



| DISCOVER
| DEVELOP
| DELIVER

**Novel Medicines for
Life-Altering CNS
Disorders**

**Q3 2015 Financial Results
November 5, 2015**



Agenda

Introduction

- Paul Cox, Director, Investor Relations

Pipeline Update

- Jeff Jonas, M.D., Chief Executive Officer

Financial Results and Upcoming Milestones

- Kimi Iguchi, Chief Financial Officer

Q&A Session

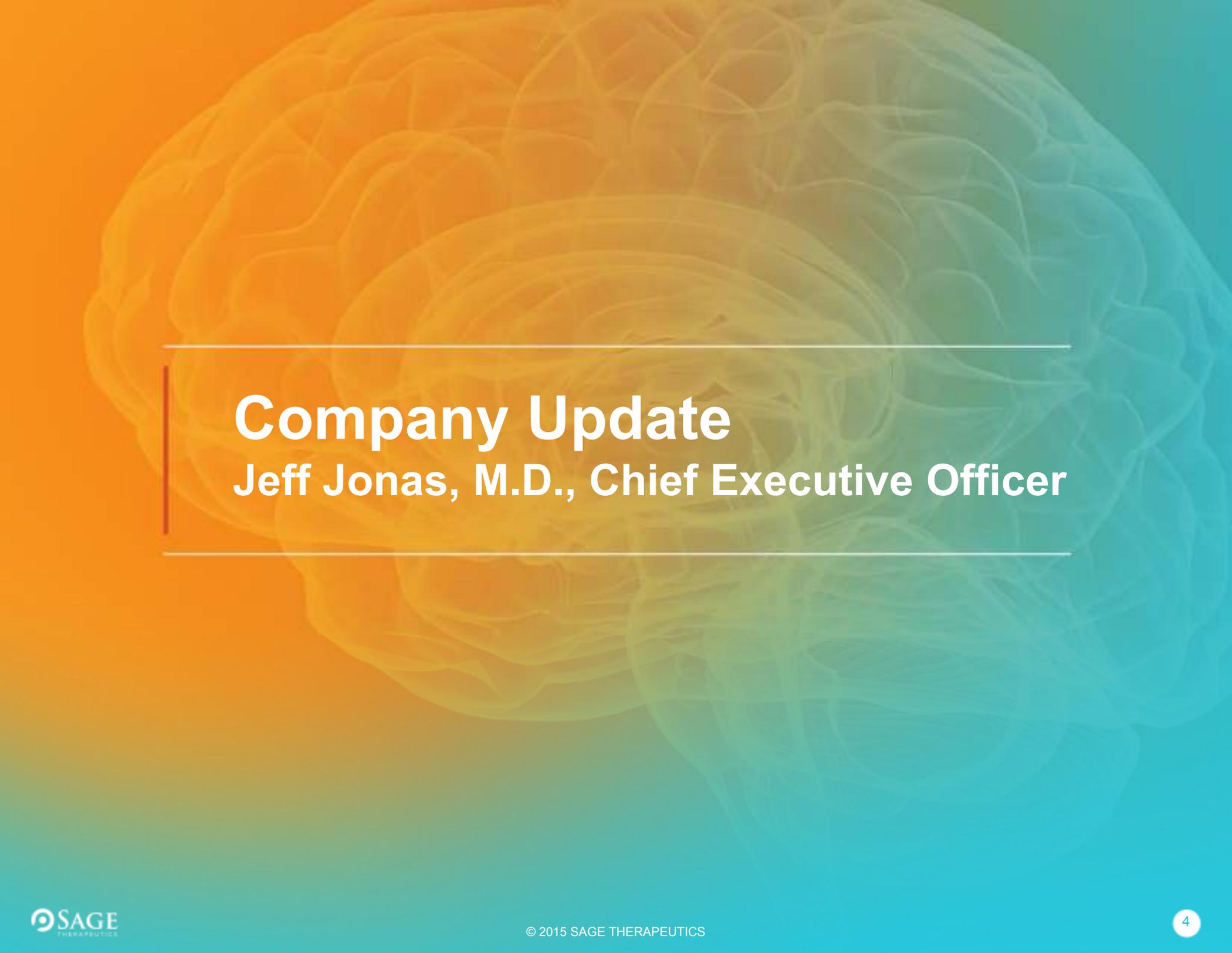
Forward-Looking Statements

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; the expected development pathway for SAGE’s product candidates; anticipated development milestones and results; the estimated number of cases of SRSE each year; expectations regarding commercialization of SAGE-547 in SRSE, if successfully developed; the anticipated impact of SAGE’s development model on future development results and on its ability to advance its pipeline; potential future indications for SAGE’s product candidates; the strength of SAGE’s intellectual property portfolio; 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;
- even if SAGE’s products are successfully developed and approved, 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, 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.

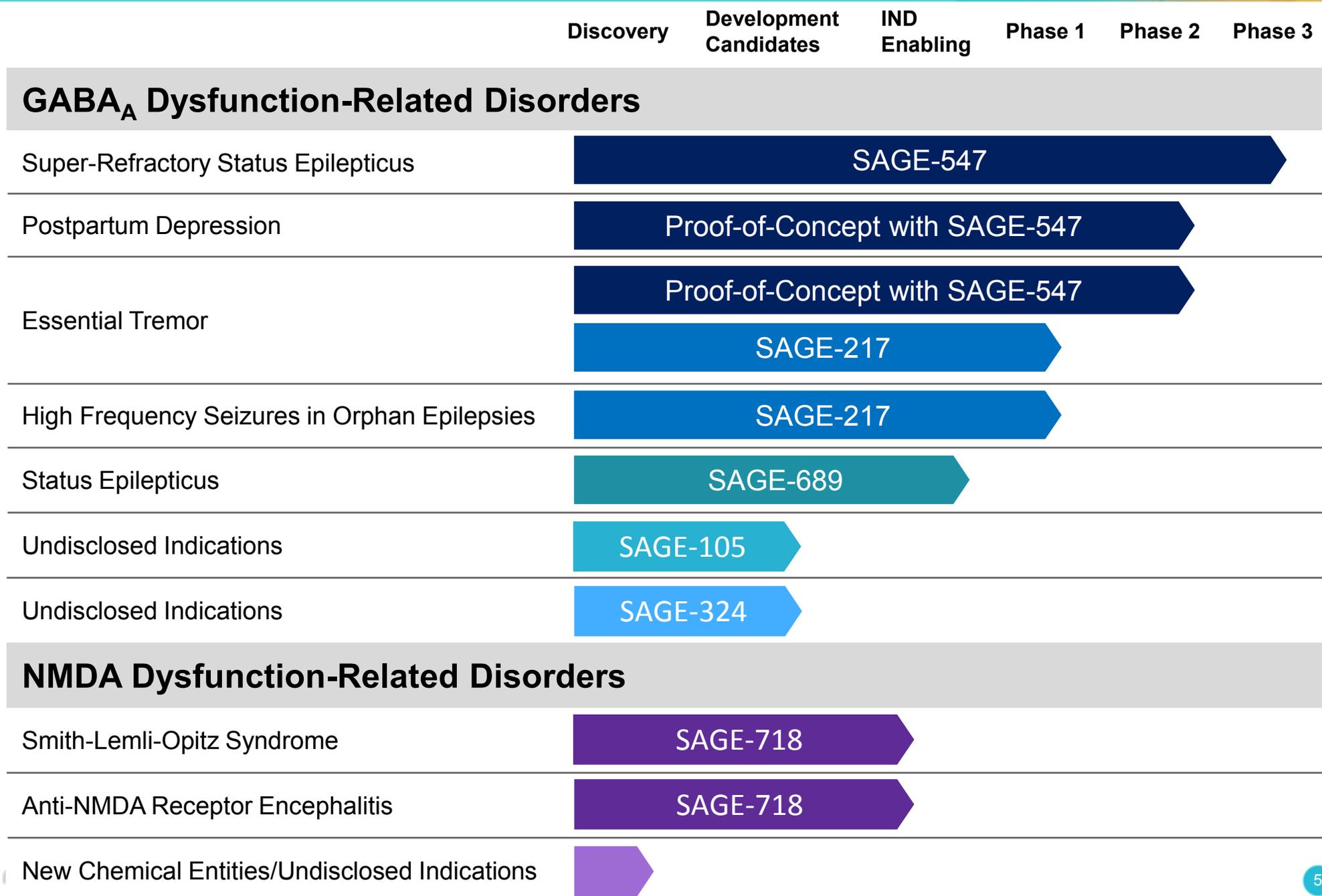
For additional disclosure regarding these and other risks SAGE faces, see the disclosure contained in the "Risk Factors" section of SAGE’s Quarterly Report on Form 10-Q filed on August 12, 2015, and in SAGE’s other public filings with the Securities and Exchange Commission, available on the SEC’s website 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.



