SAGE THERAPEUTICS

DISCOVER
DEVELOP
DELIVER

Novel Medicines for Life-Altering CNS Disorders

Q1 2016 Financial Results
May 5, 2016

Agenda

Introduction

- Paul Cox, Director, Investor Relations

Pipeline Update and Upcoming Milestones

- Jeff Jonas, M.D., Chief Executive 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; the expected development pathway for SAGE’s product candidates; anticipated development milestones and results, including expected timing; the estimated number of patients with certain disorders or diseases, including management’s estimates as to the 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; other planned activities 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 experience slower than expected clinical site initiation or slower than expected identification and enrollment of evaluable patients in our clinical trials, or may encounter delays or problems in analyzing data or the need for additional analysis, data or patients.
- 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, 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.

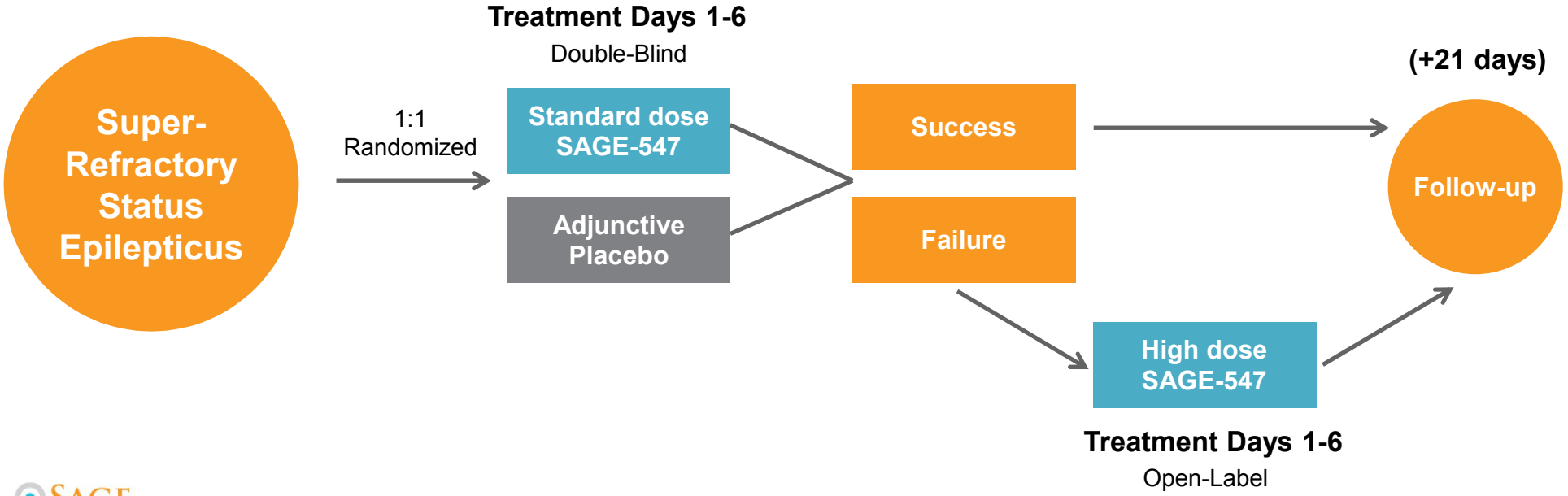
For additional disclosure regarding these and other risks SAGE faces, see the disclosure contained in the "Risk Factors" section of SAGE’s Annual Report on Form 10-K filed on February 29, 2016, and in SAGE’s other public filings with the Securities and Exchange Commission, available on the SEC's website 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.

