SAGE Therapeutics, Inc. (SAGE)

SunTrust Robinson Humphrey

Phase III Design In Line with Our Conservative Estimate

Buy

Price Target: $67.00
Prior: $67.00

Price (Apr. 1, 2015)	$50.86
52-Wk Range	$53.38-$25.86
Market Cap ($M)	$1,312
ADTV	187,698
Shares Out (M)	25.8
Short Interest Ratio/% Of Float	6.8%
TR to Target	31.7%

Cash Per Share	$4.12
Total Debt	$0.0
Cash And Equivalents ($M)	$127.8

	2014E	2015E		2016E	
		Curr.	Prior	Curr.	Prior
Revenue ($M)					
FY	0	0	0	0	0
EPS Adjusted					
FY	(1.67)A	(2.52)	(2.52)	(2.86)	(2.86)
P/E	NM	NM		NM	
Consensus Rev					
FY	0	0	0	0	0
Consensus EPS Adjusted					
FY	(2.51)A	(2.09)	(2.09)	(2.44)	(2.44)
FYE Dec					

What's Incremental

SAGE announced that, per FDA's feedback, a Phase III study of lead product SAGE-547 for SRSE be randomized, double blind. Management reiterated the guidance for a 1-2 year duration for this trial. Given the short duration of treatment (6 days/patient), the ~2 year timeline could be highly conservative, but is in line with our current estimate. We look to presentation of final Phase I/II data for SAGE-547 at AED (May 13-15, Miami) and a Late Breaker at AAN (Apr 22, Washington D.C.), mid-15 PoC for 547 in ET and PPD and YE15 disclosure of the NMDA program.

Per FDA's feedback, the Phase III study of SAGE-547 for SRSE will consist of a randomized, double blind design. This morning SAGE announced the results of an End-of-Phase II meeting with the FDA and the design of the Phase III study of lead product SAGE-547 for super refractory status epilepticus (uncontrolled seizures). The trial is on track to begin in mid-15, and will be a randomized, double blind, controlled one, to enroll 126 patients with SRSE (towards the lower end of management's guidance of 100-200 patients), at up to 150 sites in the U.S. as well as E.U. We spoke with management, who noted higher than expected interest in the study and thus a larger number of targeted clinical sites (including E.U.). Following 1:1 randomization, patients will get either SAGE-547 or placebo in addition to current standard of care 3rd line anti-seizure medication for a total of 6 days (vs. 5 days in the Phase I/II, to allow for more flexibility in the weaning process). The primary endpoint is in line with the Phase I/II endpoint, successful resolution of status epilepticus (SE) (after weaning off all 3rd line anti-seizure agents as well as SAGE-547/placebo) without resumption of SE within 24 hours post SAGE-547/placebo dosing completion. The trial is 90% powered based on Phase I/II results to date. Secondary outcomes will include other functional measurements (rate of recovery, regaining of consciousness, mental status and functional outcome). In addition, non-responders to blinded treatment (either arm) could be crossed over to an open-label follow-up arm and eligible for higher doses of SAGE-547 and followed for 30 days. Overall, management noted this was their desired study design.

Investors may be concerned that the randomized, double blind design for the SAGE-547 may translate into a study duration towards the higher end of management's guidance of 1-2 years. While there are clear advantages to the randomized design (i.e. potentially a stronger label), some investors may believe approval timelines are more protracted than previously modeled. Management reiterated the guidance for 1-2 year duration of the SAGE-547 pivotal study, to potentially be revisited as clinical trial sites are brought online. We believe a 2-year duration is conservative, but in line with our current estimates: we anticipate results from the study

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could report out in mid-2017. **However, we believe there is upside to this timeline, given that patient identification and enrollment are relatively straightforward processes (candidates for SAGE-547 are in intensive care units; per physician feedback once patients reach SRSE, their primary authorized representative is typically highly amenable to allowing for other therapies to be tested).** The time-limiting step could be site onboarding and Institutional Review Boards (IRB) agreements for the targeted 150 sites (we note 17 sites are currently involved in the Phase I/II study and would require re-contracting, though likely quick onboarding).

Phase I/II results to be presented at medical conferences could provide more information on durability. To date, SAGE has generated clinical data for SAGE-547 in super refractory status epilepticus (SRSE), continuous seizures, which is viewed as impressive by key opinion leaders (KOLs). The ~71% response rate in the Phase I/II study (N=17 patients disclosed to date) and the emergency use program (N=9) compare with a 22-43% historical response rates in SRSE per our review of literature and KOL feedback. Final results from the Phase I/II study will include a few more than 20 SRSE patients and will be presented at the Antiepileptic Drug and Device Trials XIII Conference (Miami, May 13-15). The company will also have a presence at the London/Innsbruck Colloquium in Status Epilepticus and Acute Seizures (Apr 9-11, London, satellite symposium), and SAGE-547 Phase I/II data will also be featured as a Late Breaker presentation at the American Association of Neurology meeting (Apr 18-25, Washington DC). SAGE is planning on presenting non-overlapping datasets, best suited for each audience, including the statistical plan and design of the Phase III trial and data from the eIND patients. Final results at AED may provide more granularity on physiological assessments and potentially clues on response durability, given exploratory secondary outcomes with 30 days of follow up.

