SAGE THERAPEUTICS™

January 2017

J.P. Morgan Healthcare Conference

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.

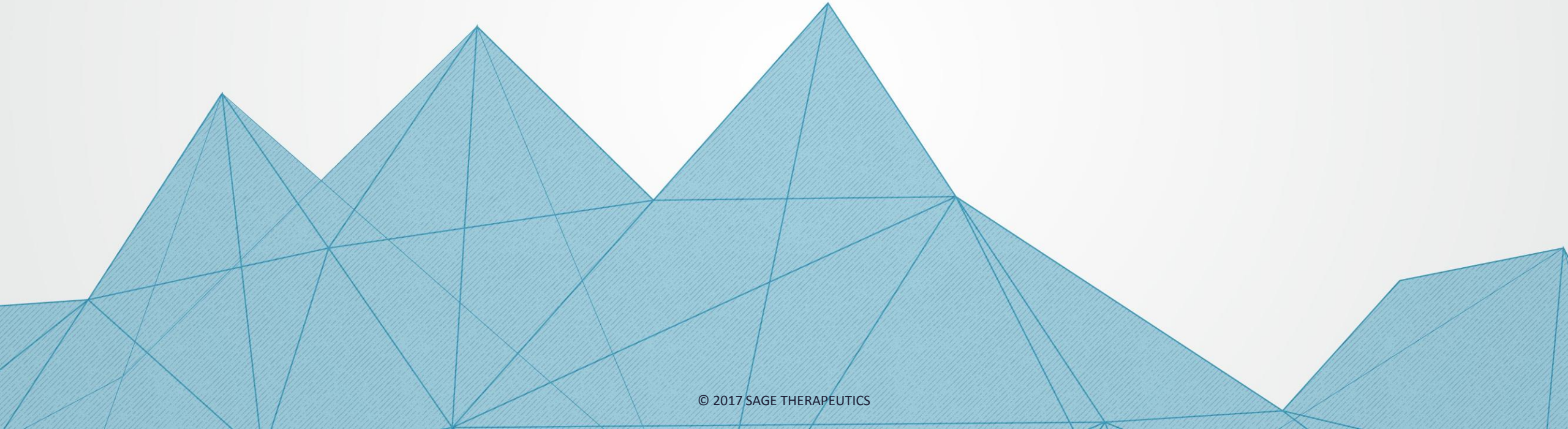
For additional disclosure regarding these and other risks SAGE faces, see the disclosure contained in the "Risk Factors" section of SAGE’s our most recent Quarterly Report on Form 10-Q, and in SAGE’s other public filings with the Securities and Exchange Commission, available on the SEC's website at http://www.sec.gov. 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.

The CNS Disease Landscape

The brain is an interactive network. Simple “target” approaches may fail.

Few CNS breakthroughs in decades.

CNS disorders represent 35% of WW disease burden.



SAGE THERAPEUTICS™

RETHINKING CNS

Pioneer New Approaches to Neuroscience R&D

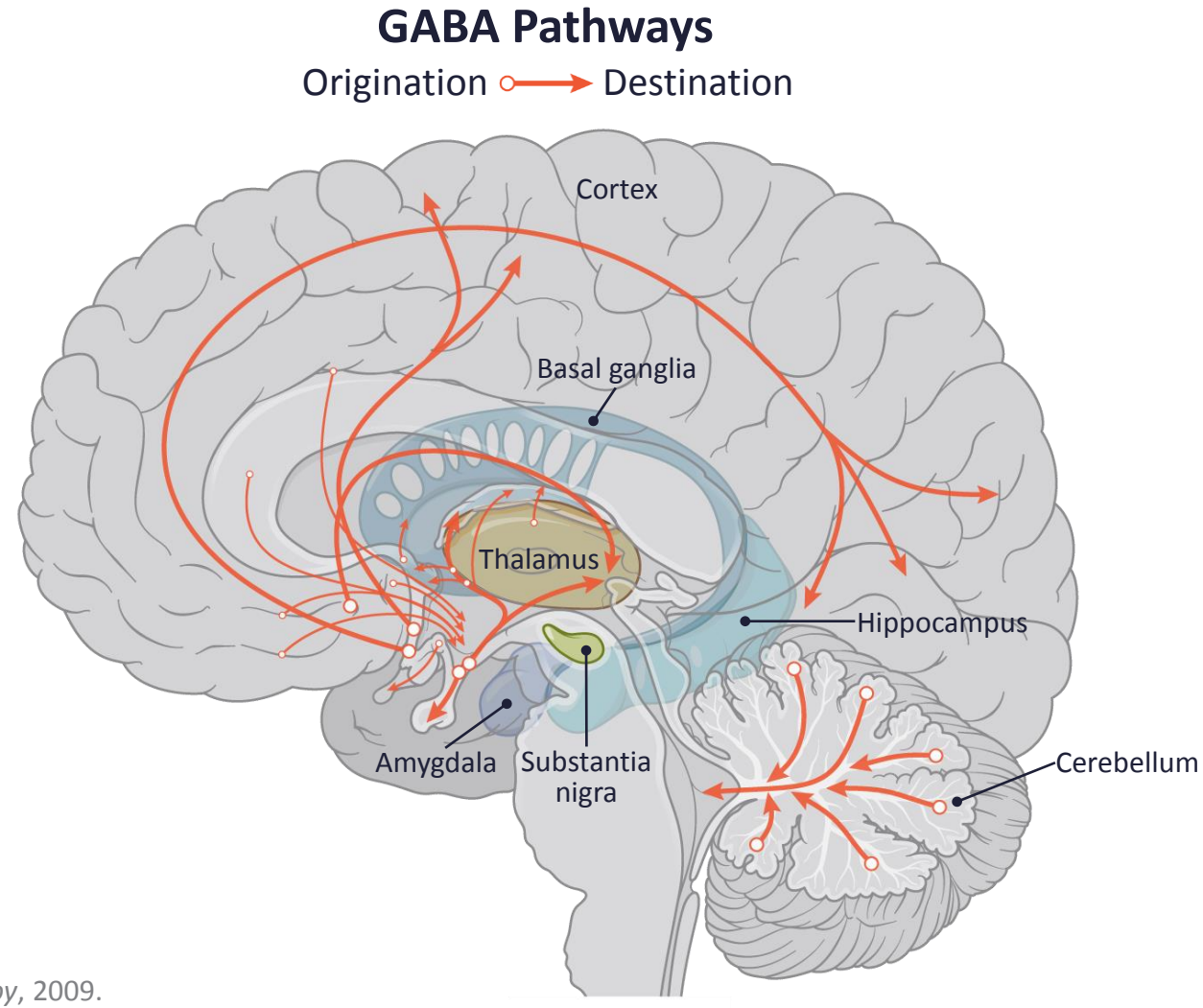
- **Lead with human data**
- Focus on **powerful mechanisms** known to have demonstrated and broad effects on brain networks
- Design **bespoke next-generation compounds** differentiated from available therapies
- Utilize new and efficient **translational approaches** to speed discovery and clinical development
- **Data-driven development** - true “serial de-risking” to “incrementally innovate”
- Clinical trials in **defined populations** with **rapid readouts** and **well-defined endpoints**

