SAGE Therapeutics, Inc. (SAGE)

SunTrust Robinson Humphrey

Signal in Postpartum Depression Supports SAGE's CNS Platform Approach

Increasing PT from $67 to $109

What's Incremental
SAGE disclosed promising data for SAGE-547 (used as test molecule) in 4 postpartum depression patients from a Phase II study. SAGE now plans to start a controlled Phase II study of 547 to confirm the proof-of-mechanism in PPD by YE15, and advance novel molecules, likely oral, for the same target (in parallel). We view potential proof-of-concept data in PPD as key to enabling SAGE to address a broader population than SRSE. We are increasing our PT to include some contribution from PPD to our R&D platform valuation, and we look towards mid-15 Ph II for 547 in essential tremor (upside to model).

SAGE-547 yields interesting signal in a small PPD patient sample. SAGE disclosed topline data from the first 4 patients with PPD (inadequate response to antidepressants), treated with SAGE-547 (proprietary formulation of the naturally-ocurring hormone allopregnanolone) in a single center, exploratory open label Phase II trial. Patients were given SAGE-547 intravenously in an inpatient setting for 60 hours (proprietary dose schedule) and evaluated at 24 hours after dosing initiation on the Hamilton Rating Scale for Depression (HAM-D, rates severity of 17 depression symptoms such as insomnia, agitation, anxiety, weight loss and low mood). The 4 patients achieved a statistically significant improvement/remission, from a mean baseline HAM-D score of 26.5 and to 1.8 post SAGE-547 dosing (p=0.001). SAGE-547 was well tolerated with no serious adverse events or treatment discontinuations. As a reminder, studies have linked PPD with abnormally low levels of allopregnanolone. We spoke with management, who discussed supportive preclinical data, and **we believe these results are the first in-human evidence for the utility of allopregnanolone/ modulation of GABA (SAGE-547's target) in PPD**. **We view these data as encouraging, given the exploratory nature of the trial** (notwithstanding the small patient numbers). We did not previously include any contribution from SAGE-547/novel molecules for PPD; we believe these data are upside to Street expectations.

Initial signs of activity in PPD could enable SAGE to address a broader population. The Phase II study was designed to enroll up to 15 PPD patients or 10 evaluable patients (whichever came first). SAGE is accelerating this program based on consistent and rapid responses achieved in the first 4 patients (placebo effects typically emerge within days rather than hours). We look for more color on durability, and note management saw consistent results. SAGE is now taking a two pronged approach with 1) a randomized

Salveen Richter, CFA
212-319-3728
salveen.richter@suntrust.com

Raluca Pancratov, Ph.D.
212-303-4178
raluca.pancratov@suntrust.com

SEE PAGE 5 FOR REQUIRED DISCLOSURE INFORMATION

Buy

Price Target: $109.00
Prior: $67.00

Price (Jun. 8, 2015)	$75.15
52-Wk Range	$80.82-$25.86
Market Cap ($M)	$1,939
ADTV	313,417
Shares Out (M)	25.8
Short Interest Ratio/% Of Float	7.1%
TR to Target	45.0%

Cash Per Share	$7.21
Total Debt	$0.0
Cash And Equivalents ($M)	$222.9

	2014E	2015E Curr.	2015E Prior	2016E Curr.	2016E Prior
Revenue ($M)					
FY	0	0	0	0	0
EPS Adjusted					
FY	(1.67)A	(2.83)	(2.83)	(3.15)	(3.15)
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					

controlled Phase II study of SAGE-547 to confirm the proof-of-mechanism of GABA modulation in PPD (to begin by YE15), and 2) parallel advancing of additional GABA-modulating compounds (likely an oral formulation) towards the clinic, with first assessments to include PK/PD and measures of sedation. **We believe ~15-20% of the ~4M postpartum U.S. women (could be conservative, excludes stillborn and miscarriages) could be addressed by SAGE's approach.** The randomized Phase II study may stratify patients by measures of severity/biomarkers, and identify a patient subgroup best suited for SAGE-547/GABA modulation. **We believe positive proof-of-concept data in a Phase II study and the ability to address a population significantly larger that SRSE (peak SAGE-547 WW sales estimate of $1.7B in 2026) represent a key value driver for SAGE.**

