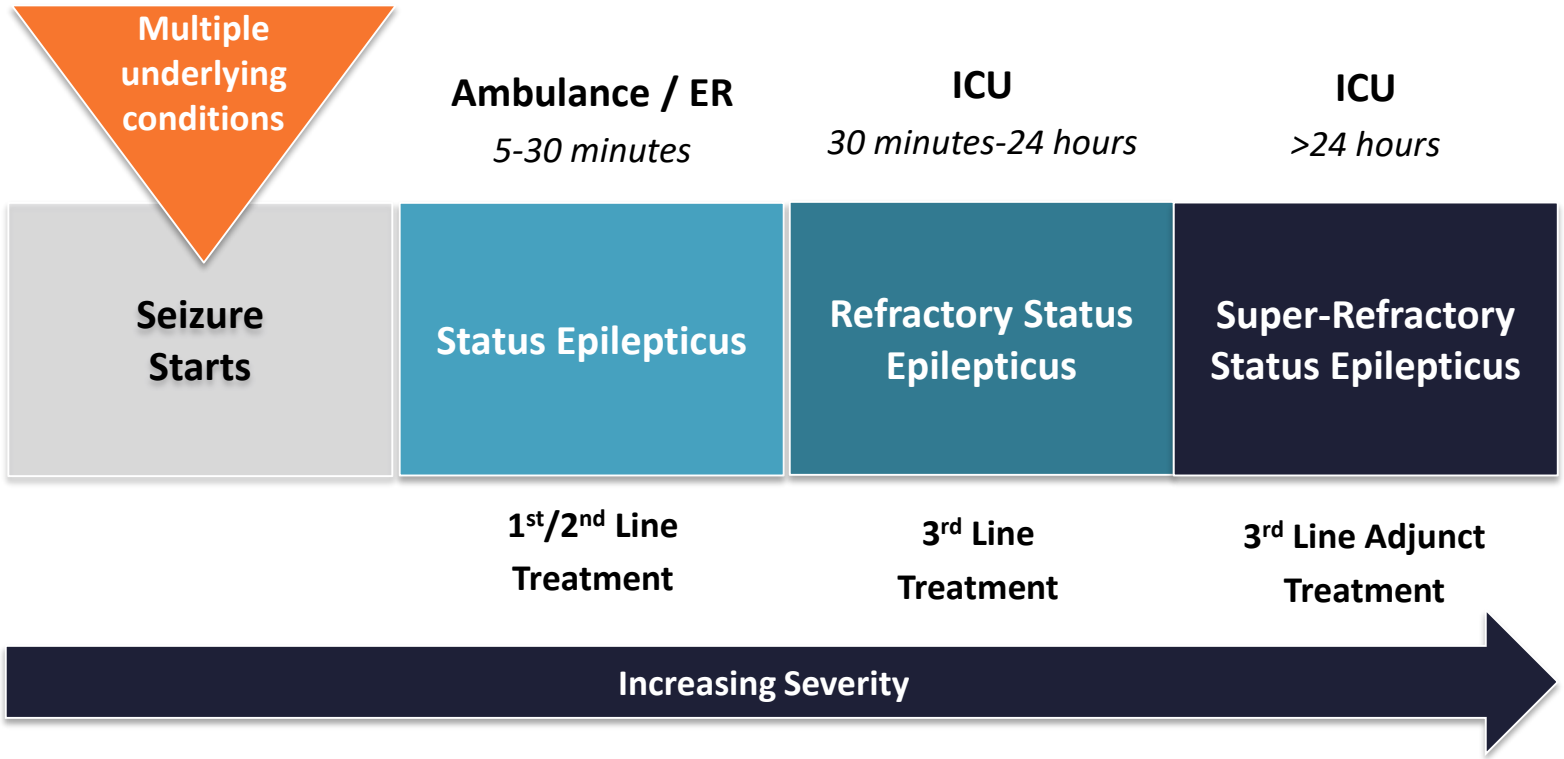
RETHINKING CNS

Multi-Compound Neuropsych Portfolio

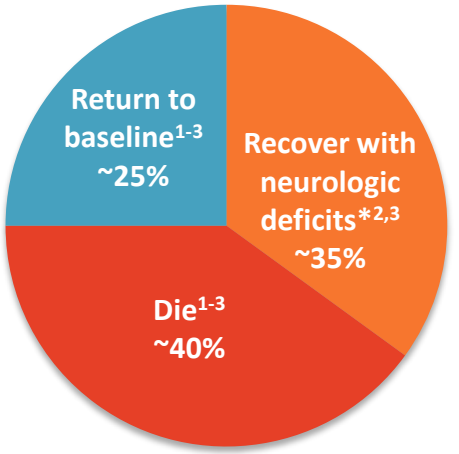
Program	Compound	Indication	Preclinical	Phase 1	Phase 2	Phase 3
GABA	Brexanolone (SAGE-547)	Super-Refractory Status Epilepticus				
		Postpartum Depression				
	SAGE-217	Postpartum Depression				
		Major Depressive Disorder				
		Essential Tremor				
		Parkinson's Disease				
	SAGE-324	GABA Hypofunction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