Multi-Compound Neuropsych Portfolio

Program	Compound	Indication	Preclinical	Phase 1	Phase 2	Phase 3
GABA	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				

GABA is the Major Inhibitory Brain Network

- GABA is an abundant and ubiquitous inhibitory neurotransmitter in the brain[1]
- GABA dysfunction can occur in many different brain regions with potential downstream effects
- The $GABA_A$ receptor family is complex with diverse physiology, pharmacology and function[2]
  - 19 different receptor subunits[3]

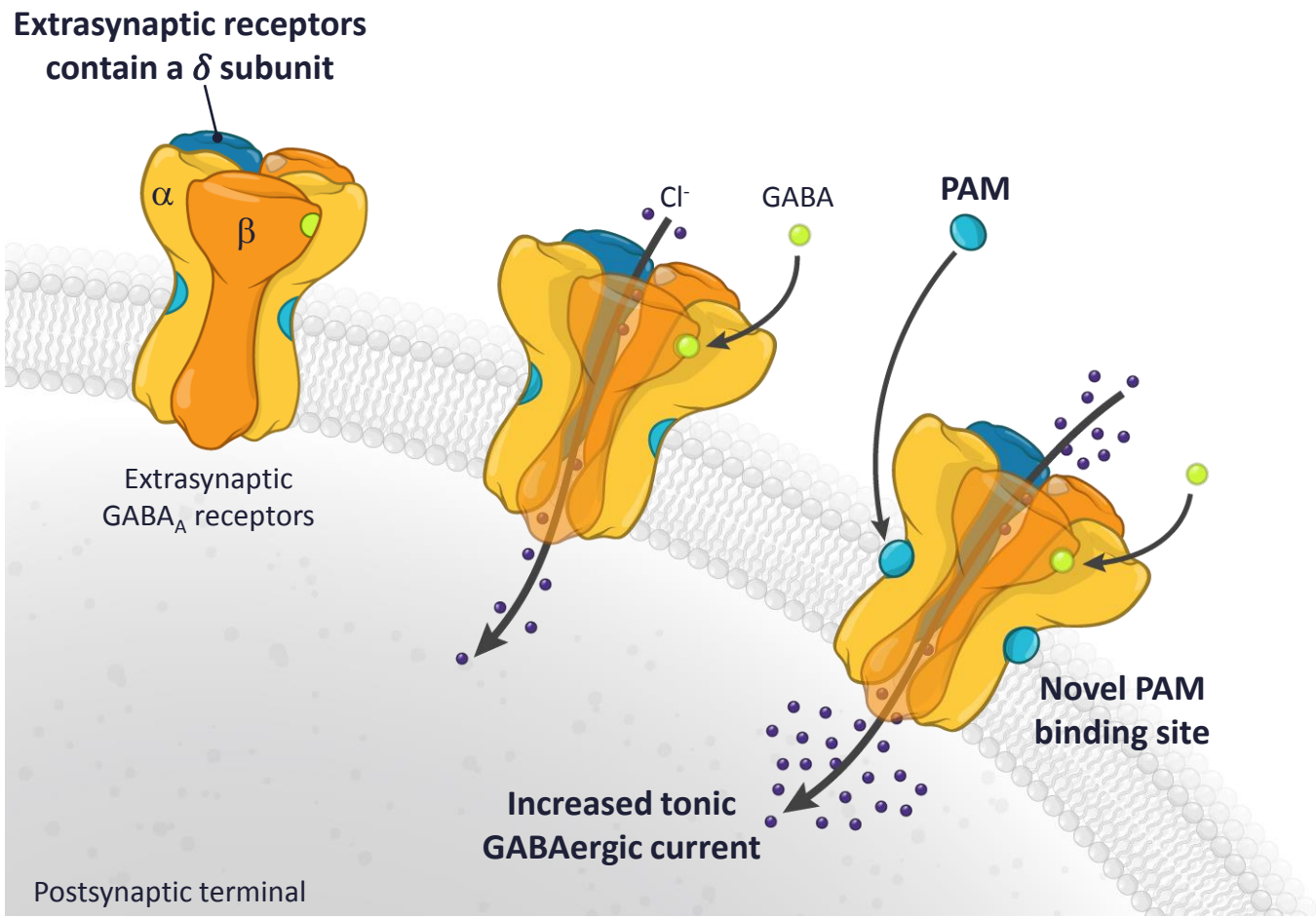


1,2. Nutt DJ, Malizia AL, *Br J Psychiatry*, 2001; 3. Olsen RW, Sieghart W, *Neuropharmacoloy*, 2009.