We are looking forward to additional catalysts for SAGE starting in mid-2015. We look towards the London/Innsbruck Colloquium on Status Epilepticus, Phase I/II data presentation at AAN (Apr 22, 6 pm ET) and at the Antiepileptic Drug and Device Trials XIII Conference (Miami, May 13-15). We anticipate additional data iterations with longer follow-up could be presented at other medical conferences in late 2015 and beyond. In addition, an open label expanded access protocol (in line with the Phase III design) could allow for additional patients to access SAGE-547 and likely provide additional data points for presentation at medical conferences. In addition to SRSE (exp. pivotal trial start in mid-15), SAGE-547 is also being used as a probe molecule for essential tremor and post-partum depression (indications whereby its mode action appears well-suited to modulate the underlying cause of the disease). Two additional products are on track to enter the clinic by YE15: SAGE-689 as adjunctive i.v. second-line therapy for RSE, and SAGE-217 in an orphan epilepsy. Another program targeting the neural NMDA receptor could also be announced in 2015 in an orphan indication.

Sage Therapeutics

(NASDAQ: SAGE)

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Consolidated Income Statement

($thousands, except per share data)	FY 2012A	FY 2013A	FY 2014A	Mar Q1 2015A	Jun Q2 2015A	Sep Q3 2015E	Dec Q4 2015E	FY 2015E	FY 2016E	FY 2017E	FY 2018E	FY 2019E	FY 2020E
Revenue													
SAGE-547	$ -	$ -	$ -	-	-	-	-	$ -	$ -	$ -	$ 63,810	$ 332,738	$ 545,591
Total Revenue	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ 63,810	$ 332,738	$ 545,591
COGS	-	-	-	-	-	-	-	-	-	-	5,105	36,601	60,015
Gross profit	-	-	-	-	-	-	-	-	-	-	58,705	296,137	485,576
Operating expense													
R&D (GAAP)	7,229	14,357	24,100	9,542	10,559	12,155	14,546	46,802	60,221	70,224	80,334	90,211	100,260
SG&A (GAAP)	2,402	3,922	9,710	3,812	4,044	5,157	5,544	18,557	23,556	48,910	74,002	79,043	84,056
Total operating expense	9,631	18,279	33,810	13,354	14,603	17,312	20,090	65,359	83,777	119,134	154,336	169,254	184,316
Operating income (loss)	**(9,631)**	**(18,279)**	**(33,810)**	**(13,354)**	**(14,603)**	**(17,312)**	**(20,090)**	**(65,359)**	**(83,777)**	**(119,134)**	**(95,631)**	**126,883**	**301,260**
Interest Income (expense), net	-	1	8	4	4	5	4	17	34	54	58	91	212
Other income (expense), net	(1)	(3)	(9)	-	-	-	-	-	-	-	-	-	-
Total Other Income	(1)	(2)	(1)	4	4	5	4	17	34	54	58	91	212
Income before income taxes	(9,632)	(18,281)	(33,811)	(13,350)	(14,599)	(17,307)	(20,086)	(65,342)	(83,743)	(119,080)	(95,573)	126,974	301,472
Provision for income taxes	-	-	-	-	-	-	-	-	-	-	-	12,697	30,147
Net gain (loss)	**(9,632)**	**(18,281)**	**(33,811)**	**(13,350)**	**(14,599)**	**(17,307)**	**(20,086)**	**(65,342)**	**(83,743)**	**(119,080)**	**(95,573)**	**114,276**	**271,325**
Accretion of redeemable convertible preferred stock	(4)	(7)	(2,294)										
Net gain (loss) applicable to common shareholders	**$ (9,636)**	**$ (18,288)**	**$ (36,105)**	**$ (13,350)**	**$ (14,599)**	**$ (17,307)**	**$ (20,086)**	**$ (65,342)**	**$ (83,743)**	**$ (119,080)**	**$ (95,573)**	**$ 114,276**	**$ 271,325**
GAAP EPS (diluted)	**$ (2.74)**	**$ (12.26)**	**$ (1.67)**	**$ (0.52)**	**$ (0.56)**	**$ (0.67)**	**$ (0.77)**	**$ (2.52)**	**$ (2.86)**	**$ (3.92)**	**$ (2.92)**	**$ 3.16**	**$ 7.15**
Weighted shares outstanding basic and diluted (k)	3,522,607	1,492	21,574	25,736	25,865	25,994	26,124	25,930	29,242	30,368	32,719	36,139	37,946
Margin Analysis:													
Cost of product sales	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	8%	11%	11%
Product gross margin	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	92%	89%	89%
R&D (GAAP)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	126%	27%	18%
SG&A (GAAP)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	116%	24%	15%
Stock-based compensation expense	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0%	0%	0%
Total operating expense	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	242%	51%	34%
Operating margin	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-150%	38%	55%
Income tax provision	N/A	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	10%	10%
Net margin (GAAP)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-150%	34%	50%
Y/Y change:													
Total revenue	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	521%	164%
SAGE-547 revenue	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	521%	164%
R&D (GAAP)	N/A	99%	68%	129%	141%	84%	63%	94%	29%	17%	14%	12%	11%
SG&A (GAAP)	N/A	63%	148%	136%	124%	80%	62%	91%	27%	108%	51%	7%	6%
Stock-based compensation expense	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total operating expense	N/A	90%	85%	131%	136%	83%	63%	93%	28%	42%	30%	10%	9%
Operating income	N/A	90%	85%	131%	136%	83%	63%	93%	28%	42%	-20%	-233%	137%
Net income (GAAP)	N/A	90%	97%	118%	88%	76%	62%	81%	28%	42%	-20%	-220%	137%
GAAP EPS (diluted)	N/A	348%	-86%	-56%	-88%	32%	59%	-51%	-14%	-37%	26%	208%	-126%
Shares outstanding - GAAP	N/A	-100%	1346%	394%	1421%	33%	2%	20%	13%	4%	8%	10%	5%