Super-Refractory Status Epilepticus (SRSE)

SRSE is a life-threatening neurologic emergency that occurs after ≥24 h in status epilepticus (SE), despite multiple therapeutic interventions (first-, second-, and third-line agents)



Estimated SRSE outcome rates[1,2,3]



* ~ 15% severe,
* ~ 15% mild,
* ~ 5% undefined[2]

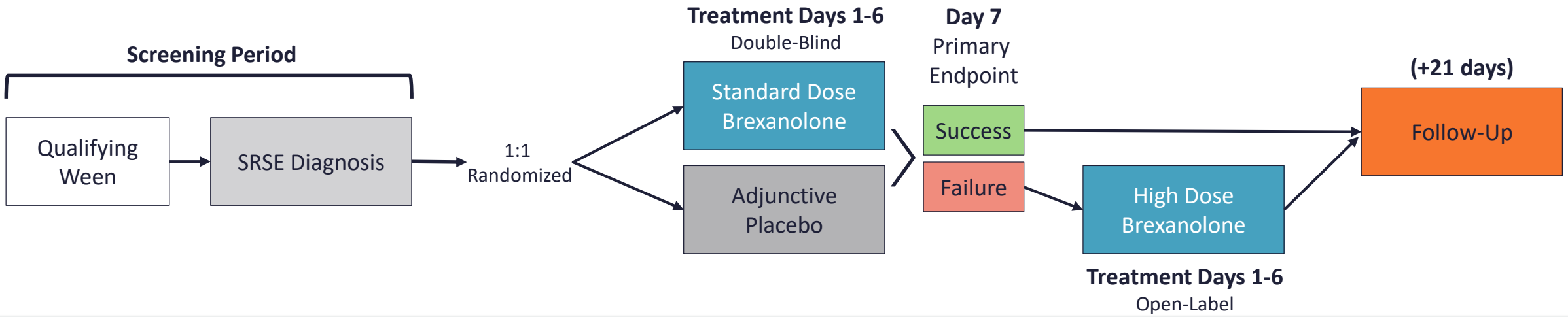
>55% of patients with SRSE die or remain severely disabled[2]

1. Shorvon et al. *Brain*. 2012;135(8):2314-28. 2. Novy et al. *Epilepsia*. 2010;51(2):251-6. 3. Claassen et al. *Epilepsia* 2002; 43(2): 146-153.

SAGE-547 Phase 3 SRSE Trial Design

STATUS TRIAL

- First-ever double-blind, placebo-controlled, randomized trial of a novel agent in SRSE
- Expect up to enroll up to 126 evaluable patients
- ~180 international sites (U.S., Canada, E.U., Israel)
- FDA Special Protocol Assessment and EMA Scientific Advice
- Primary Endpoint: continued resolution of SE for 24 hours following wean of all 3rd-line agents and brexanolone/placebo