SAGE Approach to GABA

Compounds Specifically Target both Phasic and Tonic Receptors

- **Positive allosteric modulation (PAM)** increases receptor efficacy and/or potency
- **Neuroactive steroids** (NAS) can enhance neurotransmission in both regions, unlike benzodiazepines
- **Tonic inhibitory receptors** play a critical role in regulating neuronal circuit excitability
- Certain **Sage NAS compounds** demonstrate capability *in vitro* to increase receptor function
  - PKC trafficking of receptors to cell surface
  - Not all NAS compounds have this capability



SAGE-547: Lead Phase 3 GABA Program

First Generation Compound from Sage's Robust GABA Library

- **SAGE-547 Injection** is a proprietary formulation of allopregnanolone
- Endogenous PAM of $GABA_A$ receptors[1]
- Positive data across numerous clinical and preclinical studies
- In Phase 3 development as an acute interventional treatment:
  - **SRSE** - Fast Track and Orphan Drug Designations in U.S.
  - **PPD** - Breakthrough Therapy (U.S.) and PRIME (EU) Designations

1. Majewska et al, *Science*, 1986.

SAGE-547 has Demonstrated Robust Activity in Clinical Studies

Super-Refractory Status Epilepticus

- SAGE-547 demonstrated a +73% response rate in a Phase 1/2 open-label treatment of patients with SRSE
- SAGE-547 showed a favorable tolerability profile

Robust Activity

Favorable Tolerability

Postpartum Depression

- Primary endpoint met (p=0.008) in Phase 2 placebo-controlled trial in severe PPD patients
- 70% remission achieved at 60 hours of SAGE-547 treatment and maintained at Day 30 follow-up
- SAGE-547 was generally well tolerated in Study 202A

SRSE and PPD

Two Patient populations Significantly Underserved by Current Treatments

Super-Refractory Status Epilepticus

- Life-threatening neurologic emergency
- ≥24 hours in SE despite 1st, 2nd and 3rd-line therapeutic interventions
- Lack of clinical evidence to inform treatment
- High disease burden
- High morbidity and mortality

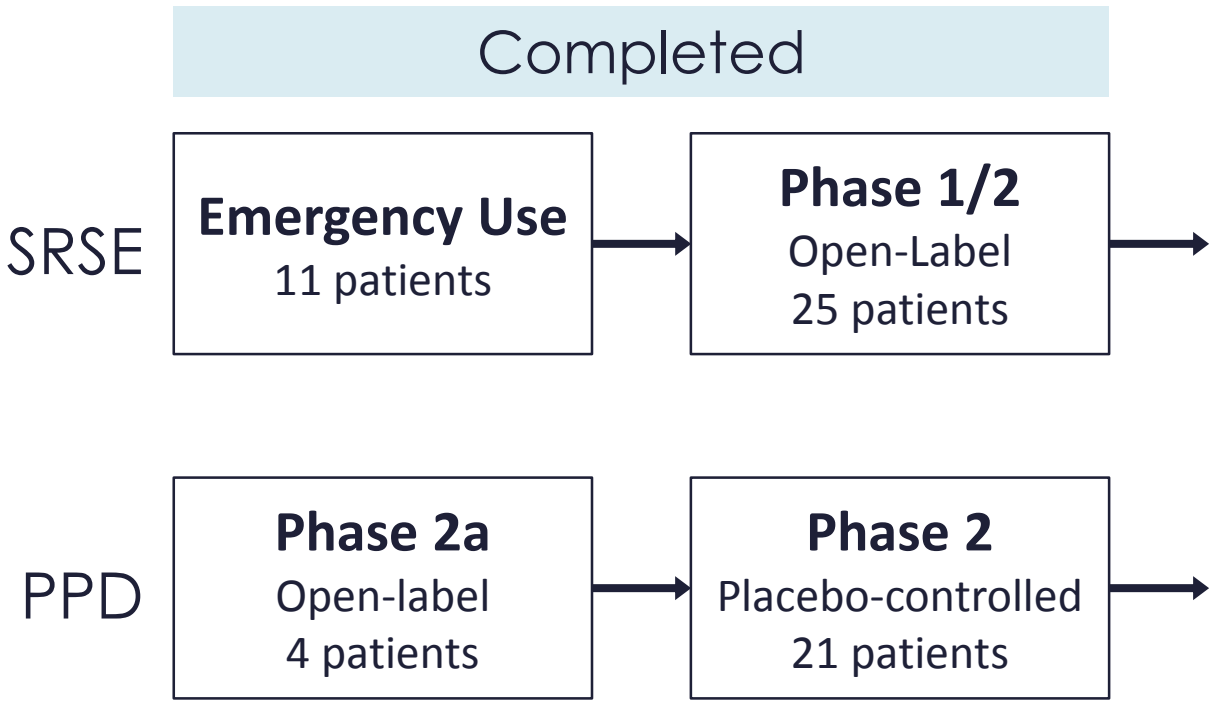
Significant Unmet Need

No Treatments Specifically FDA-Approved

Postpartum Depression

- Medical complication of pregnancy
- Depression, anxiety, difficulty sleeping, poor self-esteem
- Disassociation with baby and family members or hypervigilance about baby
- Highly stigmatizing
- Suicide is leading cause of maternal death following childbirth