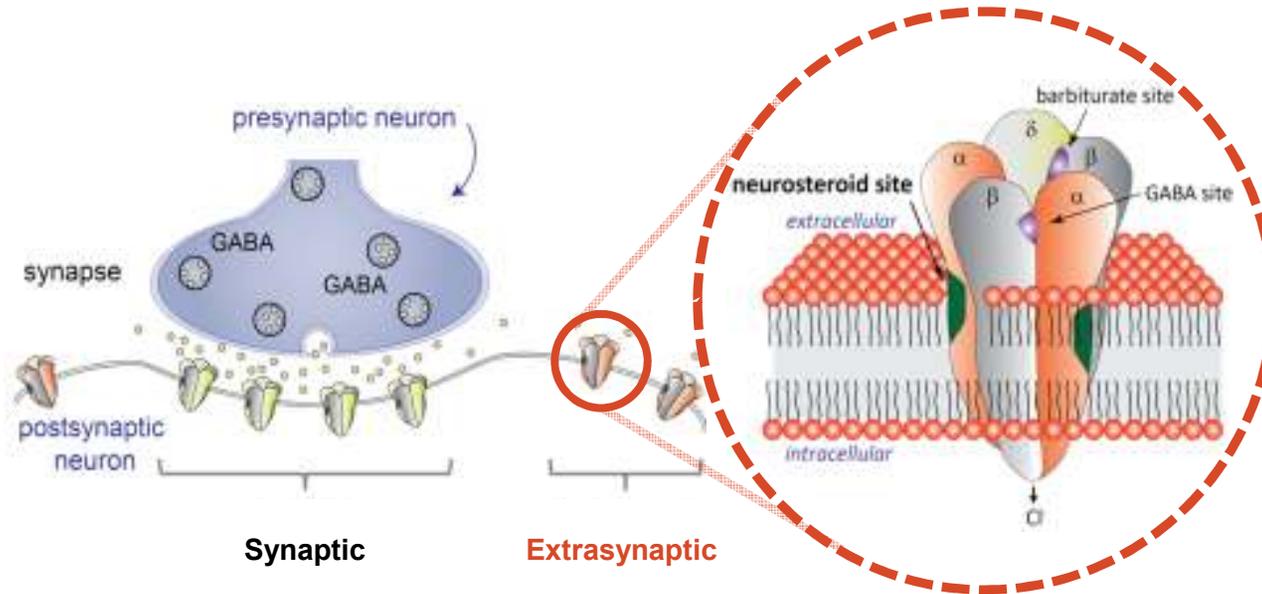
Company Update

Jeff Jonas, M.D., Chief Executive Officer

Building a Wholly-Owned Multi-Product CNS Portfolio



SAGE-547: Novel GABA_A Receptor Modulator



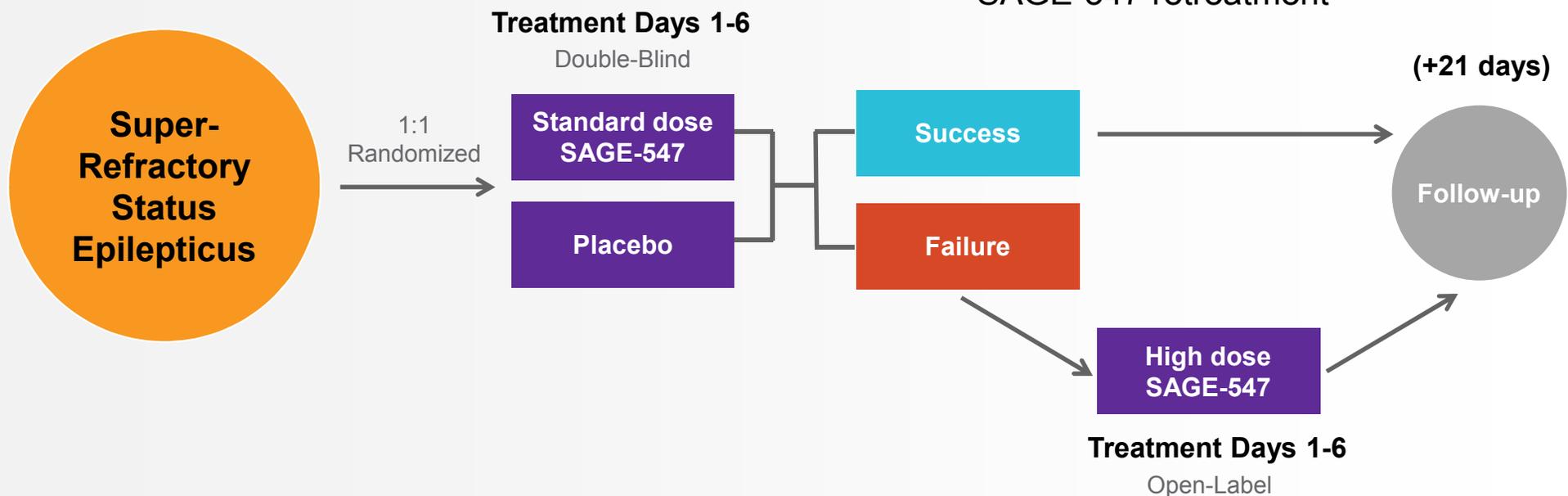
- Synaptic and extrasynaptic allosteric modulator
- Foundational molecule validating GABA_A modulator mechanism of action
- Granted orphan drug for status epilepticus, including SRSE, and Fast Track designation in U.S.
- FDA agreement on SPA for Phase 3 trial in SRSE

Enrollment is on Track in Phase 3 STATUS Trial of SAGE-547 in SRSE

STATUS TRIAL

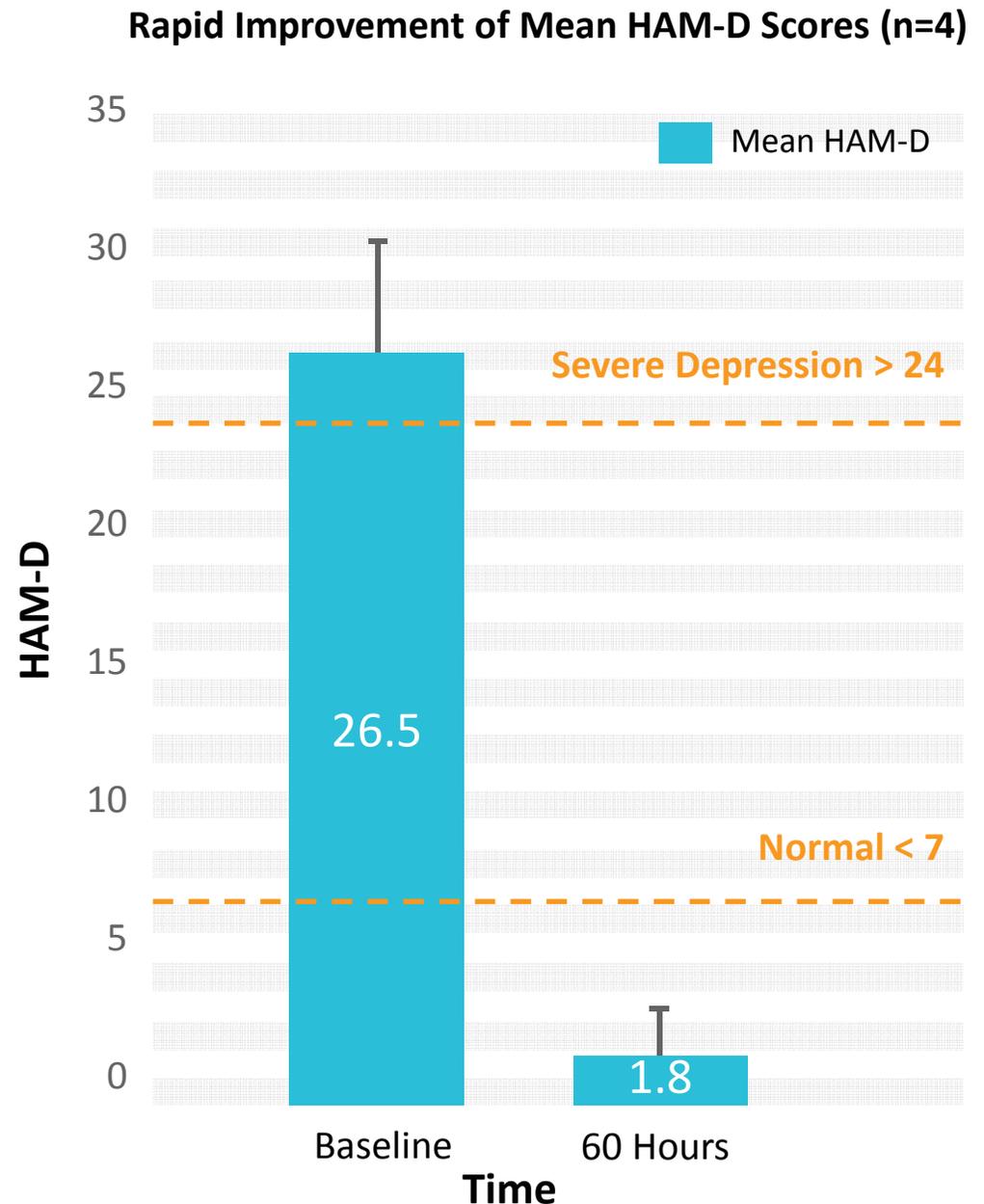
**Randomized, double-blind,
placebo-controlled Phase 3 trial**