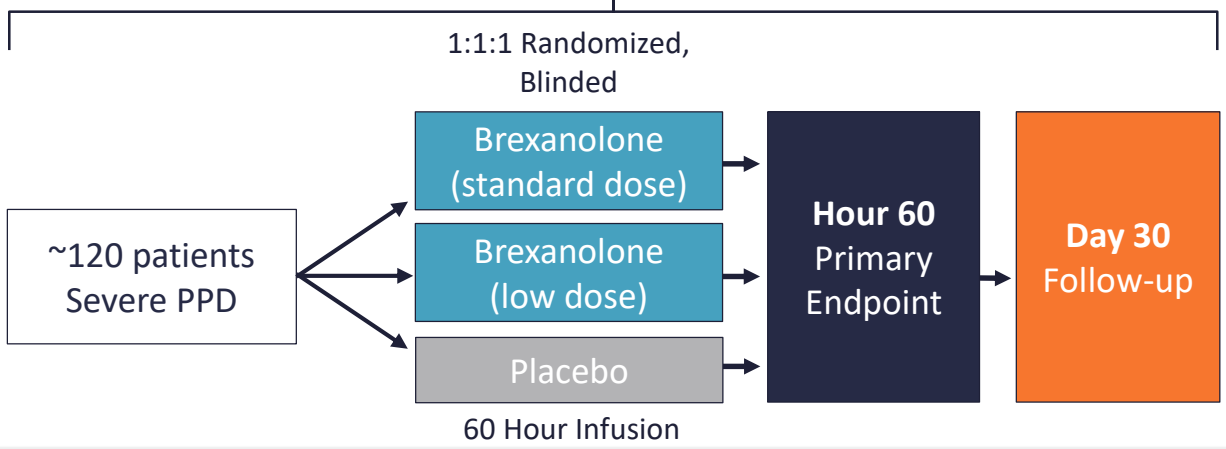
Brexanolone as a Treatment for PPD

Phase 3 HUMMINGBIRD Program

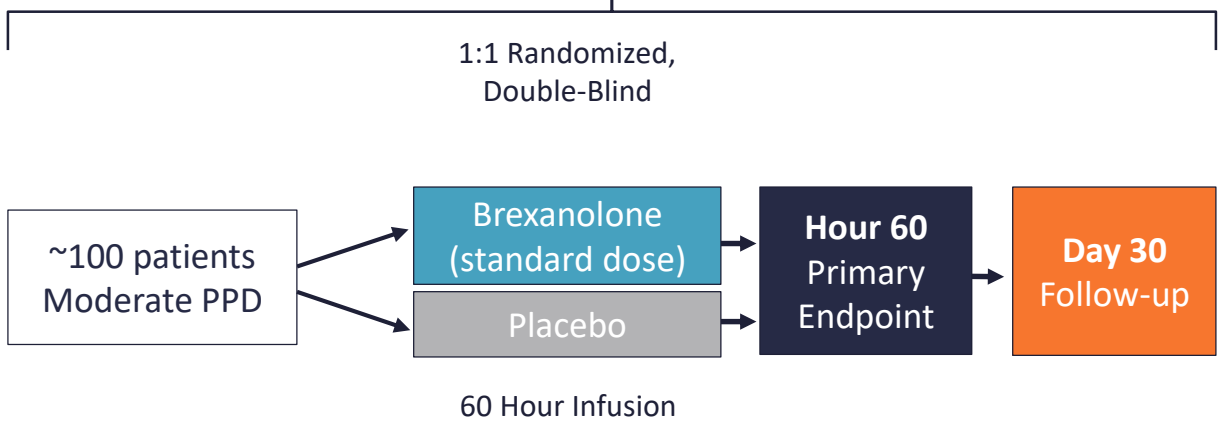
HUMMINGBIRD STUDY

Study Population	Key Endpoints
• Placebo-controlled, double-blind 1:1 randomization • Major depressive episode in 3rd trimester or within 4 weeks post-birth • HAM-D ≥26 (202B); HAM-D ≥20 and ≤25 (202C)	• 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 THERAPEUTICS

SAGE-217

Well Positioned for Development in Broad Market CNS Indications

		Estimated Total U.S. Patient Population
Mood Disorders	**Postpartum Depression:**	• ~500,000 - 750,000 new diagnoses per year[1,2,8] • ~320,000 - 400,000 patients seek treatment per year[3]
	Major Depressive Disorder:	• ~16 million adults reported at least one major depressive episode in the past year[4,8]
Movement Disorders	**Essential Tremor:**	• ~6 - 7 million total patients[5,8]
	Parkinson's Disease:	• ~700,000 total patients[6,8] • 60,000 new diagnoses per year[7,8]

1. Hamilton et al, *National Center for Health Statistics*, 2015; 2. O'Hara MW, McCabe JE, *Annual Review of Clinical Psych*., 2013; 3. Data on file. 4. Nat. Inst. of Mental Health website, 2014; 5. Louis ED, Ottman R, *Tremor Other Hyperkinet Mov*, 2014. 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 or claims analysis, as the case may be. Given limitations of methodologies on which current estimates are based, more in-depth studies are needed to better understand prevalence in each case.

Incremental Innovation

Advancing Novel Medicines through Deliberate and Data-Driven Development

Scientific Rationale

- Disease biology
- Role of mechanism
- Translatable animal models
- Right patient population