SAGE-547 Dual Phase 3 Development Path



Ongoing Efficacy Studies

STATUS TRIAL

Phase 3 Placebo-controlled
Expected to enroll ~140 patients

HUMMINGBIRD

Phase 3 Placebo-controlled
Expected to enroll ~220 total patients

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

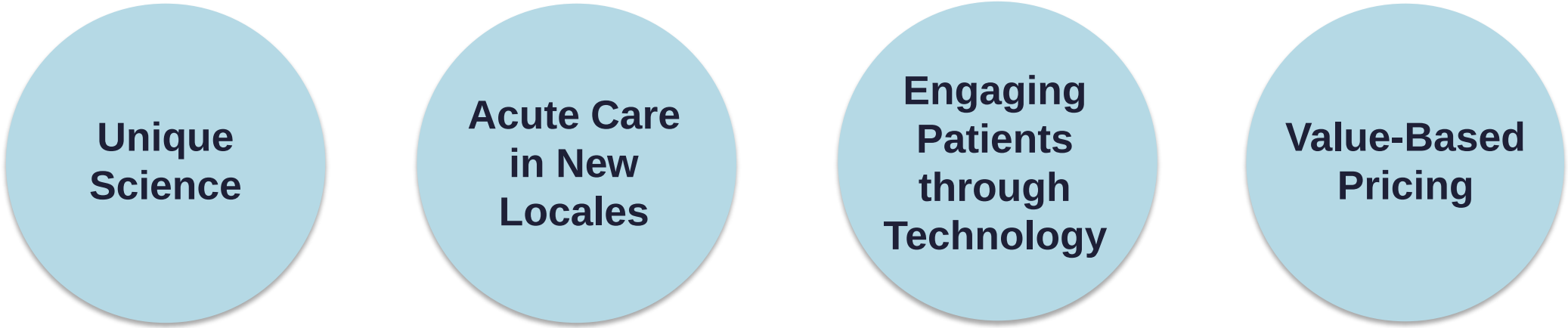
SAGE-547's Two Near-Term Commercial Opportunities

	SRSE	PPD
Estimated U.S. Patient Population:	• ~25,000 – 41,000 in per year[1,5]	• 500,00-750,000 pear year[2,3] • Claims for ~360,000 patients seeking treatment[4]
Customers:	• ~1,200 target hospitals • ICUs, hospital pharmacy • Critical care specialists, neurologists, epileptologists, pharmacists	• ~1,200 target hospitals • Clinics, home infusion, group practices • OBGYNs, psychiatrists, select PCPs
Commercial Build-Out:	• Field-based: ~125 Account Managers, Regional Business Directors and Market Access personnel at launch, if both indications approved • Patient and Provider Access network and services	
Preliminary Pricing Assumptions:	• $25,000 - $75,000 per patient	• Proportional patient pricing

1. Beg et al. *Journal of Medical Economics,* 2016. 2. Hamilton et al. *National Vital Statistics Reports*. National Center for Health Statistics, 2015. 3. O'Hara MW & McCabe JE. *The Annual Review of Clinical Psychology,* 2013. 4. Truven data on file. 5. 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.

SAGE-547 Approval Would Represent New Paradigms for the Treatment of SRSE and PPD

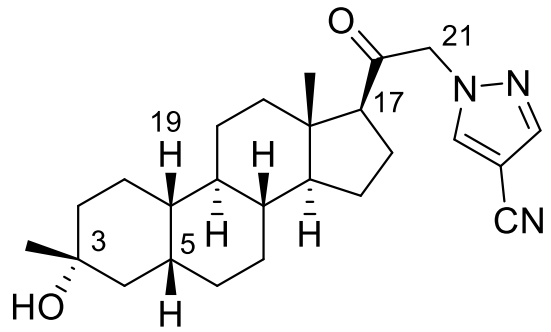
- If successful, SAGE-547 would represent the **first-ever medicine** specifically developed and approved for SRSE or PPD
- Availability of an approved **evidence-based treatment** could drive improved disease awareness, diagnosis and treatment in indications with potentially significant under-diagnosis and under-treatment
- Approval and availability of a potentially **rapid-acting and life-altering** treatment for these disorders would drive new **innovative approaches** in the marketplace



SAGE-217: First-in-Class Oral $GABA_A$ Receptor Modulator

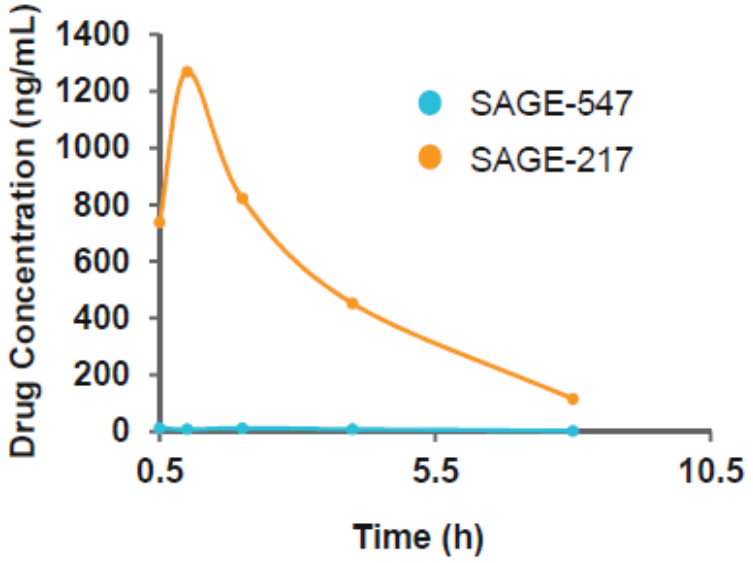
Novel Compound in Broad Phase 2 Development

- **In Phase 1:**
  - Well tolerated in over 100 human subjects
  - Clear evidence of EEG target engagement