- **1° Endpoint: Continued resolution of SE for 24 hours following wean of all 3rd-line agents and SAGE-547/placebo**
- SPA agreement with FDA
- 126 evaluable SRSE patients, aged ≥ 2 years
- ~150 sites in U.S., Canada and Europe
- Non-responders eligible for open-label, SAGE-547 retreatment



Postpartum Depression: Proof-of-Concept Observed in Exploratory Open-Label Study

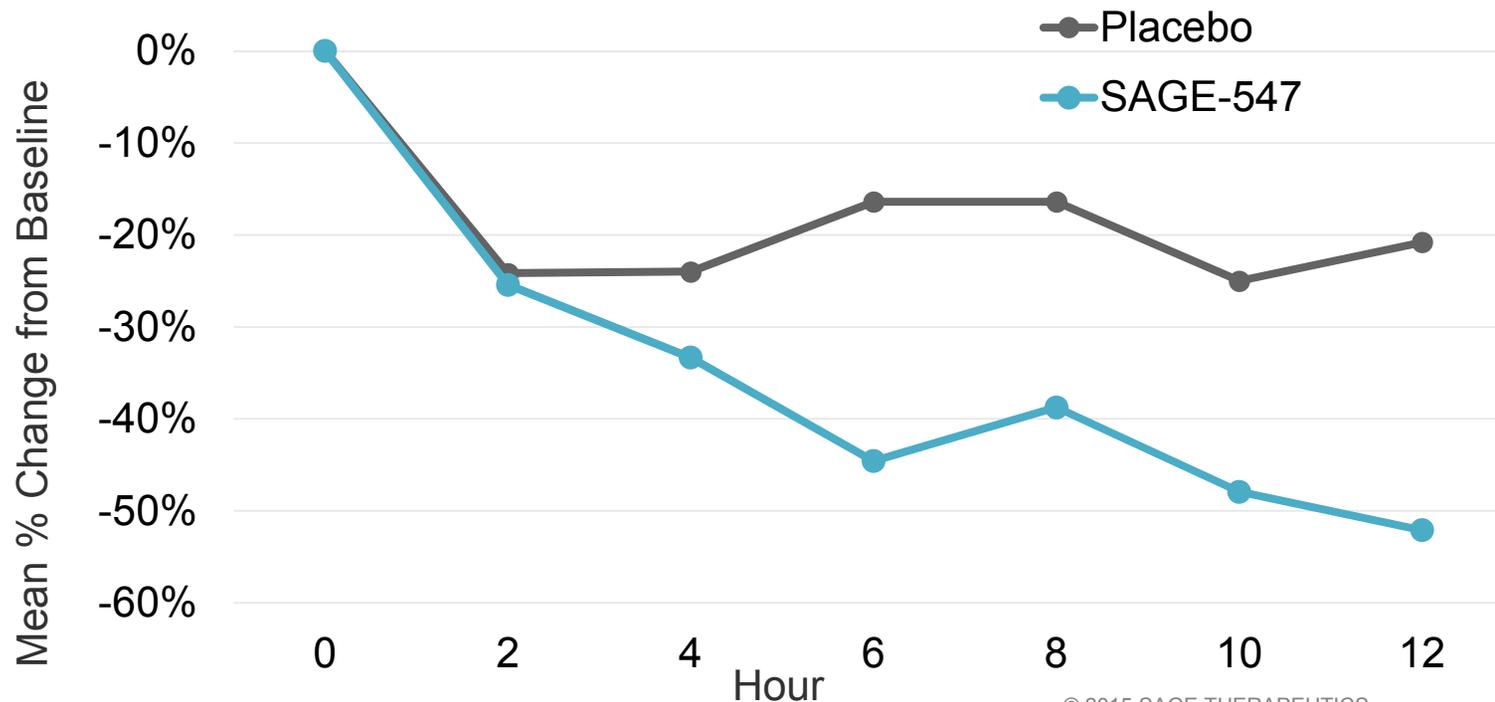
- Abnormal GABAergic function has been associated with affective disorders
- Animal data suggest dramatic changes in expression of extrasynaptic GABA_A receptors during perinatal period¹
- Significant improvement of mean HAM-D scores in 4/4 PPD patients in Proof-of-Concept SAGE-547 study
- No SAEs: only AE reported in more than 1 patient was sedation (2 patients)
- Placebo-controlled study with SAGE-547 open for enrollment



Essential Tremor Proof-of-Concept: Clinically Meaningful Reduction Shown in Tremor Amplitude

- Pretreated patients (19/25) exposed to target dose for only 2 hours
- SAGE-547 well-tolerated in conscious patients
 - Most common AEs were dizziness and fatigue (during higher dose phase)
 - One patient in higher dose phase discontinued due to hypotension
- Planning to study SAGE-217 in a Phase 2 trial in 2016

Accelerometer Kinetic Tremor Combined Score over Time (p=0.046 at 12 hours)
(Placebo-controlled patients, n=25)

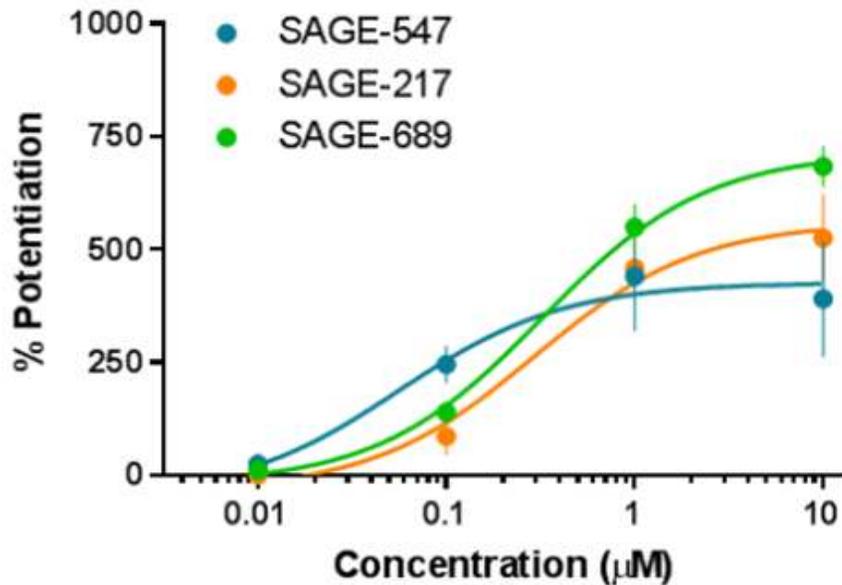


SAGE-217: A Chronic Oral GABA_A Modulator in Phase 1 Development

- Differentiated approach through a well-validated mechanism
- Highly potent and selective activity at GABA_A receptors in animal models
- Designed with optimized PK/PD profile intended for once-daily dosing