Source: STRH Research, Company Reports

Company Description

SAGE Therapeutics, Inc. is a biopharmaceutical company focused on developing and commercializing novel medicines to treat life threatening, rare central nervous system disorders. Its lead program SAGE-547 is in clinical development for super-refractory status epilepticus and is the first of several compounds the company is developing in its portfolio of potential seizure medicines. The company's robust chemistry platform has generated multiple new compounds that target the GABA-A and NMDA receptors, which are well-characterized with regard to their role in many psychiatric and neurological disorders.

Investment Thesis

SAGE is positioning itself as a premier orphan play, focused on central nervous system (CNS) diseases of high unmet need, with well-defined molecular characteristics and likely short drug development timelines. SAGE is one of the few players in the CNS space, a field with significant unmet need – that has been historically difficult to tackle in drug development. The company recently went public, with the key strategy to use its broad platform (chemical modulators of brain molecules) to focus on drug development for CNS indications that are: 1) well-defined from a molecular perspective, and 2) have short drug development timelines (small numbers of patients, short clinical trial duration). SAGE's lead drug candidate is SAGE-547, a modulator of the neural gamma-amino butyric acid (GABA) receptor. SAGE-547 is about to enter pivotal testing in mid-2015 for super-refractory status epilepticus, a rare type of epilepsy characterized by persistent seizures (>24 hours), in spite of treatment with multiple rounds of anesthetics. The company has two second generation molecules in the wings (SAGE-217 and SAGE-689) expected to enter the clinic in late-2015, as well as a platform of early stage modulators (N-Methyl-D-aspartic acid receptor, NMDA) of cellular brain function, slated to expand the epilepsy/CNS orphan disease franchise.

Valuation and Risks

We arrive at our price target of $67 by means of a sum-of-the-parts discounted cash flow analysis, which ascribes $53.49/share to SAGE-547 U.S. sales, $8.76 to SAGE-547 E.U. sales, $0.62 to SAGE-547 ROW sales, and $4.38/share to cash. We assign SAGE-547 in a probability of success of 58% in the U.S., 25% in the E.U., and 25% in ROW. We assume a discount rate of 12% and a 1% terminal growth rate to SAGE-547 in the U.S. and the E.U., and no terminal value for SAGE-547 in ROW.

Risks:

- **Clinical Risk:** SAGE-547 may fail to repeat its 71-78% response rate from Phase II trials and eIND use in a pivotal trial. It is possible that both the Phase II and eIND patients had a higher chance of recovering from SRSE than the ~30% chance quoted by SAGE, and of the 30-50% chance quoted by our physician consultants. This could be due to the inclusion/exclusion criteria used in Phase II, or another reason altogether. Although preclinical rationale for SAGE-547 is suggestive that the compound could have utility in ET and PPD, the benefit in animals may not translate well in humans. Finally, although they have similar putative mechanisms of action, there is some chance that proof-of-concept for SAGE-547 does not read through to other GABA modulators SAGE-689 and SAGE-217.