Next catalyst for SAGE could be SAGE-547 Phase II data in ET by mid-15. SAGE-547 is also being tested as a probe molecule in a Phase II study of essential tremor (ET), a common movement disorder similar to seizures (and SAGE-547's lead indication, super refractory status epilepticus), albeit less severe) given abnormal electrical signaling in the brain. ET patients are currently managed with benzodiazepines, a class of drugs that address only a subset of a patient's GABA molecules (at the neuronal synapse). SAGE-547 addresses a broader range of GABA molecules, thus could have activity in this indication. Topline data from an ongoing Phase IIa double-blind, placebo-controlled proof-of-concept crossover study of SAGE-547 in ET are expected to readout by mid-15. However, management is looking for a meaningful and consistent signal in this indication for a go/no go decision. **While we believe SAGE-547's mode of action makes sense for ET, this indication currently remains upside to our expectations.**

We are increasing our PT to $109 from $67 on increased visibility for SAGE-547's outlook and SAGE's platform. Based on the increased visibility for SAGE-547 in super refractory status epilepticus (see our discussion of updated Phase I/II data here) and encouraging signs of activity in PPD, we are increasing our price target to $109 from $67. We are 1) adjusting the discount rate for our sum-of-the-parts DCF from 12% to 10% and 2) including $25 value for SAGE's R&D platform, including SAGE-547/novel compounds addressing PPD.

Figure 1: Upcoming Expected Milestones

Product	Timing	Indication	Event
SAGE-547	**By mid-2015**	**Essential Tremor**	**Phase II topline data**
SAGE-547	By Mid-2015	Super refractory status epilepticus (IV)	Initiate the Phase III STATUS trial
SAGE-689	Late-2015	Adjunctive Status Epilepticus (IV)	Initiate Phase I testing
SAGE-217	Late-2015	Orphan Genetic Seizure Disorders (oral)	Initiate Phase I testing
NMDA modulator	Late-2015	Undisclosed orphan indication	Announce next program
SAGE-547	End-2015	Postpartum Depression	Initiate placebo-controlled Phase II study

Source: STRH analysis and Company reports

Sage Therapeutics

(NASDAQ: SAGE)

Salveen Richter, CFA
(212) 319-3728
salveen.richter@suntrust.com

Consolidated Income Statement

($thousands, except per share data)	FY 2012A	FY 2013A	FY 2014A	Mar Q1 2015A	Jun Q2 2015E	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	12,900	14,412	15,003	16,002	58,317	70,223	80,232	90,152	100,242	110,532
SG&A (GAAP)	2,402	3,922	9,710	3,997	5,002	5,157	6,002	20,158	30,122	50,033	82,823	90,232	100,213
Total operating expense	9,631	18,279	33,810	16,897	19,414	20,160	22,004	78,475	100,345	130,265	172,975	190,474	210,745
Operating income (loss)	**(9,631)**	**(18,279)**	**(33,810)**	**(16,897)**	**(19,414)**	**(20,160)**	**(22,004)**	**(78,475)**	**(100,345)**	**(130,265)**	**(114,270)**	**105,663**	**274,831**
Interest Income (expense), net	-	1	8	21	50	85	96	252	65	85	87	115	230
Other income (expense), net	(1)	(3)	(9)	5	-	-	-	5	5	10	20	40	75
Total Other Income	(1)	(2)	(1)	26	50	85	96	257	70	95	107	155	305
Income before income taxes	(9,632)	(18,281)	(33,811)	(16,871)	(19,364)	(20,075)	(21,908)	(78,218)	(100,275)	(130,170)	(114,162)	105,818	275,136
Provision for income taxes	-	-	-	-	-	-	-	-	-	-	-	5,291	27,514
Net gain (loss)	**(9,632)**	**(18,281)**	**(33,811)**	**(16,871)**	**(19,364)**	**(20,075)**	**(21,908)**	**(78,218)**	**(100,275)**	**(130,170)**	**(114,162)**	**100,527**	**247,623**
Accretion of redeemable convertible preferred stock	(4)	(7)	(2,294)										
Net gain (loss) applicable to common shareholders	**$ (9,636)**	**$ (18,288)**	**$ (36,105)**	**$ (16,871)**	**$ (19,364)**	**$ (20,075)**	**$ (21,908)**	**$ (78,218)**	**$ (100,275)**	**$ (130,170)**	**$ (114,162)**	**$ 100,527**	**$ 247,623**
GAAP EPS (diluted)	**$ (2.74)**	**$ (12.26)**	**$ (1.67)**	**$ (0.66)**	**$ (0.70)**	**$ (0.70)**	**$ (0.76)**	**$ (2.83)**	**$ (3.15)**	**$ (3.95)**	**$ (3.22)**	**$ 2.58**	**$ 6.04**
Weighted shares outstanding basic and diluted (k)	3,522,607	1,492	21,574	25,655	27,805	28,551	28,694	27,676	31,838	32,989	35,472	39,029	40,980
		$ 4											
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	141%	30%	20%
SG&A (GAAP)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	130%	27%	18%
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	271%	57%	39%
Operating margin	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-179%	32%	50%
Income tax provision	N/A	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	5%	10%
Net margin (GAAP)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-179%	30%	45%
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%	209%	229%	127%	79%	142%	20%	14%	12%	11%	10%
SG&A (GAAP)	N/A	63%	148%	147%	177%	80%	76%	108%	49%	66%	66%	9%	11%
Stock-based compensation expense	N/A	N/A	N/A	650%	0%	0%	0%	0%	N/A	N/A	N/A	N/A	N/A
Total operating expense	N/A	90%	85%	192%	214%	113%	78%	132%	28%	30%	33%	10%	11%
Operating income	N/A	90%	85%	192%	214%	113%	78%	132%	28%	30%	-12%	-192%	160%
Net income (GAAP)	N/A	90%	97%	176%	149%	104%	77%	117%	28%	30%	-12%	-188%	146%
GAAP EPS (diluted)	N/A	348%	-86%	-44%	-85%	40%	58%	-69%	-11%	-25%	18%	180%	-135%
Shares outstanding - GAAP	N/A	-100%	1346%	393%	1535%	46%	12%	28%	15%	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 $109 by means of a sum-of-the-parts discounted cash flow analysis, which ascribes $65.17/share to SAGE-547 U.S. sales, $10.89 to SAGE-547 E.U. sales, $0.63 to SAGE-547 ROW sales, $25.00 to the R&D platform including SAGE-547/other molecules contribution to postpartum depression, and $7.21/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 10% 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, $75.15, Buy)