Early Proof-of-Concept

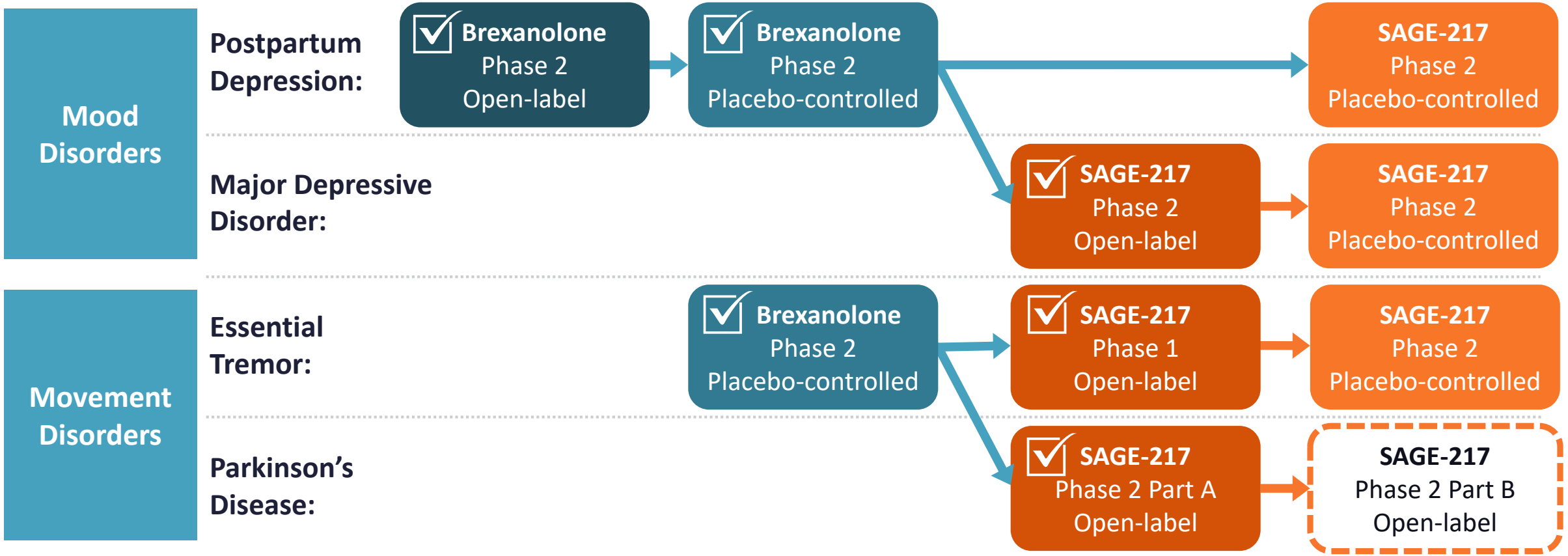
- Open-label signal finding
- Proof of activity
- Increased investment for next development phase
- Methodology for future studies

Controlled Validation

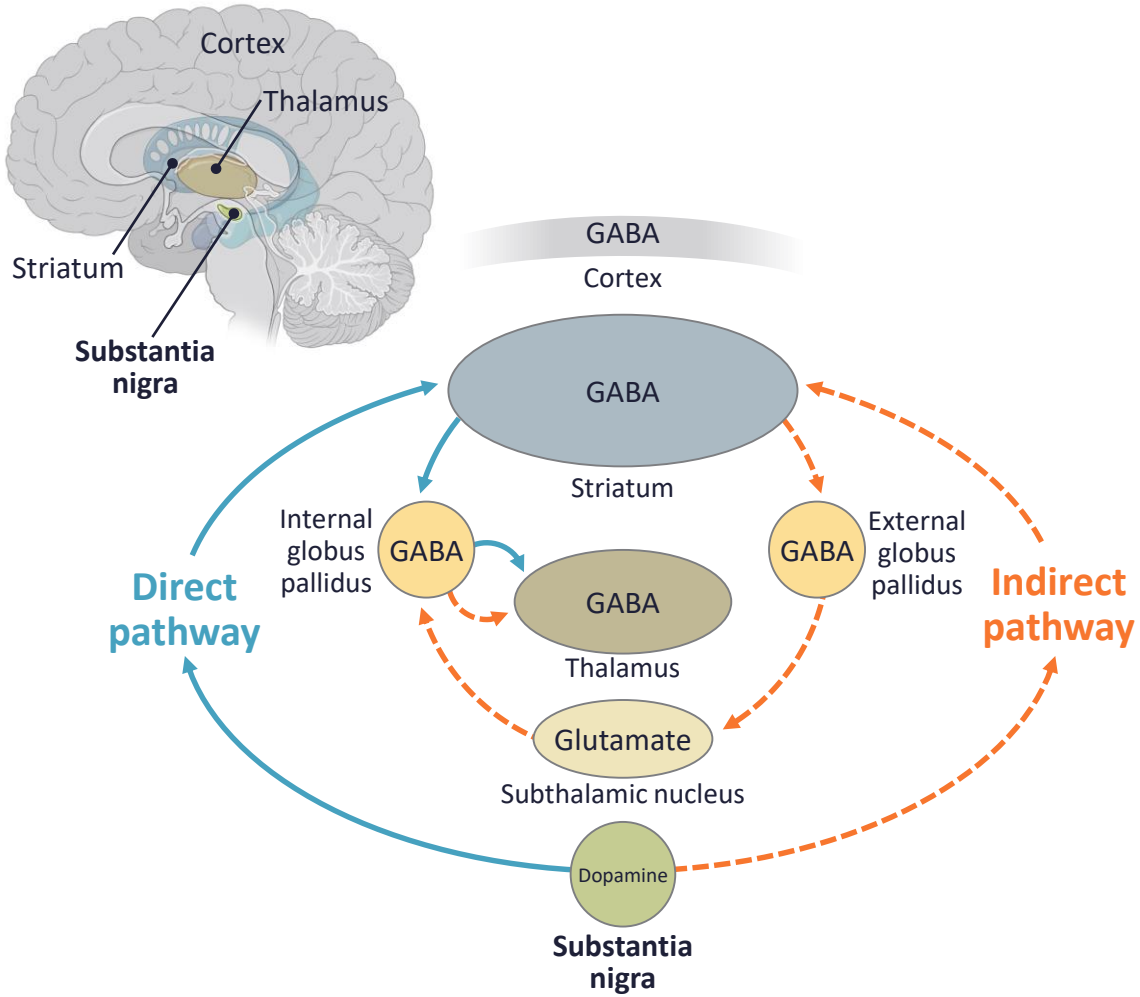
- Definitive, late-stage
- Multi-center, global
- Replicate earlier studies
- Goal to generate valuable data for regulatory discussions