Global Phase 3 STATUS Trial of SAGE-547 in SRSE

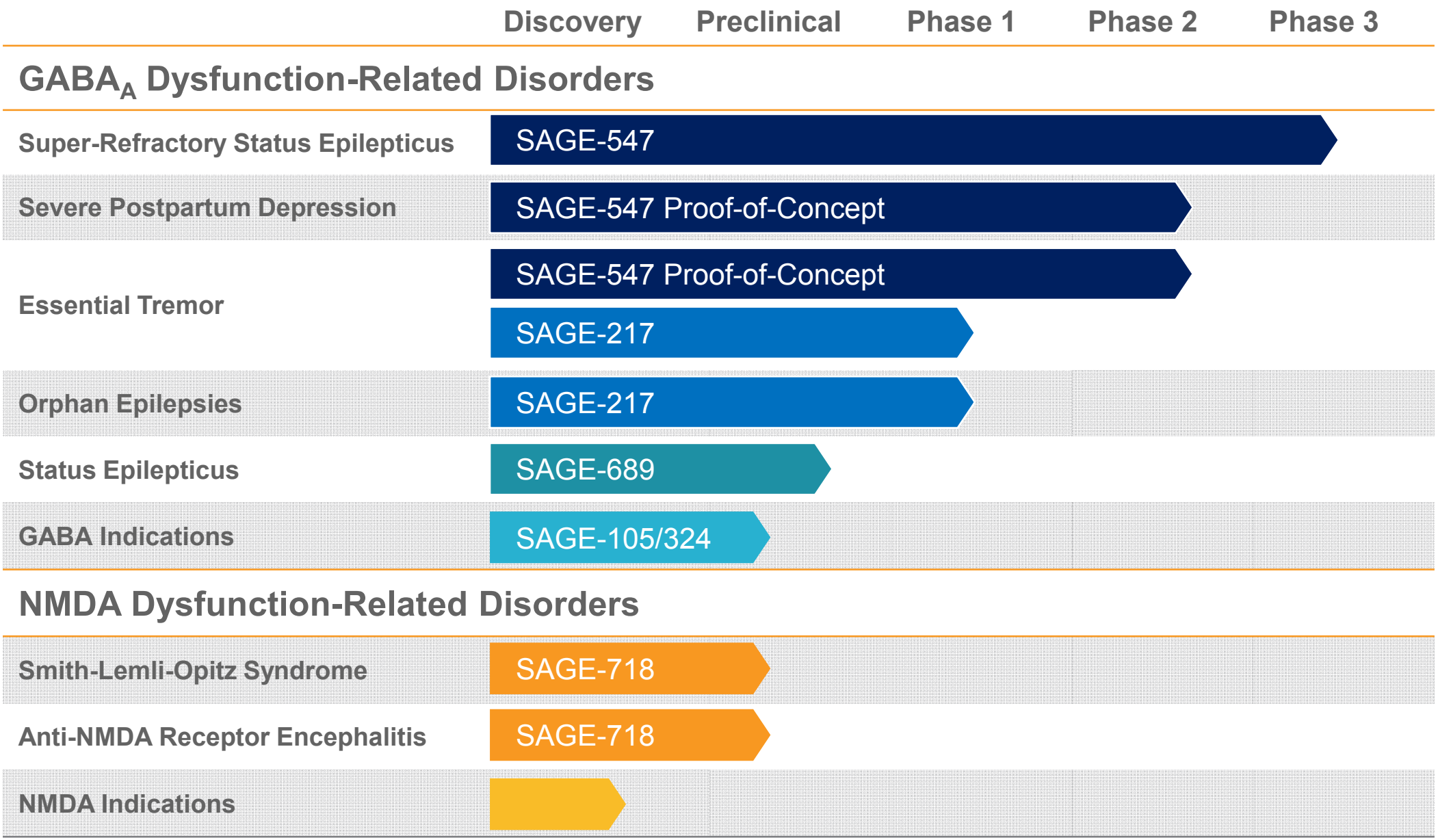
STATUS TRIAL

Top-line results expected 2H 2016

- Randomized, double-blind, placebo-controlled
- Expect up to 140 patients enrolled to get 126 evaluable patients
- Anticipate ~150 sites in U.S., Canada and Europe
- Non-responders eligible for open-label, SAGE-547 retreatment
- SPA agreement with FDA
- Primary Efficacy Endpoint: Continued resolution of SE for 24 hours following wean of all 3rd-line agents and SAGE-547/placebo