- **In preclinical studies:**
  - Highly potent and selective next generation $GABA_A$ receptor PAM
  - PK/PD profile strongly differentiated from 1st Gen NAS
  - Oral bioavailability
  - Brain penetrant in preclinical studies (B/P > 3)

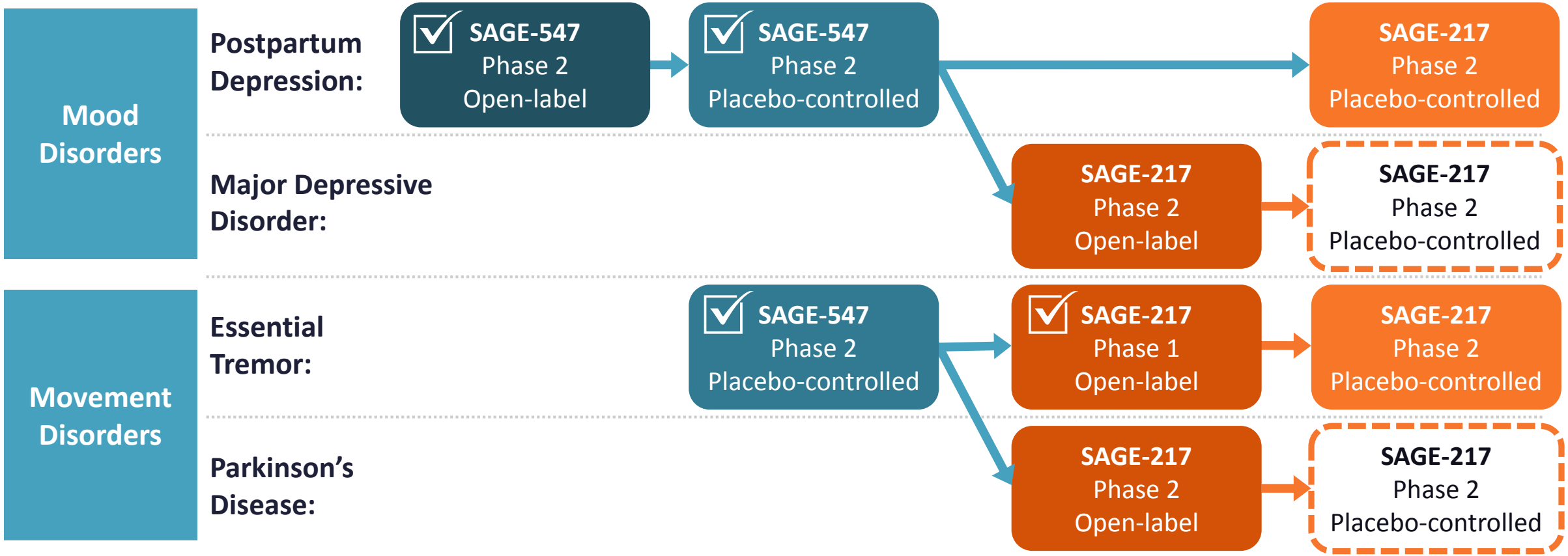
Oral Bioavailability vs. SAGE-547 (*in vivo*) [1]



1. Belfort et al, American Epilepsy Society Annual Meeting, 2016.

SAGE-217 Clinical Development Strategy

Positive Data Drive Incremental De-Risking



SAGE-217

Well Positioned for Development in Broad Market CNS Indications

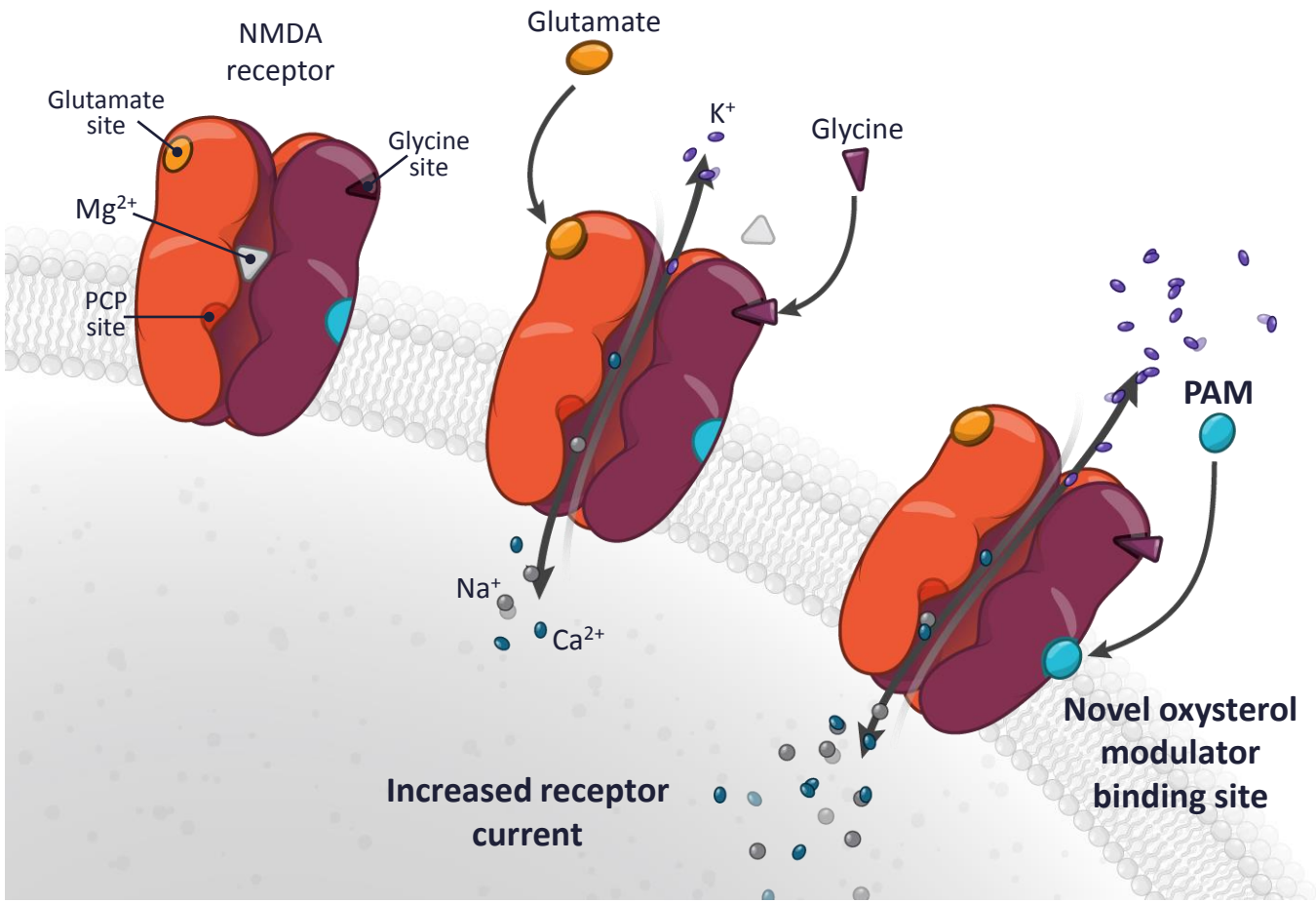
		Estimated Total U.S. Patient Population
Mood Disorders	**Postpartum Depression:**	• ~500,000 - 750,000 new diagnoses per year[1,2,8] • Claims for ~360,000 patients seeking treatment[3]
	Major Depressive Disorder:	• ~16 million adults reported at least one major depressive episode in the past year[4,8]
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. Truven 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.