SAGE-217 Clinical Development Strategy

Positive Data Drive Incremental De-Risking



Why Parkinson's Disease?



Disease Overview

- Parkinson's disease (PD) is a neurodegenerative disorder with motor and non-motor symptoms, including resting tremor and mood disorders
- Current treatment consists of dopamine replacement (levodopa/carbidopa), however, treatment is associated with motor complications

Pathophysiology

- PD is associated with loss of dopaminergic cells in the substantia nigra and alteration of the basal ganglia circuitry[1]
- The substantia nigra produces high levels of allopregnanolone ($GABA_A$ modulator)[2]
- Dopamine neurons are under control of the GABA system
- Decreased levels of allopregnanolone have been measured in plasma and cerebrospinal fluids in PD patients[3]

1. Siderowf A, Lang AE, *Movement Disorders*, 2012; 2. di Michele et al, *Front Neuroendocrinol*, 2013; 3. di Michele et al, *Neurol Sci,* 2003.

SAGE-217 in Parkinson's Disease

Phase 2 Proof-of-Concept Program

Study Population	Key Endpoints
• PD patients with duration less than 7 years and moderate severity (stage 2 or 3) • Stable dosing of levodopa/carbidopa prior to study • 12 patients (Part A); ~10 patients (Part B) • Positive Part B could lead to placebo-controlled studies	• Safety, tolerability and pharmacokinetics • Change from baseline in MDS-UPDRS Part III score

SAGE-217 in Parkinson's Disease

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

Top-Line Results Summary

- For overall study population (N=12), levodopa/carbidopa activity was primarily focused on the motor symptoms of bradykinesia and rigidity, while SAGE-217 activity as monotherapy was primarily focused on tremor symptoms
- ~20-30% improvement in tremor symptoms was observed on the 4 days of SAGE-217 open-label treatment in patients with overt tremor (n=5; tremor score >5 at baseline MDS-UPDRS Part III tremor score)
- Improvement in tremor score during the SAGE-217 dosing phase was longer-lasting than effect on tremor observed in these patients during the levodopa/carbidopa-only phase

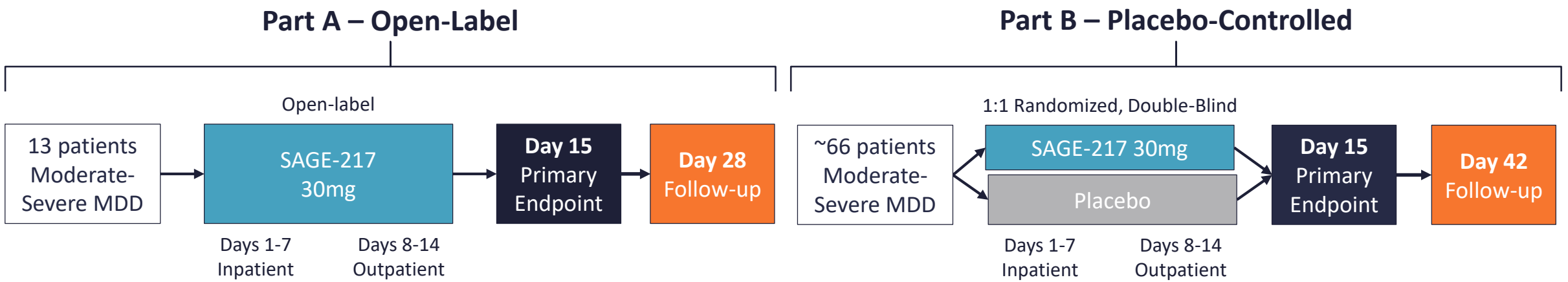
Safety and Tolerability (Primary Endpoint)