- **Regulatory risk:** The FDA may require more rigorous clinical trials than we anticipate. We believe that SAGE's expected Phase III endpoint of being seizure-free after the patient is weaned from both general anesthesia and SAGE-547 should be appropriate. However, the FDA may ask for a randomized controlled study, which may be difficult to set up given the variability in standard of care among different treatment centers. Longer term follow-up could be required, for example an endpoint such as % of patients who are seizure free 1 month after wean. We expect clarity on this endpoint in Q1 2015, when SAGE communicates the results of their end-of-Phase II meeting with FDA.

- **Commercial risk:** SAGE plans to target the relatively small number of ICUs (~900 hospitals in the U.S.) and epilepsy treatment centers (~200 in the U.S.), where SRSE patients are treated. E.U. has

a comparable number of centers. The remains a commercial risk (albeit low) that SAGE is unable to effectively reach these patients.

- **Competitive Risk:** Although we are not aware of any significant competitive drugs in development for status epilepticus (SE), Marinus Pharmaceuticals (MRNS) is developing ganaxolone, a similar GABA-receptor targeted agent (although restricted to hitting the synaptic receptors), for the treatment of other forms of epilepsy and Fragile X syndrome. Although ganaxolone is unlikely to be approved for SE without clinical trials in that population, if the drug does become available it could be used off-label.
- **Financial risk:** Given the expenses associated with conducting clinical trials and launch of the product, we anticipate that SAGE may have to issue additional equity through follow-on offerings

Companies Mentioned in This Note

SAGE Therapeutics, Inc. (SAGE, $50.86, Buy)
Marinus (MRNS, $10.00 , NR)

Analyst Certification

I, Salveen Richter , hereby certify that the views expressed in this research report accurately reflect my personal views about the subject company(ies) and its (their) securities. I also certify that I have not been, am not, and will not be receiving direct or indirect compensation in exchange for expressing the specific recommendation(s) in this report.

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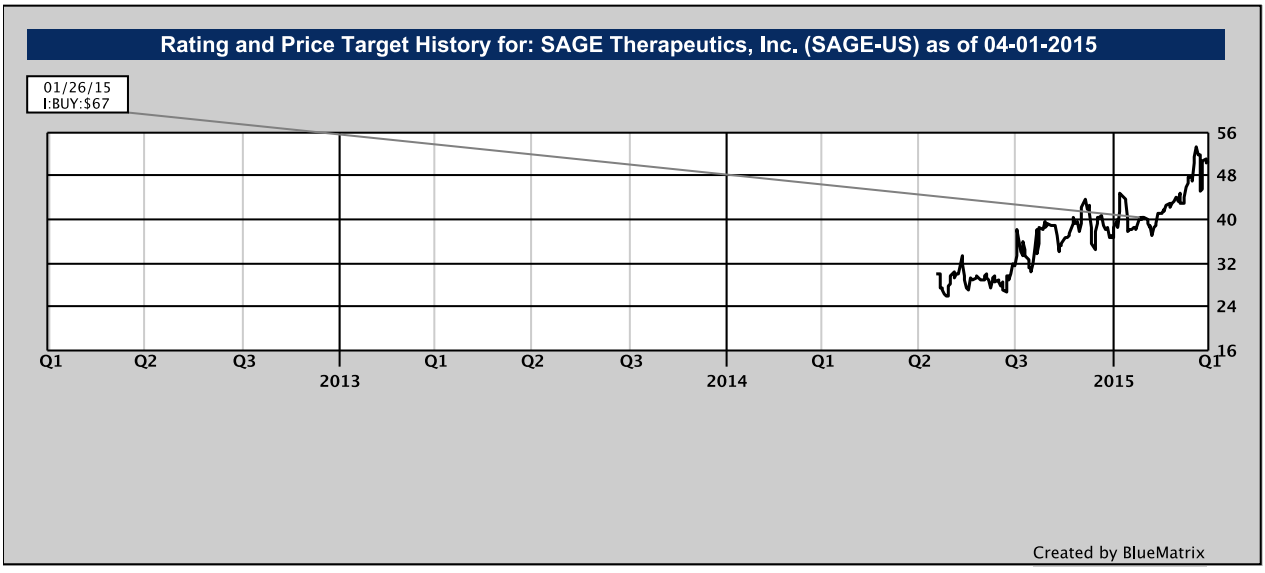

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3 designations based on total returns* within a 12-month period**

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*Total return (price appreciation + dividends)
**Price targets are within a 12-month period, unless otherwise noted
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Legend for Rating and Price Target History Charts:
D = drop coverage
I = initiate coverage
T = transfer coverage

SunTrust Robinson Humphrey ratings distribution (as of 04/02/2015):

Coverage Universe			Investment Banking Clients Past 12 Months		
Rating	**Count**	**Percent**	**Rating**	**Count**	**Percent**
Buy	279	52.25%	Buy	100	35.84%
Neutral	243	45.51%	Neutral	45	18.52%
Sell/Reduce	12	2.25%	Sell/Reduce	3	25.00%

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