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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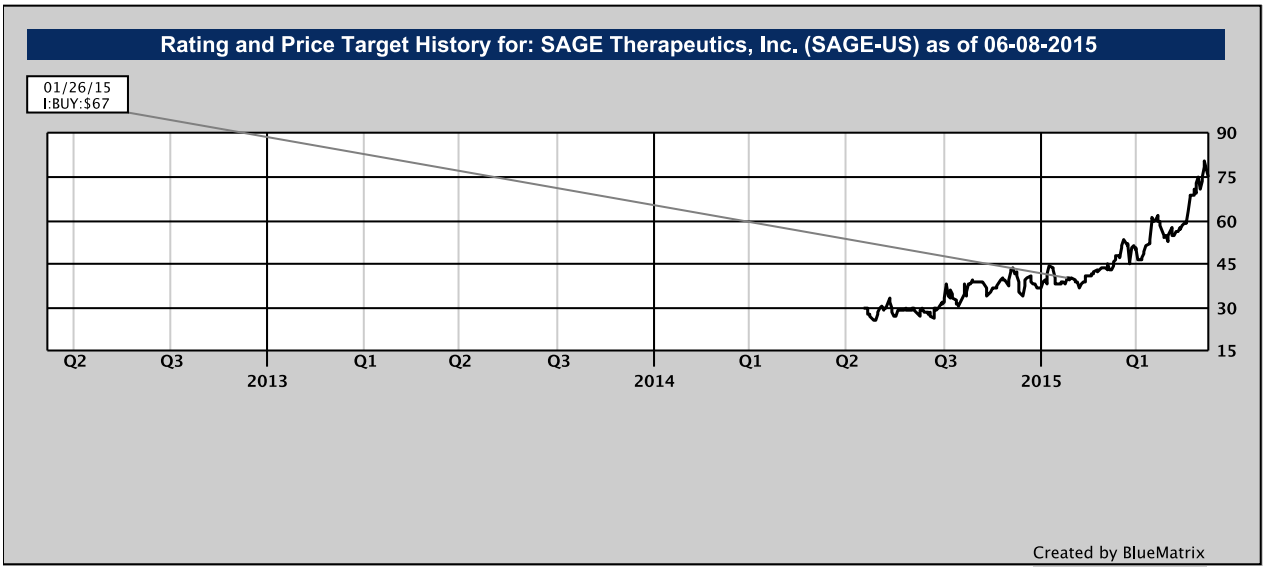

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