- SAGE-217 was generally well-tolerated with no SAEs or discontinuations
- Similar to findings in Phase 1 program, most common AEs were sedation and somnolence
- Dosing was initiated at 30 mg/day MTD established in Phase 1 - majority of patients were down-titrated to 10-20 mg/day of SAGE-217

SAGE-217 in MDD

Phase 2 Clinical Program

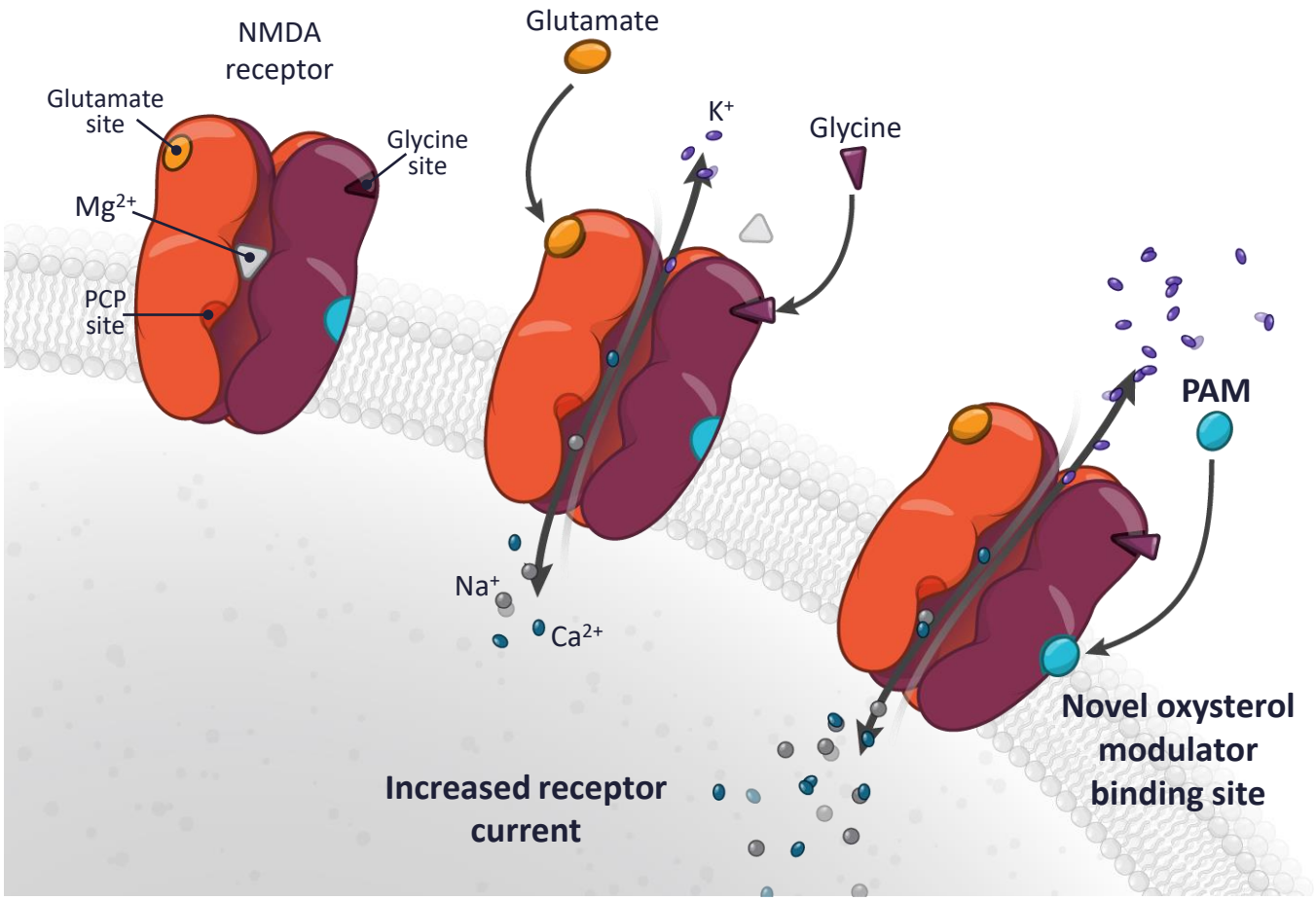
Study Population	Key Endpoints
• Patients with MDD present for 4-week period • HAM-D ≥22 • 13 patients (Part A); ~66 patients (Part B)	• Safety, tolerability and pharmacokinetics • Change from baseline in HAM-D total score



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

Now in Phase 1 Clinical Development

- NMDA receptor system plays a critical role in brain network balance and plasticity
- Loss of NMDA function may have significant impact on neuropsych disorders
- SAGE-718 is a novel, oral, first-in-class, oxysterol-based positive allosteric modulator (PAM) of the NMDA receptor
- Good oral pharmacokinetic profile in animal models