SAGE Differentiated Approach to NMDA

Key Regulator of Excitatory Neurotransmission

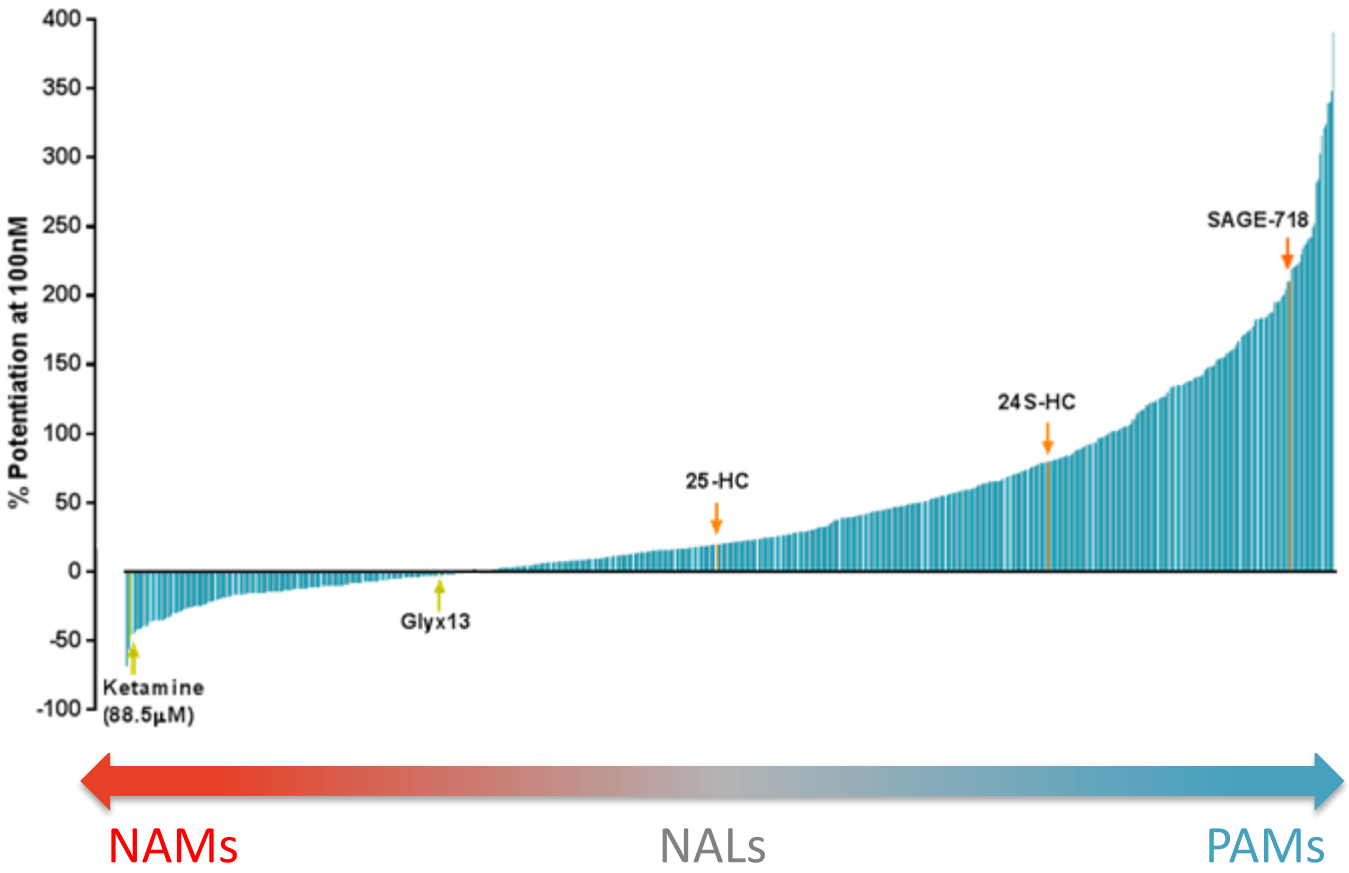
- NMDA plays a critical role in brain plasticity and neuronal network stabilization
- Loss of NMDA function may have significant impact on neuropsych disorders
- Existing NMDA agonists/antagonists have faced side effects and excitotoxity
- Sage has discovered a novel endogenous oxysterol-based modulatory mechanism
  - Potential for greater selectivity and minimal off-target effects