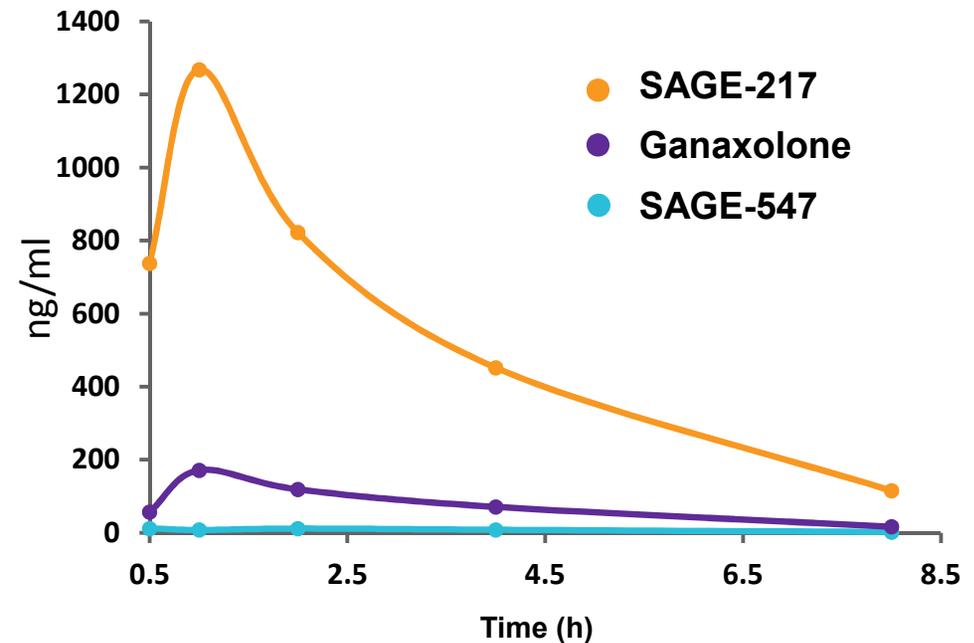
Enhanced Activity at GABA_A Receptors

Activity at Extrasynaptic GABA_A Receptor



Optimized Profile for Oral Use

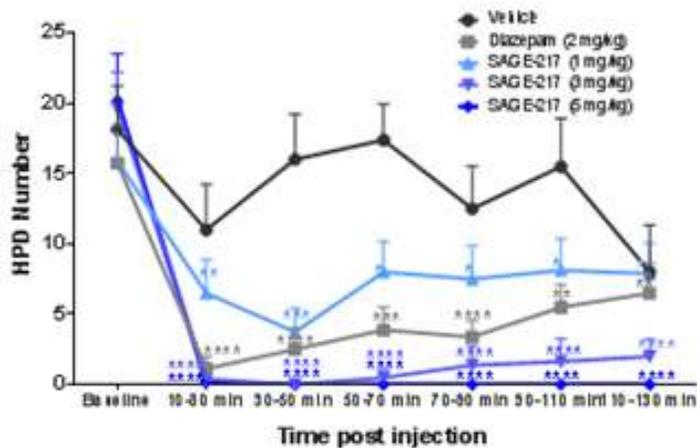
Oral Bioavailability Over Time



SAGE-217 and Related Tool Compounds Have Shown Efficacy Across Numerous Preclinical Models of Seizure

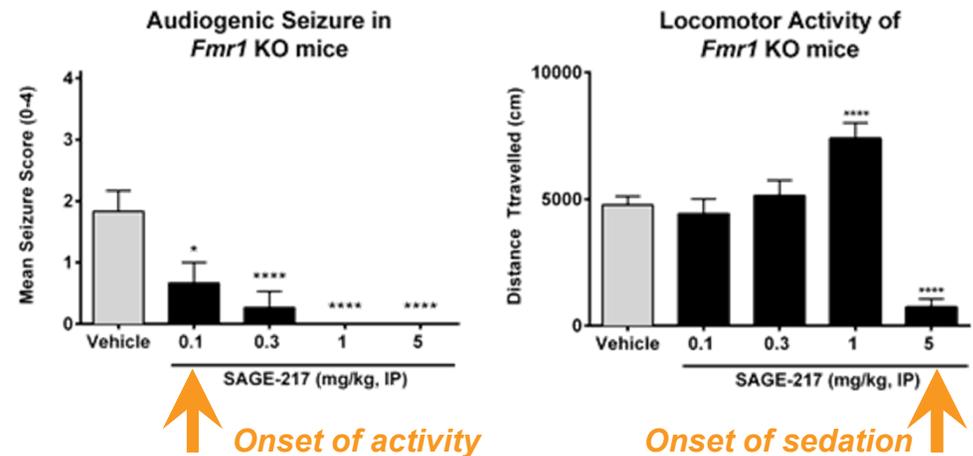
Seizure Suppression in Chronic Epilepsy Model

Rat model of mesial temporal lobe epilepsy



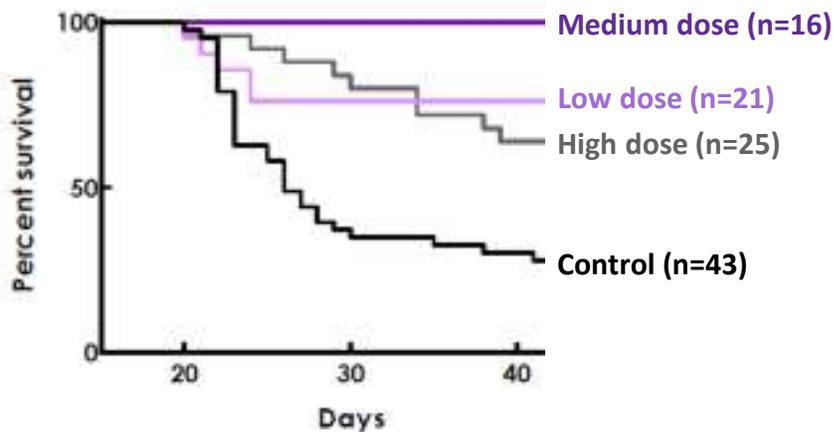
Activity in Genetic Epilepsy Model

Model of audiogenic seizures in *Fmr1* knockout mice



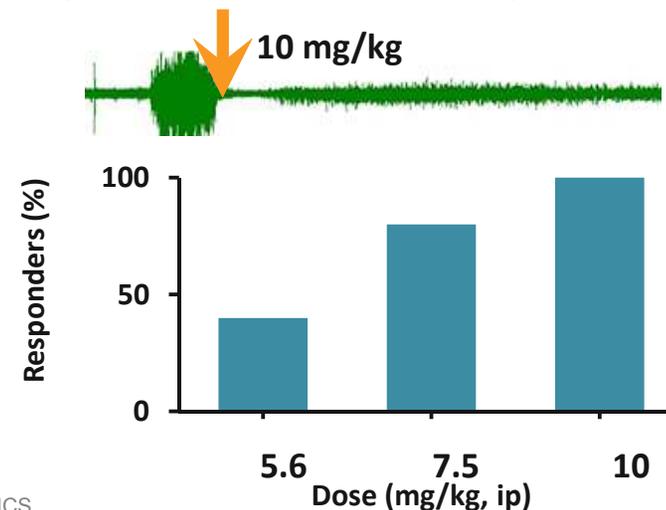
Increased Survival in Genetic Epilepsy Model

Tool compound in model of Dravet syndrome (*Scn1a*^{+/-} mice)