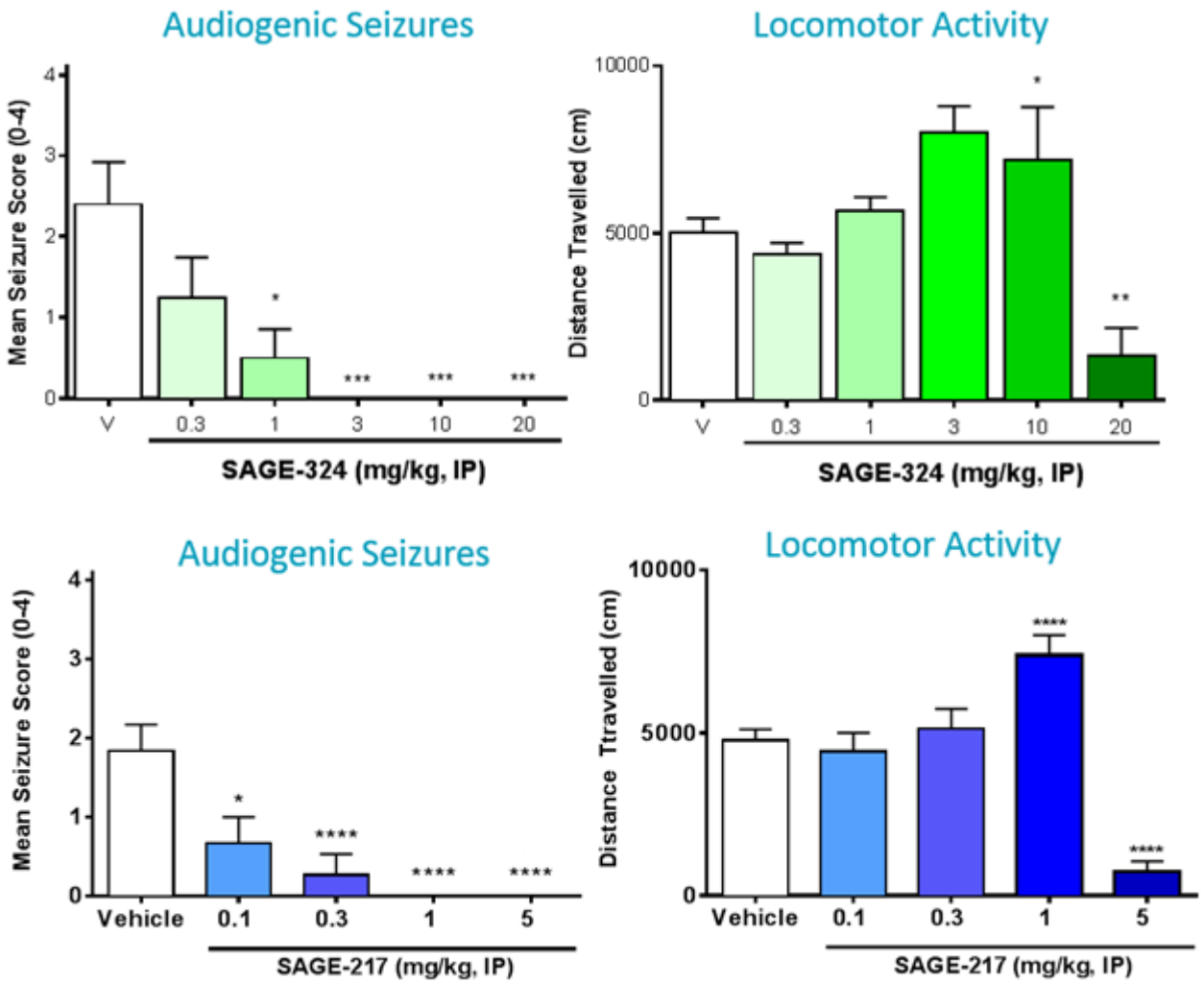
SAGE-324: Next Generation Oral $GABA_A$ Receptor PAM

Progressing in IND-Enabling Studies

- Potent anti-seizure activity in preclinical models
- Wider dose range before locomotor impairment in animals (compared with SAGE-217)

SAGE-324 activity in Fmr1 Knockout Mice

SAGE-217 activity in Fmr1 Knockout Mice



Solid Financial Position to Advance Programs

Q1 2017 Financial Results (as of 3/31/2017)

	Q1 '17	Q4 '16
Cash and Marketable Securities	$342.6M	$397.5M

	Q1 '17	Q1 '16
Research & Development	$45.2M	$23.6M
General & Administrative	$12.3M	$7.1M
Net Loss	$56.8M	$30.5M

Guidance:

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

Recent and Expected Milestones

Program	Compound	Indication	1H 2017	2H 2017	1H 2018
GABA	Brexanolone (SAGE-547)	Super-Refractory Status Epilepticus		○ Ph 3 top-line data (Q3)	
		Postpartum Depression		○ Ph 3 top-line data ▪ 202B - Severe ▪ 202C - Moderate	
	SAGE-217	Postpartum Depression		○ Ph 2 top-line data	
		Major Depressive Disorder	✓ Ph 2 open-label data ✓ Initiate Ph 2 Part B		○ Ph 2 Part B top-line data
		Essential Tremor		○ Ph 2 top-line data	
		Parkinson's Disease	✓ Ph 2 Part A initiation ✓ Ph 2 Part A data ○ Initiate Ph 2 Part B	○ Ph 2 Part B top-line data	
NMDA	SAGE-718	Cerebrosterol Deficit Disorders	✓ Ph 1 SAD initiation	○ Ph 1 SAD data	
		Anti-NMDA Receptor Encephalitis			
		NMDA Hypofunction			

Commitment to Neuroscience Leadership

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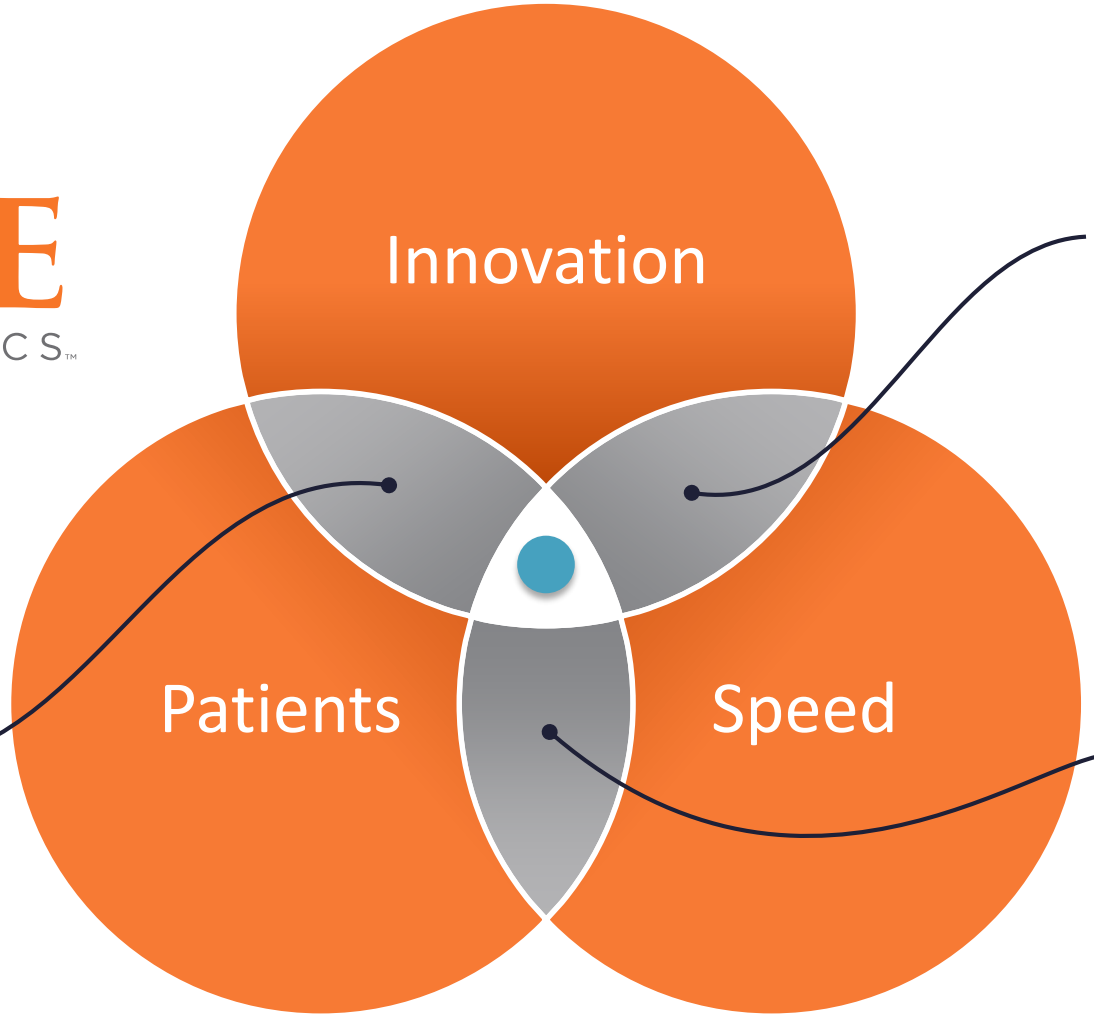

Advancing novel medicines through deliberate, stepwise and data-driven development

Tackling the **innovation** gap in CNS

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