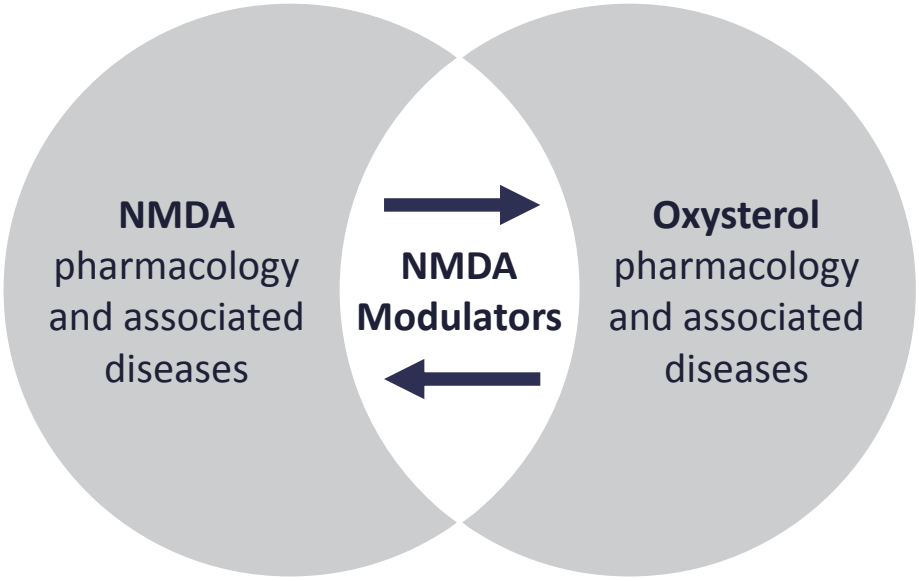


Sage's Robust NMDA Chemical Library

Over 800 Compounds with Broad Therapeutic Potential

Designed for Purpose Compound Library





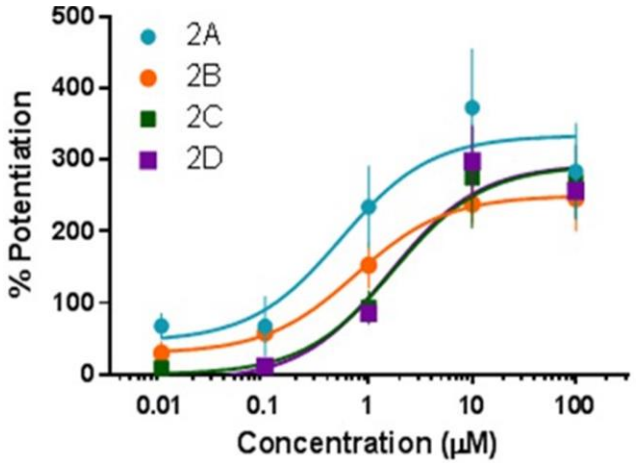
- Anti-NMDA Receptor Encephalitis
- Schizophrenia
- Depression
- Mood disorders
- Cognition
- Dementia
- Cerebrosterol Deficit Disorders
- Autism Spectrum Disorders
- Huntington's

SAGE-718: Developing as a First-in-Class NMDA Modulator

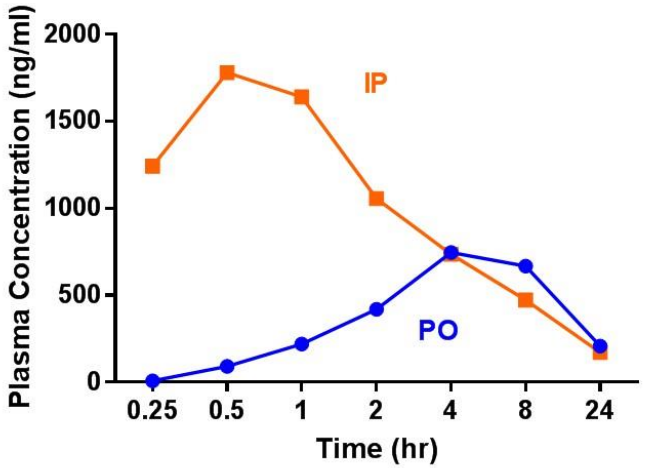
Expect to Begin Phase 1 Clinical Development in 1H 2017

- Potent and selective oxysterol-based NMDA PAM
- Good oral pharmacokinetic profile in animal models
- No off-target effects in a panel of 81 receptors and ion channels
- 24S-HC may serve as a peripheral biomarker for development