Acute Suppression of Soman-Induced SE

Tool compound administered 20 mins post-soman treatment



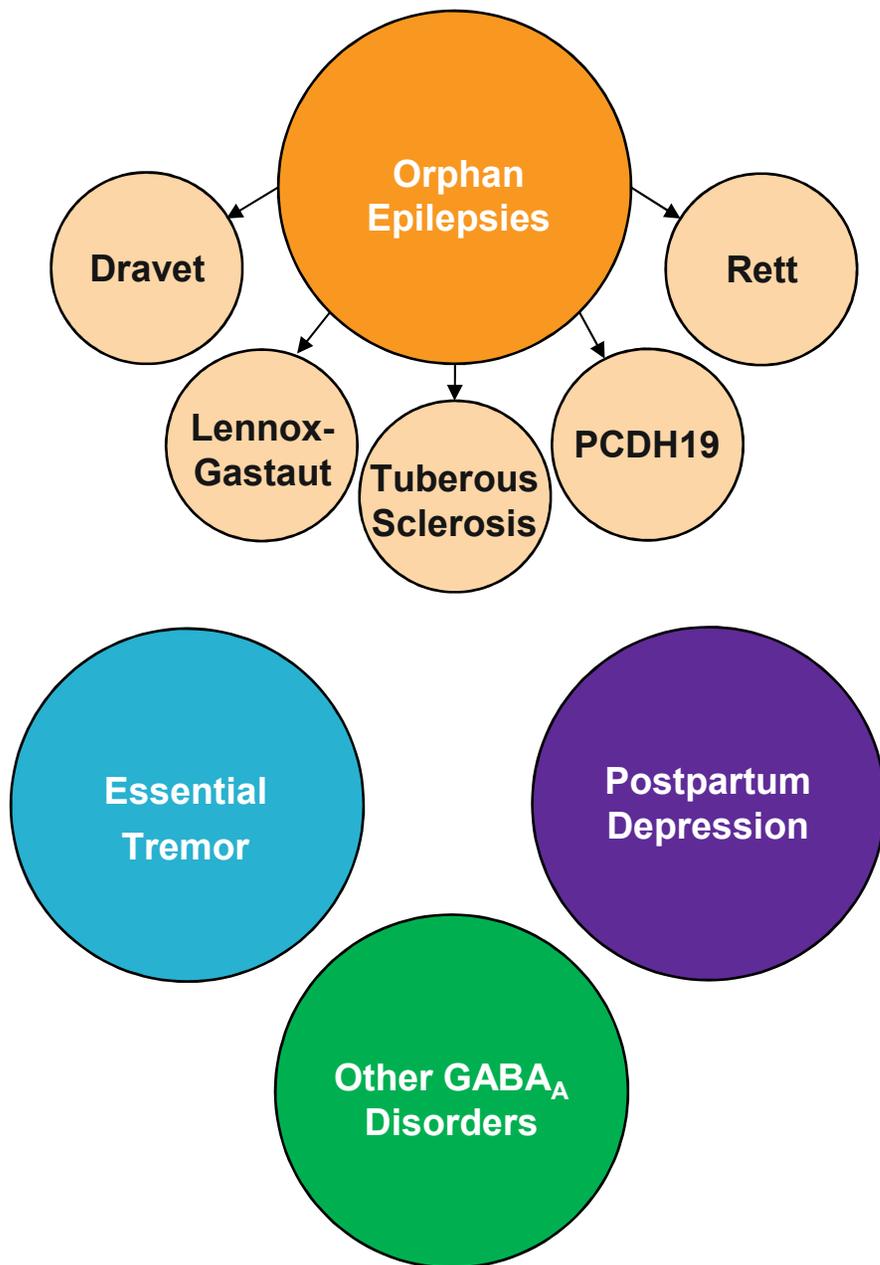
High Frequency Seizure Burden is Significant Across Orphan Epilepsies

Prevalence of Seizures Across Indications

Seizure Type		Lennox-Gastaut	PCDH19	Tuberous Sclerosis	Dravet	Rett
Generalized Seizures	Tonic-clonic	High	High	High	High	High
	Atonic	High	Moderate	Low	Low	Low
	Partial	Moderate	High	High	High	High
	Tonic	High	Low	Moderate	High	Moderate
	Myoclonic	High	Low	Low	Moderate	Low
	Absence	High	Low	Low	Moderate	Low

Seizure Burden: ■ High ■ Moderate ■ Low

Potential to Develop SAGE-217 Across a Broad Range of GABA_A-Related Disorders



High Frequency Seizures Associated with Orphan Epilepsies

- Opportunity to target high frequency seizure phenotype across orphan epilepsies
- Severely impacts patients' lives with a large number of patients refractory to current treatments
- ~100,000 combined orphan epilepsy patients in U.S.¹

Essential Tremor

- Debilitating neurological disorder that causes involuntary, rhythmic shaking with no known cause
- Current treatments only moderately effective
- ~10 million affected in U.S.²

Postpartum Depression

- Distinct and readily identified form of depression
- Potentially devastating consequences for mother and family
- ~800,000 mothers with perinatal mood disorders in U.S.³

Other GABA_A Dysfunction-Related Disorders

¹ Company estimate; data on file

² International Essential Tremor Foundation website, <http://www.essentialtremor.org/about-et/>

³ O'Hara MW, Wisner KL. Perinatal mental illness: definition, description and etiology. *Best Pract Res Clin Obstet Gynaecol* 2014;28(1):3-12.

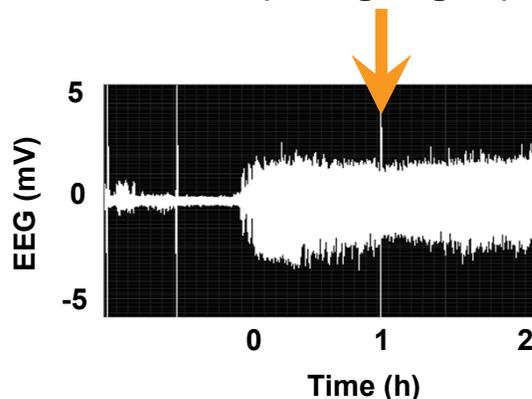
SAGE-689: Acute IV Treatment for Status Epilepticus

- Rapidly aborted seizure in pharmaco-resistant SE model
- Clean drug-drug interaction profile, wide therapeutic window
- Short half-life allows dose titration based on response
- Potential uses beyond SE

Diazepam Fails to Abort RSE (60 min post-onset)

Lithium-pilocarpine rat model

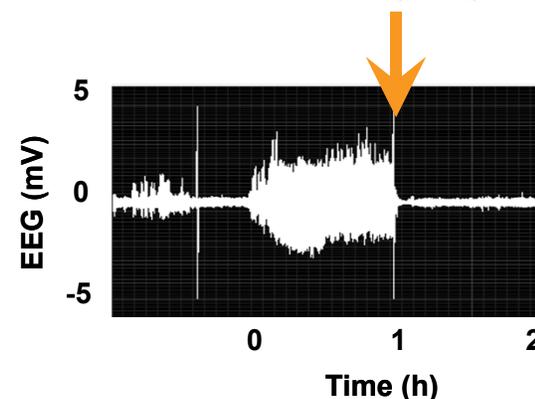
DZ (10 mg / kg *iv.*)