Building an Innovative Multi-Product CNS Portfolio

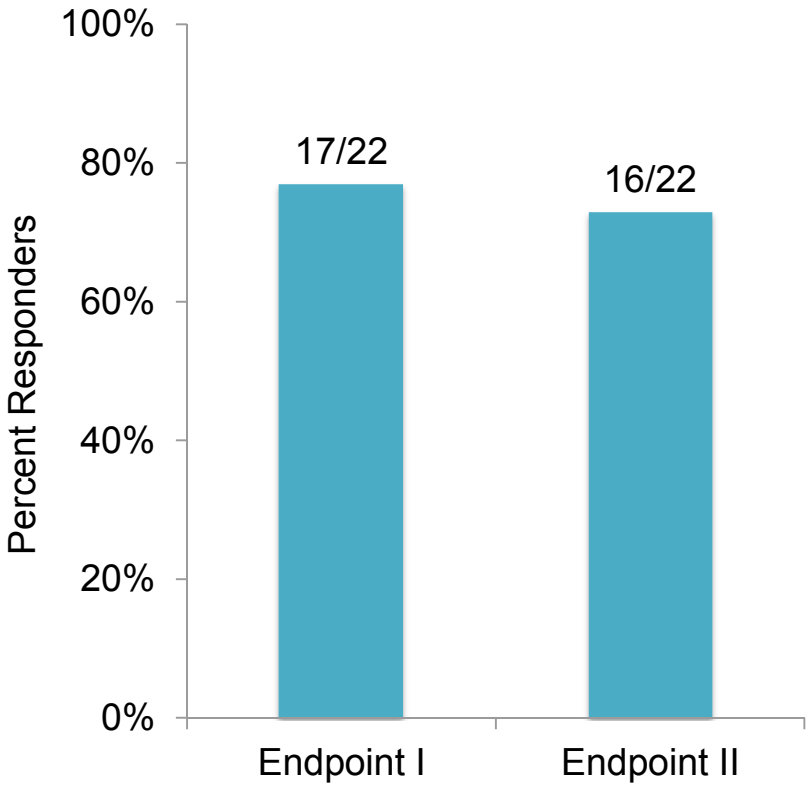


AAN 2016 Presentations

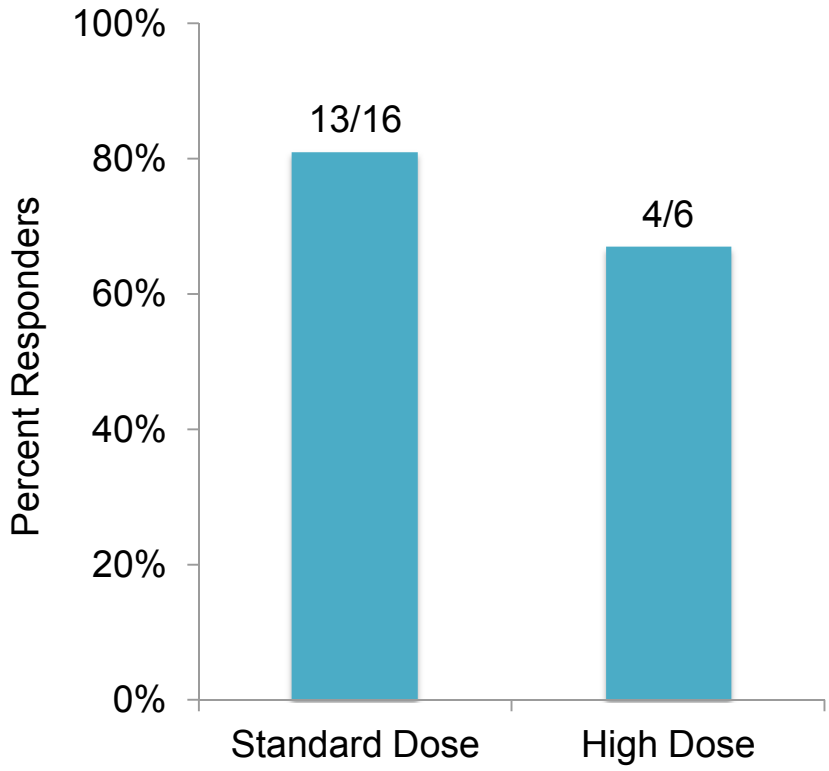
- **Super-Refractory Status Epilepticus**
  - S14.003 - 547-SSE-201 for Super-Refractory Status Epilepticus: Response and Relationship to Underlying Patient Characteristics
  - P4.210 - Phase 2 Data Suggest Heterogeneity of Presentation and Comorbidity Burden Do Not Impact Activity of SAGE-547 in Patients with Super-Refractory Status Epilepticus
  - P4.197 - Quantitative Burst Suppression as a Biomarker in the Phase 2 Trial of SAGE-547: Lessons Learned for the First International Phase 3, Randomized, Controlled Trial for Super-Refractory Status Epilepticus (The STATUS Trial)
  - P4.214 - Defining the Health Economic Burden of Treatment for Super-Refractory Status Epilepticus Patients
- **Essential Tremor**
  - P4.297 - Exploratory Trial Results for SAGE-547 in Essential Tremor