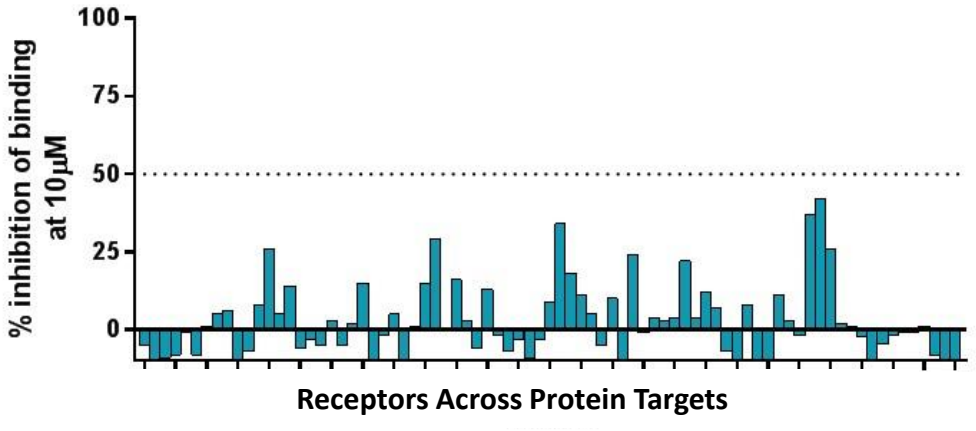
SAGE-718 Activity at NMDA Receptors (*in vitro*)



SAGE-718 Plasma PK (*in vivo*)



SAGE-718 Minimal Off-Target Activity (*in vitro*)



Source: Lewis et al, Society of Biological Psychiatry Annual Meeting, 2016.

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	
		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			

Our Goal:
A Commercial CNS Product Portfolio with Global Reach

Leadership in CNS Development

- Robust pipeline of differentiated and novel GABA and NMDA drug candidates

SAGE-547 **Opportunities**

- Two parallel Phase 3 programs in SRSE and PPD with upcoming data readouts

Developing SAGE-217

- First-in-class extrasynaptic GABA oral modulator
- Multiple Phase 2 studies with opportunities in large CNS markets

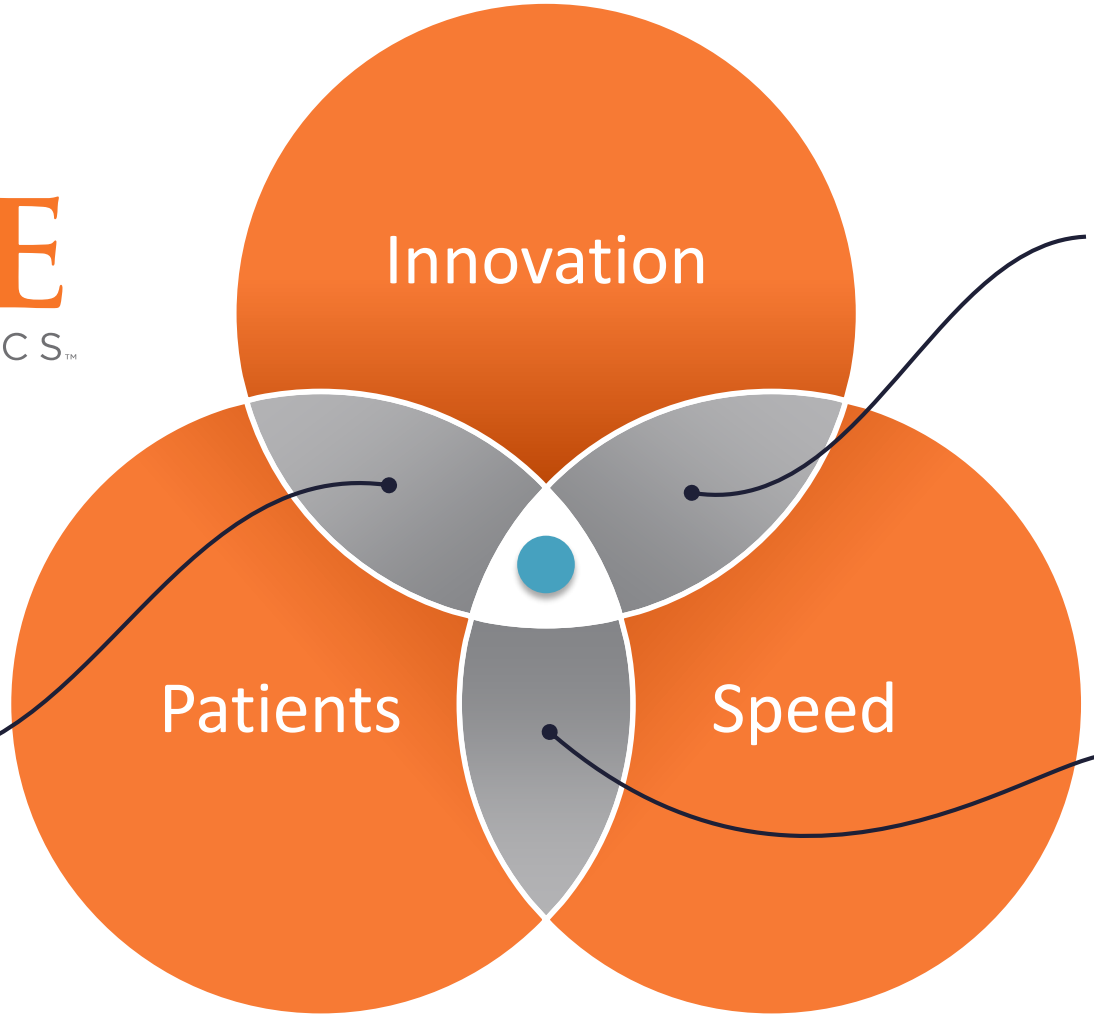
Uniquely **Positioned**

- 8 data readouts across pipeline with optionality for portfolio expansion
- Value inflection opportunities and continued momentum expected in 2017

Abbreviation: CNS, central nervous system; GABA, γ-aminobutyric acid; NMDA, *N*-Methyl-D-aspartic acid; SRSE, super-refractory status epilepticus; PPD, postpartum depression.

Commitment to Neuroscience Leadership

SAGE THERAPEUTICS™



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

Tackling the **innovation** gap in CNS

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