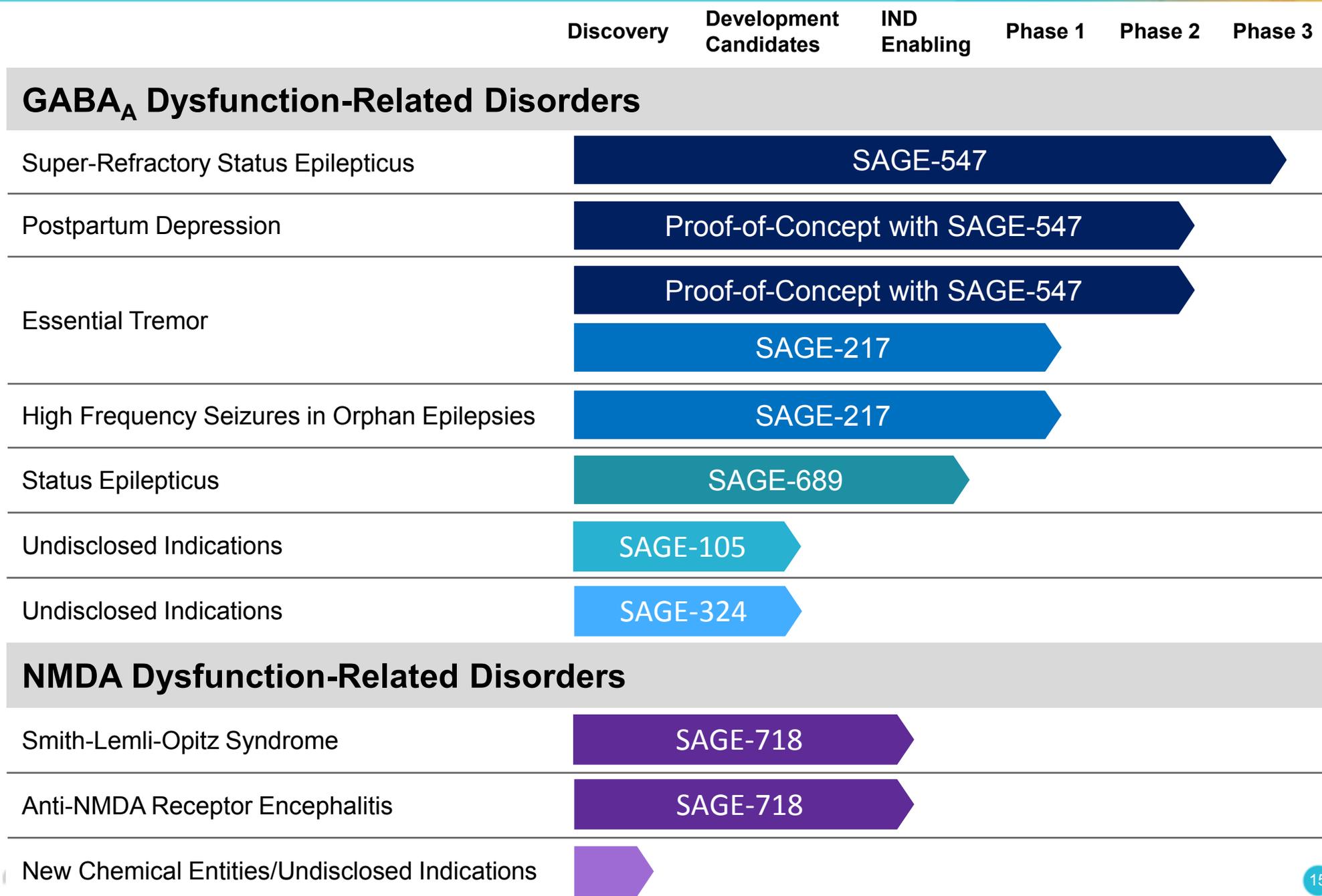
SAGE-689 Aborts RSE (60 min post-onset)

Lithium-pilocarpine rat model

SAGE-689 (5 mg / kg *iv.*)



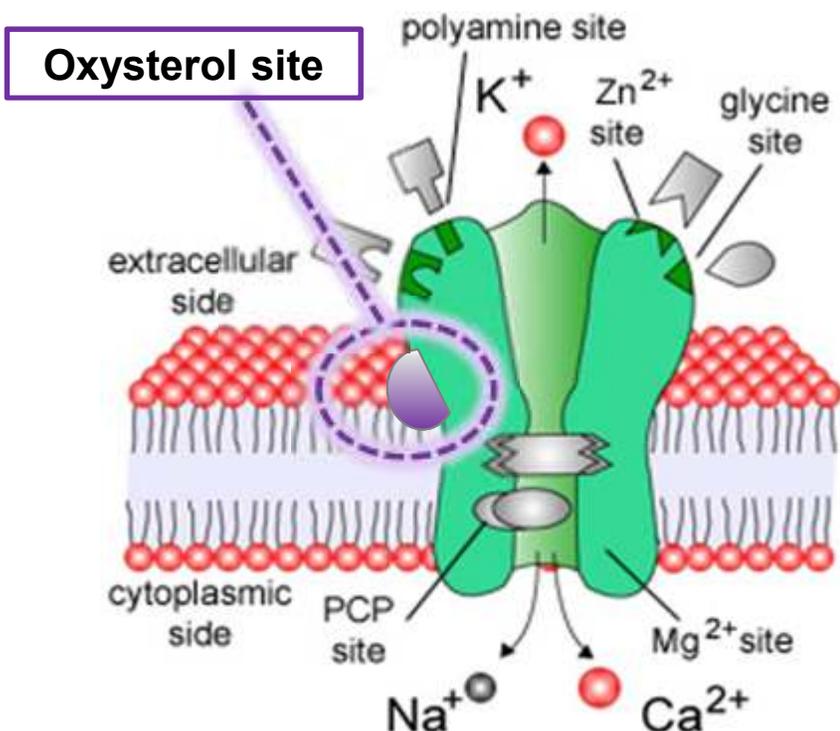
Building a Wholly-Owned Multi-Product CNS Portfolio



NMDA: Opportunity to Unlock Therapeutic Activity of Novel Modulatory Mechanism

- NMDA receptor dysfunction implicated in multiple cognitive and mood disorders
- SAGE discovery of cerebrosterol as potent positive allosteric modulator of NMDA
- Acts at novel oxysterol NMDA receptor modulatory binding site

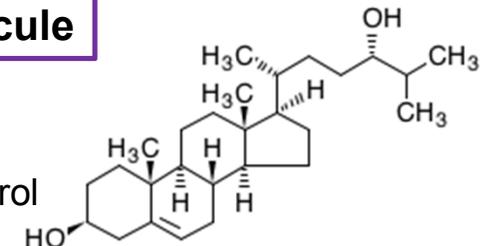
NMDA Receptor



SAGE NMDA Platform

Foundational molecule

Cerebrosterol
24(S)-Hydroxycholesterol



SAGE series of novel NMDA allosteric modulators with potential for:

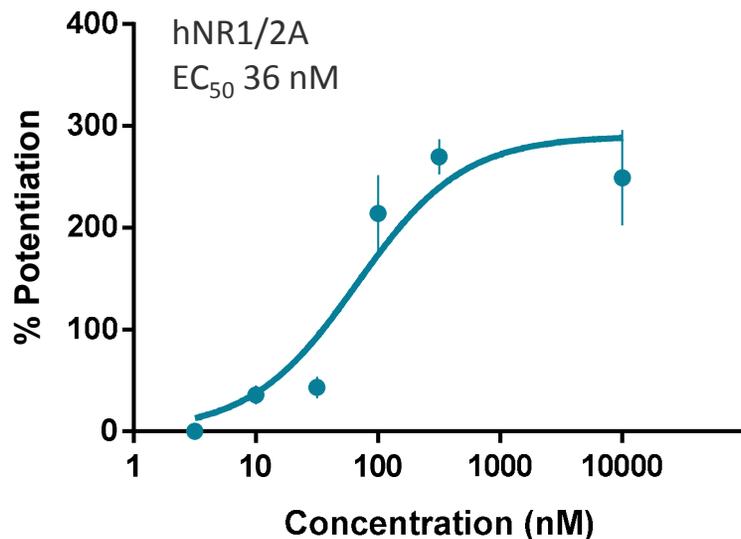
- Higher potency and receptor selectivity
- Better oral bioavailability
- Improved brain penetration

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

- Potent oxysterol-based NMDA positive allosteric modulator
- Optimized PK profile designed for oral dosing
- Demonstrates robust activity in preclinical models of cerebrosterol deficit disorder and neuropsychiatric symptoms resulting from NMDA hypofunction

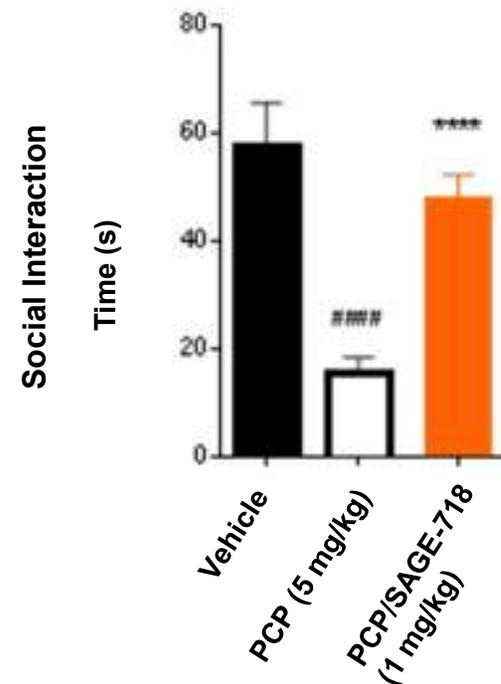
Activity at NMDA Receptors

SAGE-718 potent and selective positive modulation of NMDA Receptors



NMDA Hypofunction Model

SAGE-718 reverses social deficits associated with subchronic PCP treatment in vivo