547-SSE-201: Overall Efficacy Results

Response by Endpoint, Evaluable Patients



Endpoint I Response by Dose, Evaluable Patients



Endpoint I: wean of TLA prior to end of SAGE-547 maintenance

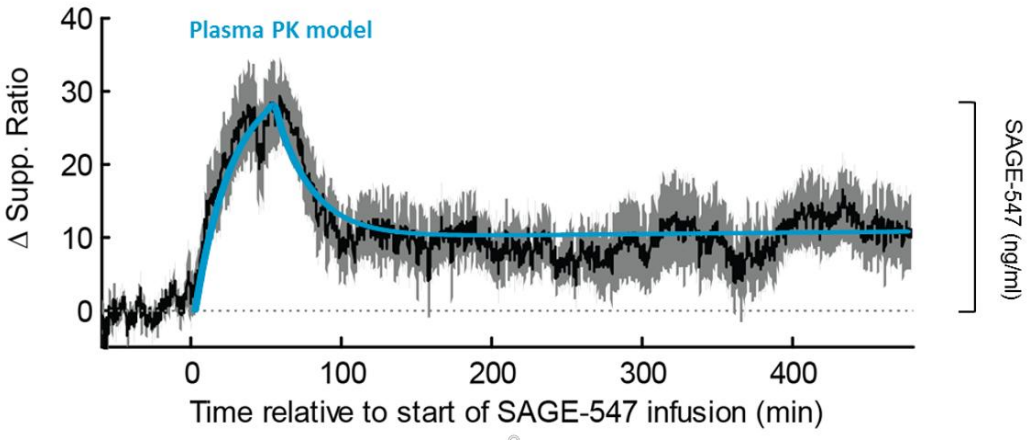
Endpoint II: wean of TLA prior to end of SAGE-547 taper

N=22 total evaluable patients

EEG Suppression Ratio as an Exploratory Pharmacodynamic Biomarker

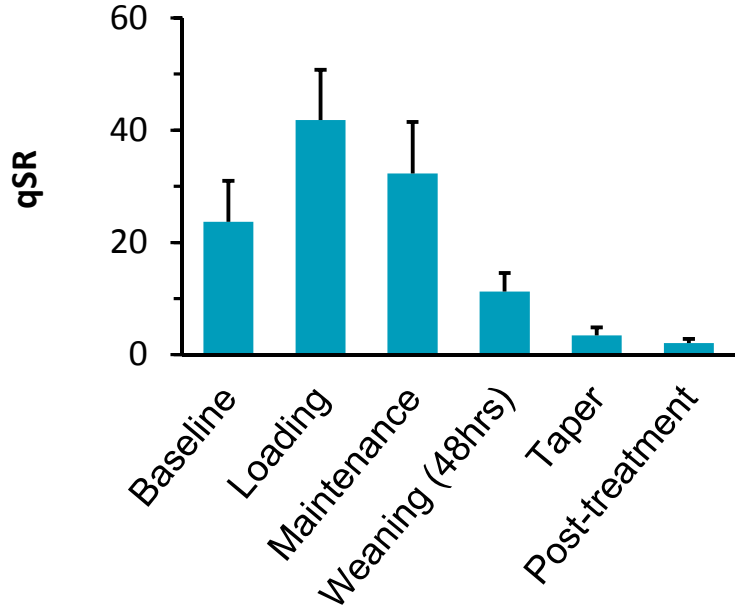
- Increase in EEG suppression ratio (qSR) during loading infusion ($p<0.001$; $n=14$), followed by sustained maintenance elevation ($p<0.005$)
- Increase in qSR significantly correlated with SAGE-547 administration and steady-state plasma concentration of SAGE-547 despite high baseline variability and presence of background medications

Mean qSR (n=14) with Plasma PK Model and Third-Line Agents



Black line is mean qSR; gray area is measured standard deviation

Suppression ratio from baseline through post-treatment time points



Poster P4.197 (Tuesday, April 19): "Quantitative burst suppression as a biomarker in the phase 2 trial of SAGE-547: lessons learned in preparation for the first international phase 3, randomized, controlled trial for super-refractory status epilepticus (the STATUS trial)"

547-SSE-201 Safety Data

Adverse Events (over 10%)	n (%)
Pyrexia	5 (20%)
Anaemia	4 (16%)
Blood urea increased	4 (16%)
Diarrhoea	4 (16%)
Hypotension	4 (16%)
Oedema peripheral	4 (16%)
Convulsion	3 (12%)
Decubitus ulcer	3 (12%)
Deep vein thrombosis	3 (12%)
Haematuria	3 (12%)
Hypertension	3 (12%)
Metabolic acidosis	3 (12%)
Pneumonia	3 (12%)
Respiratory failure	3 (12%)
Sepsis	3 (12%)
Sinus tachycardia	3 (12%)
Urinary tract infection	3 (12%)

Serious Adverse Events* (over 8%)	n (%)
Respiratory failure	3 (12%)
Convulsion	2 (8%)
Pulmonary embolism	2 (8%)
Renal failure acute	2 (8%)
Sepsis	2 (8%)

Cause of Deaths*	n
Respiratory failure or arrest	2
Cardiopulmonary arrest	1
Organophosphate toxicity	1
Metastatic breast cancer	1
Multi-organ failure	1

* None assessed as drug related by Sponsor

Hospital Claims Data Support U.S. SRSE Incidence Estimated from the Literature

Literature Analysis Estimates

Status Epilepticus (SE)
~150,000 patients/year
DeLorenzo et al, 1995

2nd-Line SE
~50,000 patients/year
Silbergleit et al, 2012
Claassen et al, 2002

Refractory SE
~35,000 patients/year
Novy et al, 2010

Estimated SRSE
~25,000 patients/year
Rossetti et al, 2011
Sage Analysis

Hospital Claims Data Analysis[1]

- Database included ~6M discharges in 2012 (~20% of U.S. inpatient discharges)
- SRSE does not have specific ICD-9 code
- Study algorithm included:
  - Seizure-related ICD-9 code;
  - ICU stay of at least 2 days;
  - Treatment with benzos or AEDs;
  - Continuous treatment with both IV AEDs and a ventilator;
  - Treatment with AEDs and benzos together or a definite SE ICD-9 diagnosis code

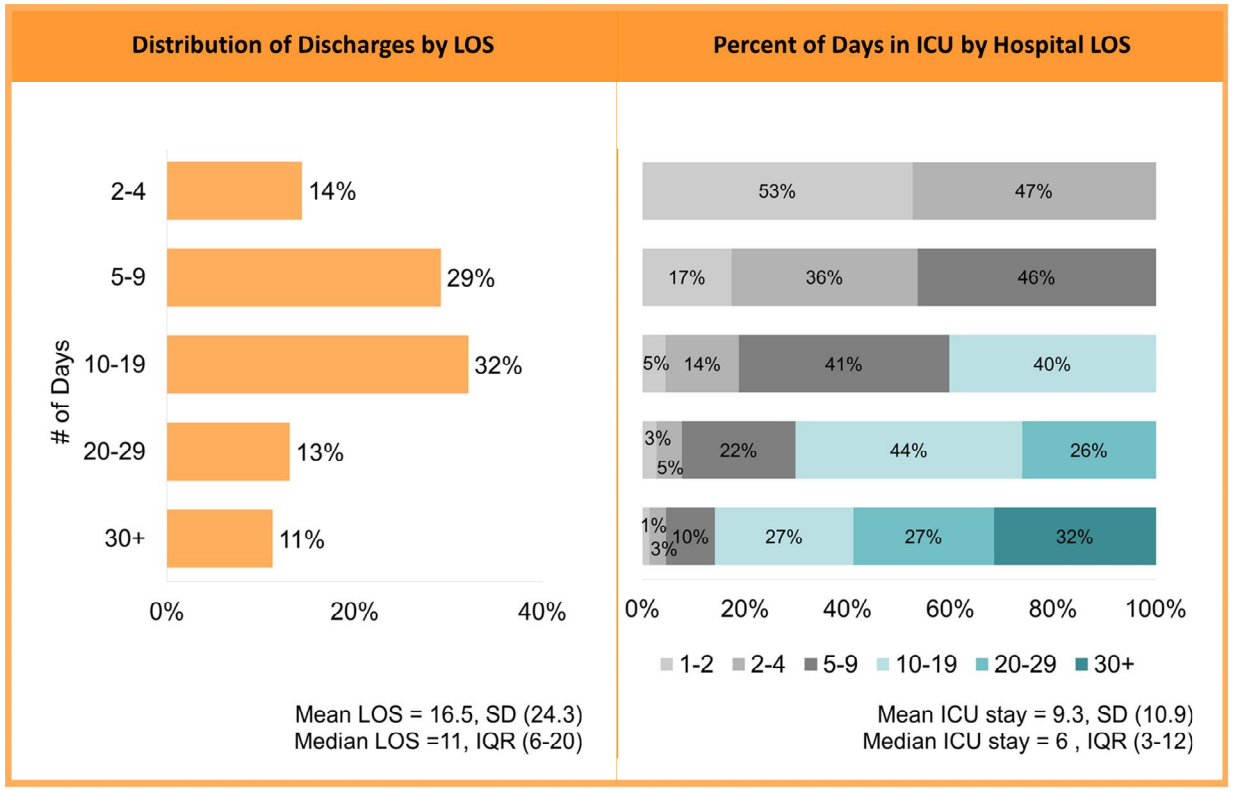
Estimated SRSE
+25,000 patients/year in the U.S.[2]

[1] "Burden of Illness for Super Refractory Status Epilepticus Patients" poster, London-Innsbruck SE Colloquium, 2015
[2] Projection for U.S. extrapolated from cases classified as SRSE using the algorithm. Estimates vary depending on criteria used.