Initial Focus on Biomarker-Defined Rare Diseases Characterized by NMDA Hypofunction

Smith-Lemli-Opitz Syndrome (SLOS)

- Metabolic disorder caused by mutations in the DHCR7 cholesterol synthesis gene
- Associated with significantly decreased plasma levels of cerebrosterol, suggesting that normal oxysterol-based NMDA modulation is disrupted
- Patients are affected by a broad range of neuropsychiatric and neurodevelopmental symptoms

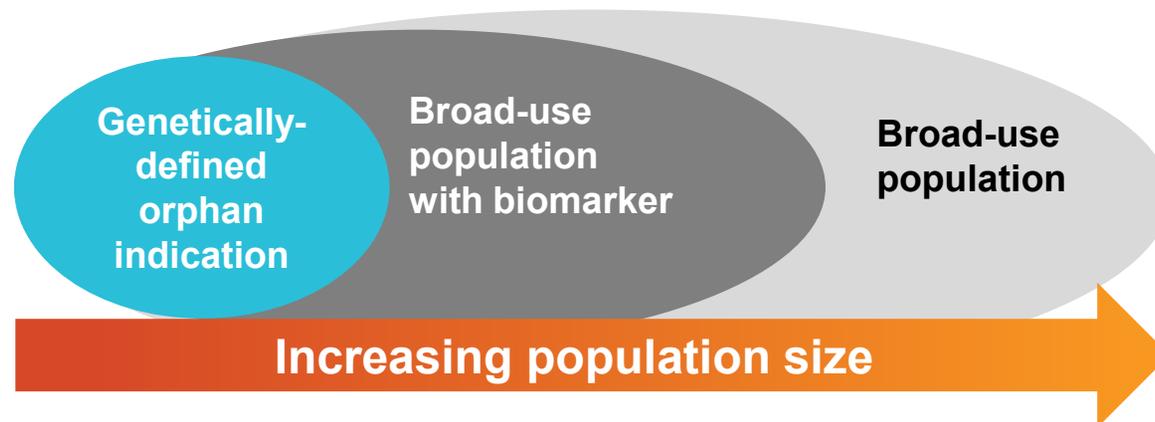
Anti-NMDA Receptor Encephalitis (ANRE)

- Autoimmune disorder in which antibodies attack NMDA receptors
- Characterized by NMDA hypofunction
- Symptoms include a highly characteristic set of neuropsychiatric deficits, including cognitive and behavioral disturbances, movement disorders and loss of consciousness

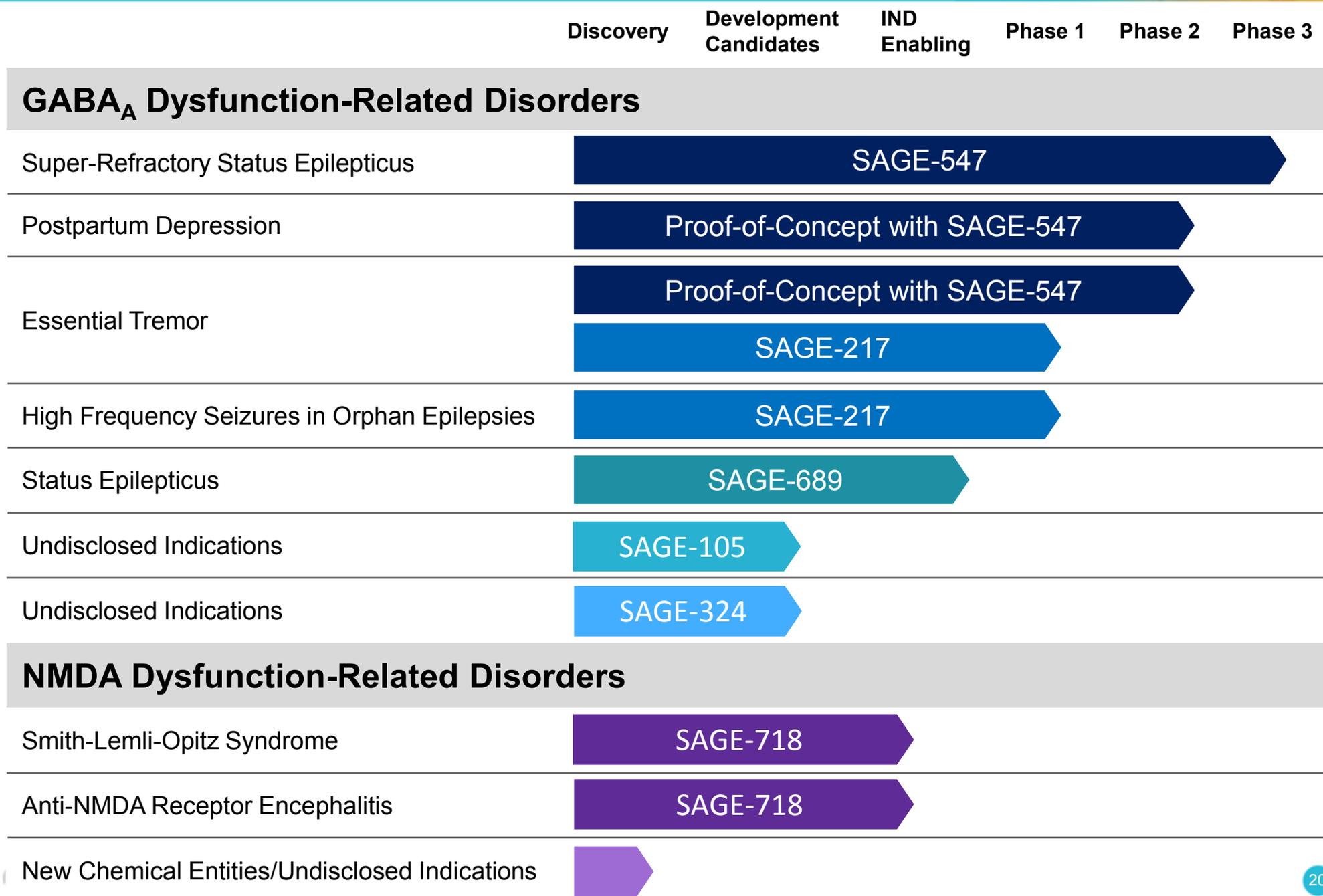
- Currently no approved treatments for these orphan disorders
- Initial focus of SAGE-718 development to address neurological symptoms of these disorders through enhancing NMDA receptor function