SRSE Has a Significant Burden of Illness

Hospital Length of Stay (LOS) and ICU Percept of Stay for SRSE Patients

- SRSE has significant resource utilization due to lengthy hospitalizations, intense ICU resource utilization and overall hospital resource use
- Mean LOS was 16.5 days with significant ICU LOS (mean 9.3 days) in the SRSE cases classified using the primary algorithm
- LOS in the analysis ranged from 2 to over 800 days

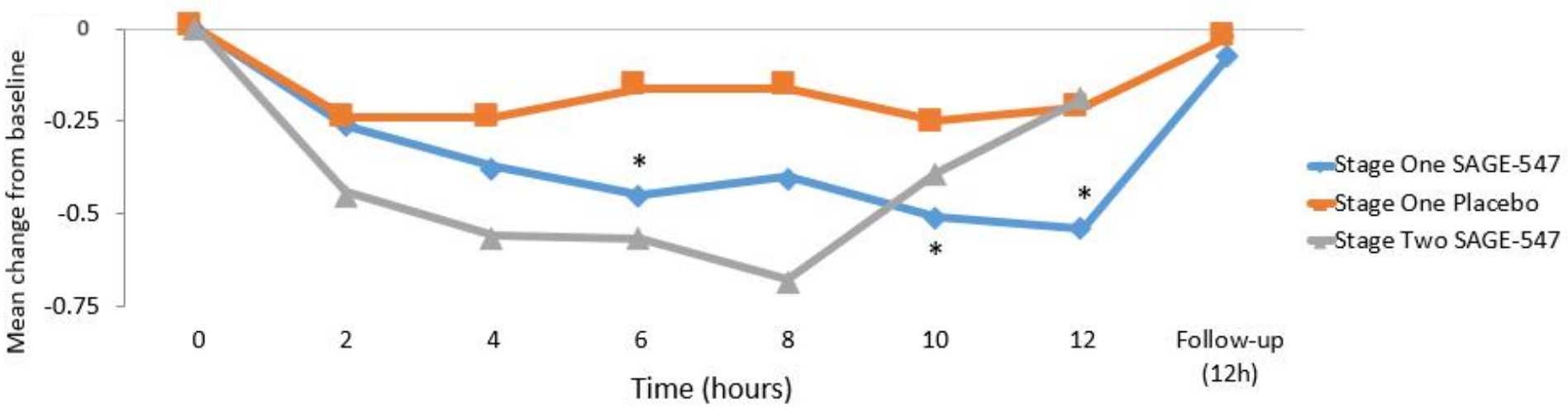


SAGE-547 Response: Kinesia Kinetic Tremor

Mean change from baseline in Kinesia kinetic tremor (combined) score over time

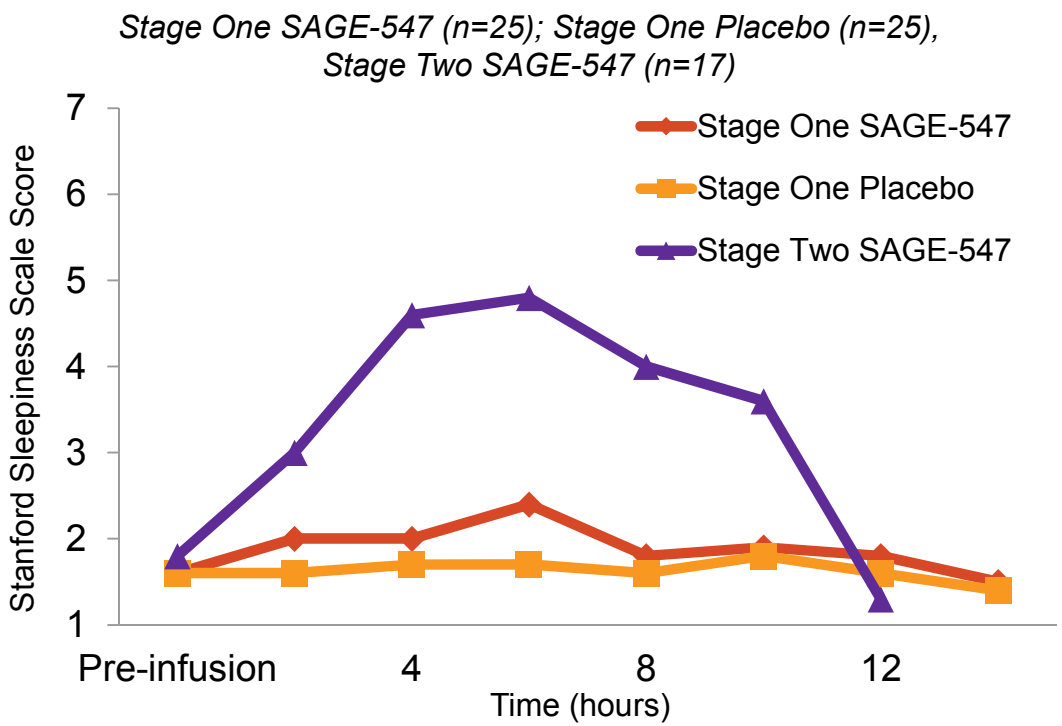
Stage One SAGE-547 (n=24); Stage One Placebo (n=25), Stage Two SAGE-547 (n=16)

*Stage One comparisons of SAGE-547 vs. placebo significant at 6 hours (p=0.02), at 10 hours (p=0.04), and at 12 hours (p=0.03)



SAGE-547 Safety Summary

Mean Stanford Sleepiness Scale score over time.



Stanford Sleepiness Scale

- 1 = feeling active, vital, alert, or wide awake
- 2 = functioning at high levels, but not at peak, able to concentrate
- 3 = awake, but relaxed; responsive but not fully alert
- 4 = somewhat foggy, let down
- 5 = foggy; losing interest in remaining awake, slowed down
- 6 = sleepy, woozy, fighting sleep; prefer to lie down
- 7 = no longer fighting sleep, sleep onset soon; having dream-like thoughts

Summary of Treatment Emergent Adverse Events (TEAEs)

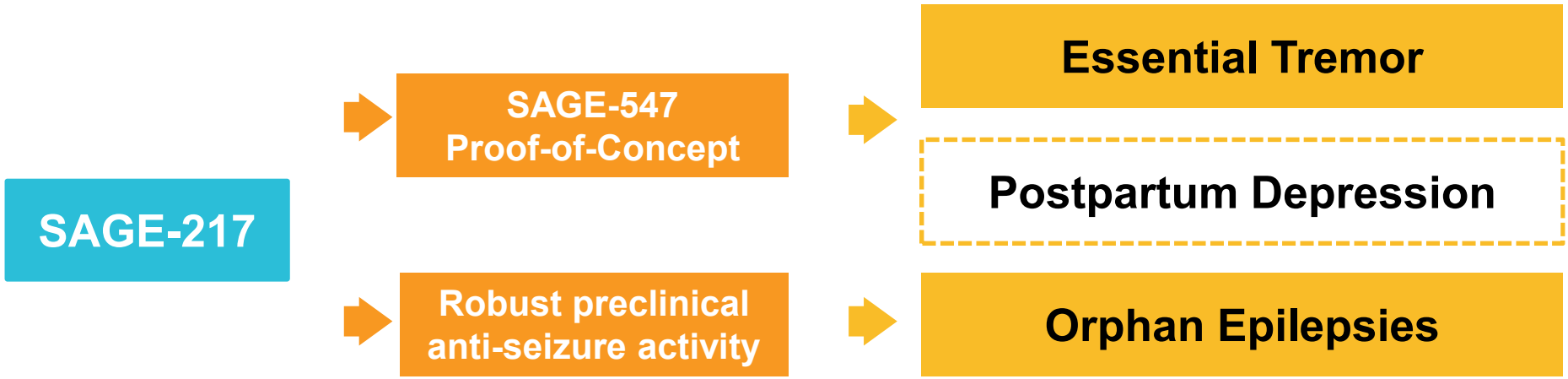
	Stage One SAGE-547 (n = 25)	Stage One Placebo (n = 25)	Stage Two SAGE-547 (n = 17)
Any TEAE, n (%)	3 (12%)	5 (20%)	8 (47.1%)
Any TEAE Considered Related to Treatment, n (%)	3 (12%)	1 (4%)	8 (47.1%)
Any TEAE Leading to Discontinuation, n (%)	0	0	1 (8.3%)