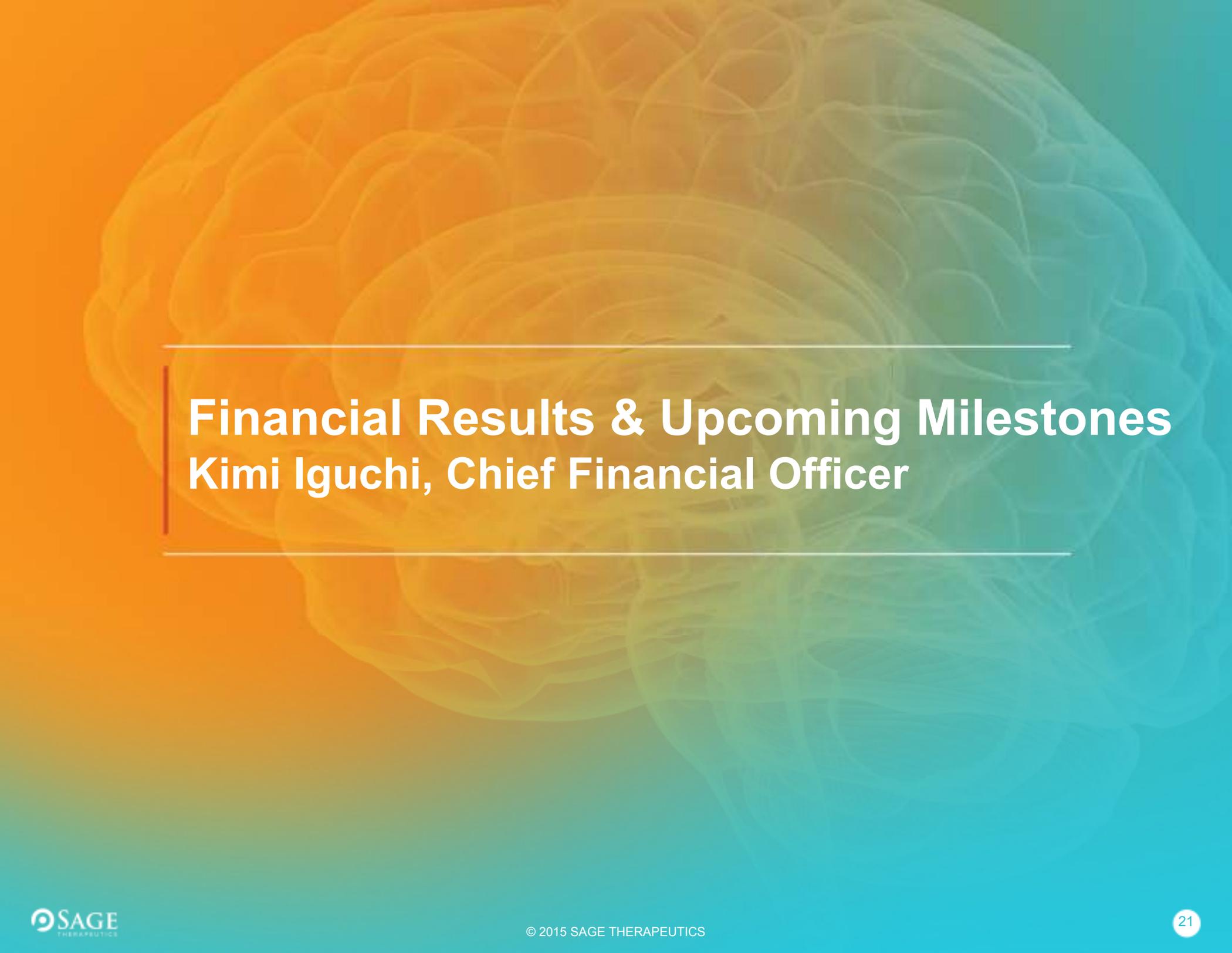
Potential to Explore Broader Indications of NMDA Receptor Hypofunction for Further Study Based on Clinical Biomarkers

- SLOS** → Decreased cerebrosterol levels may represent a biomarker to identify a range of indications characterized by phenotypes of cognitive dysfunction and neuropsychiatric symptoms
- ANRE** → Anti-NMDA antibodies may represent a biomarker to identify other indications within dementia and psychosis



Building a Wholly-Owned Multi-Product CNS Portfolio





Financial Results & Upcoming Milestones

Kimi Iguchi, Chief Financial Officer

Financial Summary

Q3 2015 Financial Results (as of 9/30/2015)

	Q3 '15	Q4 '14
Cash and Cash Equivalents	\$204.9M	\$127.8M
	Q3 '15	Q3 '14
Research & Development	\$17.5M	\$6.6M
General & Administrative	\$6.6M	\$2.9M
Net Loss	\$24.0M	\$9.9M

Guidance: Cash position expected to fund operations through mid-2017

Near-Term Clinical Milestones and Data Readouts Across Portfolio

- Developing SAGE-547 in Phase 3 trial in SRSE
- Advancing wholly-owned pipeline of first-in-class NCEs
- Establishing human proof-of-concept (PoC) data in broader CNS disorders
- Replicating GABA_A strategy with NMDA portfolio

2H 2015 – Expected Milestones

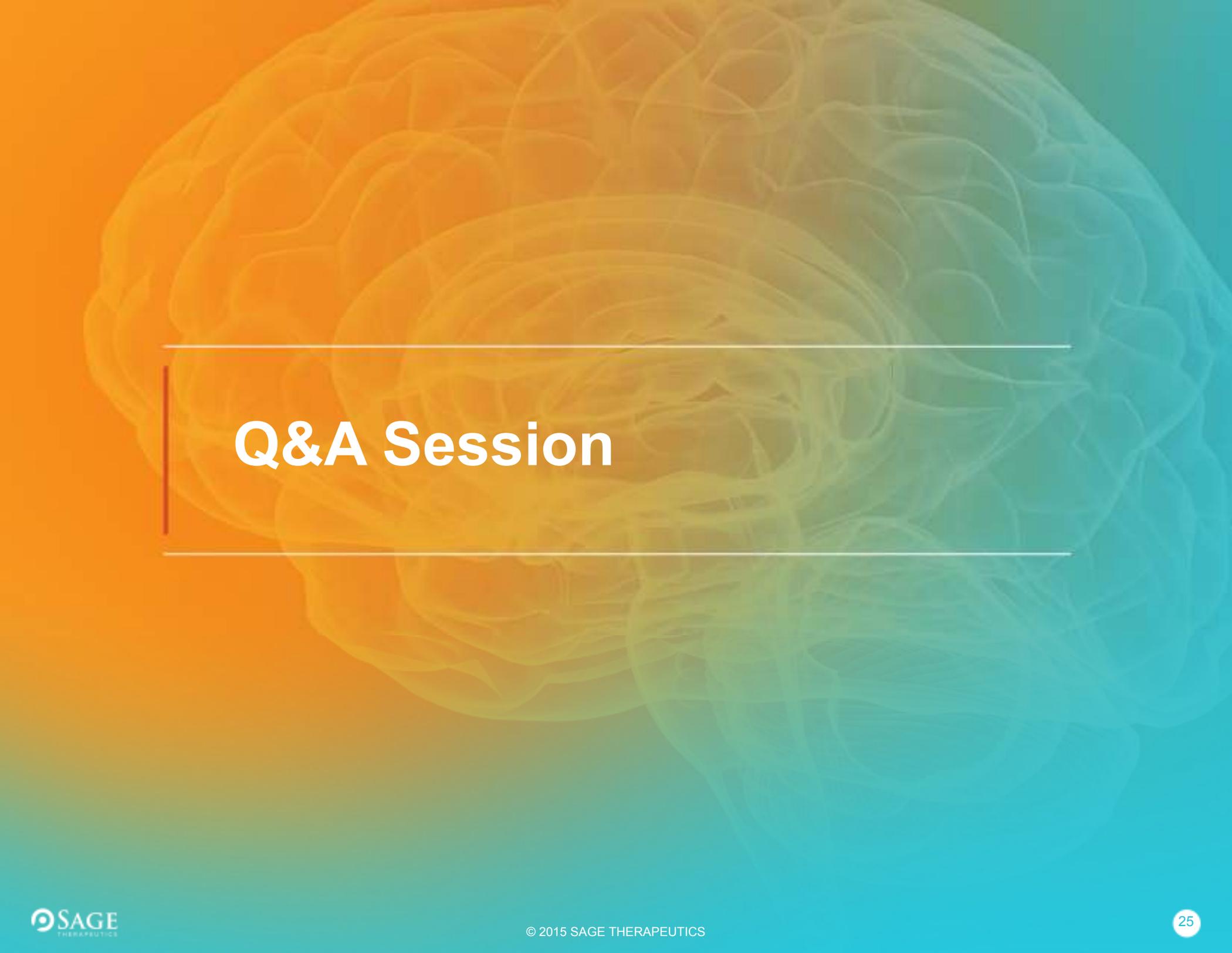
- ✓ Phase 3 SPA agreement with FDA
- ✓ SAGE-547 PoC essential tremor data
- ✓ SAGE-217 Phase 1 initiation
- ✓ NMDA candidate selection
- SAGE-547 PoC PPD trial initiation

2016 – Expected Milestones

- SAGE-217 Phase 1 data
- SAGE-547 PoC PPD data
- SAGE-217 Phase 2 initiations
- SAGE-689 Phase 1 initiation
- SAGE-547 NDA planning

Upcoming Conferences

- **24th Annual Credit Suisse Healthcare Conference**
 - November 10, 2015
 - Scottsdale, AZ
- **Stifel Healthcare Conference 2015**
 - November 18, 2015
 - New York, NY
- **Goldman Sachs US Emerging/SMID Cap Growth Conference**
 - November 19, 2015
 - New York, NY
- **27th Annual Piper Jaffray Healthcare Conference**
 - December 2, 2015
 - New York, NY
- **American Epilepsy Society (AES) Annual Meeting**
 - December 4 – December 8, 2015
 - Philadelphia, PA



Q&A Session