SAGE-217: A Chronic Oral $GABA_A$ Modulator

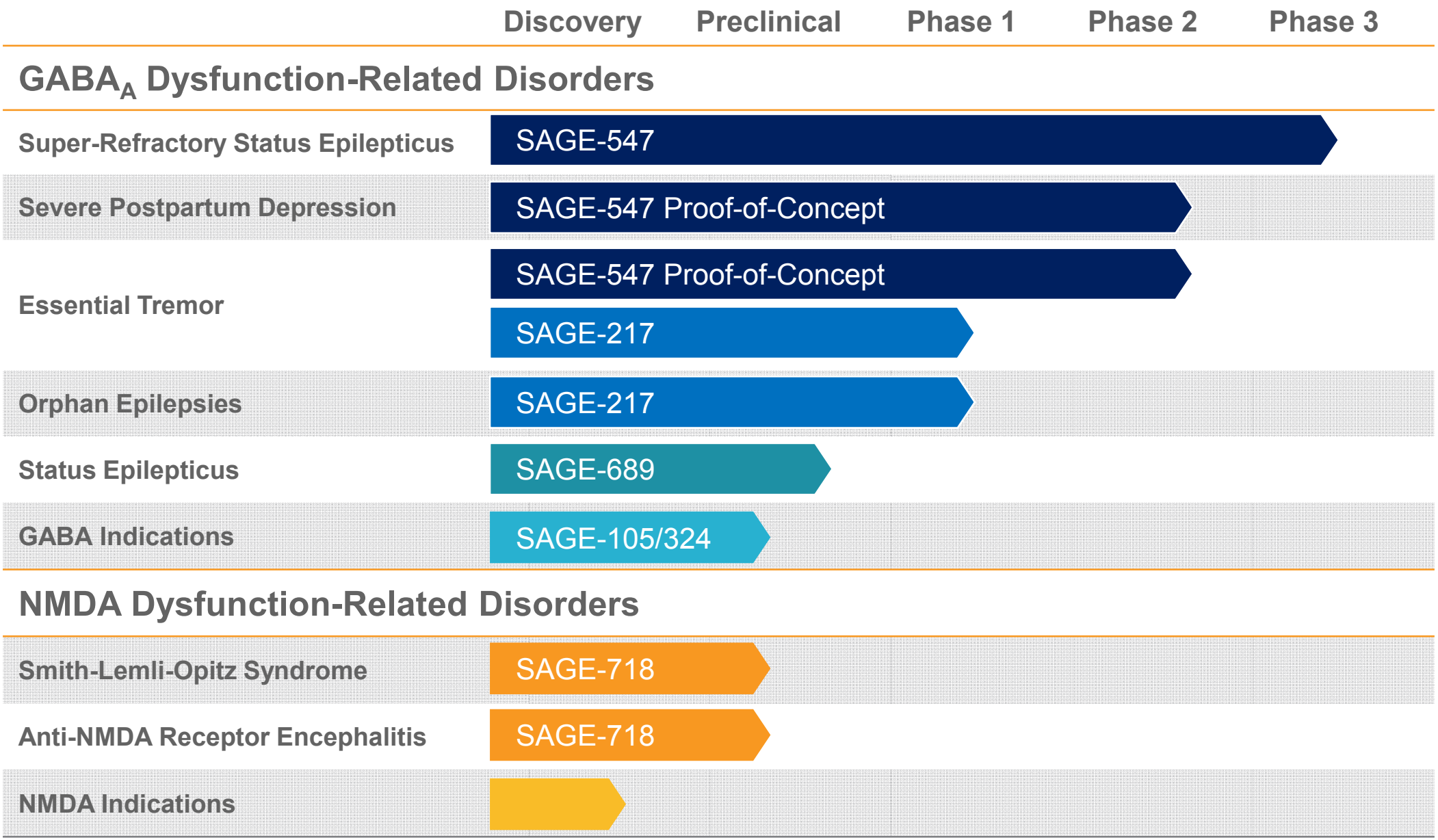
Phase 1 clinical program results expected in 1H 2016

Highly potent and selective activity at $GABA_A$ receptors in animal models	Designed with optimized PK/PD profile intended for once-daily dosing

Robust Phase 2 Development Programs Planned



Building an Innovative Multi-Product CNS Portfolio



2016 Expected Milestones

Program	1H 2016	2H 2016
SAGE-547	Severe postpartum depression • **Phase 2 top-line results**	SRSE • **Phase 3 top-line results** • **NDA planning and pre-commercial activities**
SAGE-217	**Phase 1 clinical program results**	Essential tremor • **Phase 2 initiation** Orphan epilepsies • **Phase 2 initiation**
SAGE-689		**Phase 1 clinical program initiation**

Strong Financial Position to Advance Programs

Q1 2016 Financial Results (as of 3/31/2016)

	Q1 '16	Q4 '15
Cash and Cash Equivalents[1]	$299.7M	$186.8M

	Q1 '16	Q1 '15
Research & Development	$23.6M	$12.9M
General & Administrative	$7.1M	$4.0M
Net Loss	$30.5M	$16.9M

[1]Q1 2016 includes approximately $140.4M in net proceeds from January 2016 follow-on offering

Guidance:

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

Upcoming Events and Conferences

- **Society of Biological Psychiatry 71st Annual Scientific Meeting (SOBP)**
  - May 12 - 14, 2016
  - Atlanta, GA
- **2nd Congress of the European Academy of Neurology (EAN)**
  - May 28 - 31, 2016
  - Copenhagen, Denmark
- **American Society of Clinical Psychopharmacology 2016 Annual Meeting (ASCP)**
  - May 30 – June 3, 2016
  - Scottsdale, AZ
- **Goldman Sachs Global Healthcare Conference**
  - June 7 - 9, 2016
  - Rancho Palos Verdes, CA
- **Eilat Conference on New Antiepileptic Drugs (Eilat XIII)**
  - June 26 - 29, 2016
  - Madrid, Spain

Q&A Session

