William Blair

April 24, 2015

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Therapeutics

2015 AAN Wrap-Up: In-Line SAGE-547 Data With More Expected in Miami, New Epilepsy and DMD Therapies Continue Development

Sage Therapeutics, Inc.

SAGE (NASDAQ)	$59.94
Stock Rating:	**Outperform**
Company Profile:	**Aggressive Growth**
Price Target:	$75.00

Sarepta Therapeutics, Inc.

SRPT (NASDAQ)	$13.66
Stock Rating:	**Outperform**
Company Profile:	**Aggressive Growth**
Price Target:	$34.00

- In this note, we detail Wednesday and Thursday data presentations and final conclusions from the 2015 Annual Meeting of the American Academy of Neurology. During Wednesday's Emerging Science presentations Sage Therapeutics CMO Dr. Steve Kanes reviewed Phase I/II data from SAGE-547's ongoing trial in severe refractory status epilepticus. In line with what has been previously reported, 71% (12/17) of patients were successfully weaned from their medically induced coma. In exhibits 1 and 2, on page 2, we show the etiology of disease and most common serious adverse events (SAEs), which were in line with other therapies used within the intensive care unit setting. As the company looks to begin its Phase III trial in mid-2015, we believe that physician education and site enrollment will be important. Following discussions with management, we believe higher doses of SAGE-547 and potentially 5 to 10 more patients' data should be reported at the Antiepileptic Drug and Device Trials Conference in Miami from May 13 through May 15.

- Sarepta Therapeutics' poster presentations showed pharmokinetic and pharmacodynamics data from in vitro, in vivo, and clinical studies done with eteplirsen as well as follow-on candidates SRP-4045 and SRP4053. The preclinical work presented shows that the company's PMO chemistry is well-tolerated with exposures up to 320 mg/kg in animal studies (human dose 30 mg/kg-50 mg/kg) after 12 weeks of weekly IV therapy. The clinical data presented from the company's 201/202 study with eteplirsen shows a 3- to 4-hour half-life in humans with an average renal clearance of 221 ± 53.5 mL/kg/hr in the 30 mg/kg dose and 234 ± 154 mL/kg/hr in the 50 mg/kg dose. In addition, there were no clinically significant treatment-related adverse events in doses up to 50 mg/kg/week through 168 weeks. To date, over 2,080 doses have been administered to DMD-affected boys. Given that a portion of requested data by the FDA to be included in the NDA includes safety data from eteplirsen, SRP-4045 and SRP-4053, the preclinical data gives us increased confidence that the company should be able to show safety and tolerability. However, with ongoing discussions with the FDA surrounding differing methods for dystrophin expression, there remains risk in the near term depending on the results from the company's fourth biopsy of treated patients. While our estimates do not call for a successful approval based on the company's Phase I/II data, the outcome of the company's NDA, which is set to be filed (and hopefully accepted) in the near term, and the outcome of the drisapersen review will be the major driver for share performance through year end.

- A higher level conclusion from the conference was an analysis of the increases in prevalence (as well as incidences of mortality) over the past decade in neurological disorders, such as multiple sclerosis, migraine headache, epilepsy, and Parkinson's disease (exhibit 3). As new therapies emerge with the heavy focus on development stage programs in Alzheimer's, multiple sclerosis, and the below-mentioned diseases we continue to believe that CNS therapies will be a key platform for innovation in the therapeutics space and should continue to attract investor interest.

- Lastly, we note that data presentations from Ultragenyx (RARE $68.90), Biogen (BIIB $430.28; Outperform), and GW Pharmaceuticals (GWPH $120.77) at the Emerging Science Session captured much of the Street's attention at the conference despite the abbreviated presentations. Ultragenyx's triheptanoin dosed at 1g/kg body weight per day for 2 months showed significant reduction in paroxysmal movement disorders in a study of eight GLUT1 deficiency syndrome patients that could provide an alternative approach to ketogenic diets. GW Pharmaceuticals presented new physician reports of its lead candidate, Epidiolex, in children and young adults with treatment-resistant epilepsy with a median reduction of 54% in seizures after 12 weeks of treatment. Patients were also stratified by Dravet (65% median reduction in seizure frequency) and non-Dravet syndrome (50% median reduction in seizure frequency at 12 weeks with 16% of patients seizure-free). As the company conducts its Phase III program in the treatment of Dravet syndrome, we note the efficacy of Epidiolex in the data presented at the conference. In addition, we anticipate that Phase III results could be cofounded by high placebo rates that have been observed in other seizure studies, given the caregiver measurement tools often employed. However, if approved for Dravet and/or Lennox-Gastaut syndrome, key opinion leaders we spoke with suggested that off-label use by epilepsy specialists would be prevalent given current disease outcomes with standard-of-care therapies used to date.

Exhibit 1
Etiology of SRSE in SAGE-547 Phase I/II Trial

Etiology	Patients	Percentage
Brain Hemmorhage	4	24%
Worsening of Seizures	4	24%
Infection	3	18%
Primary or Metastatic Brain Tumors	2	12%
Other	5	24%

Source: 2015 AAN Meeting

Exhibit 2
Summary of Most Common SAEs

SAE	Percentage
Pneumonia	15%
Sepsis	10%
Infection	10%
Brian Tumor	10%
Pulmonary Embolism	10%
Convulsion	10%

Source: 2015 AAN Meeting

Exhibit 3
Change in Deaths and Prevalence at Global Level 1990-2013

	Number of deaths (thousands)		Prevalent cases (thousands)	
Cause	1990	2013	1990	2013
Ischemic stroke	2183	3272	12204	18306
Hemorrhagic stroke	2402	3174	5238	7364
Alzheimers and other dementias	796	1655	28144	53051
Parkinsons disease	44	103	3244	5866
Epilepsy	111	116	16923	21712
Multiple Sclerosis	12	20	1057	2294
Migraine	0	0	581472	848367
Tension-type headache	0	0	1073159	151445
Medication overuse headache	0	0	28513	62899
Other neurological disorders	55	84	-	-

Source: 2015 AAN Meeting

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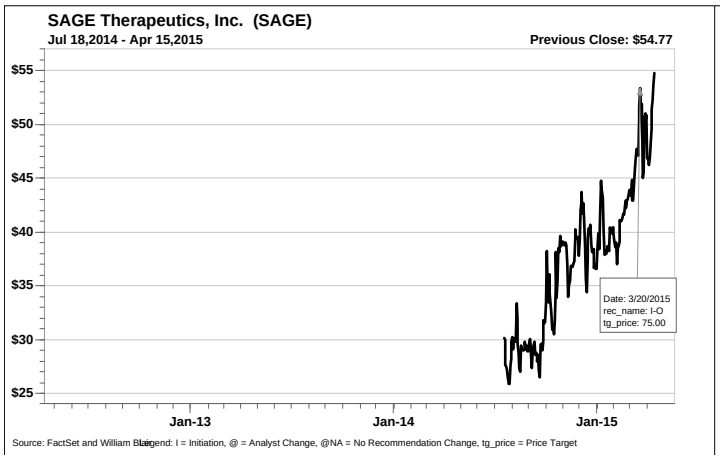
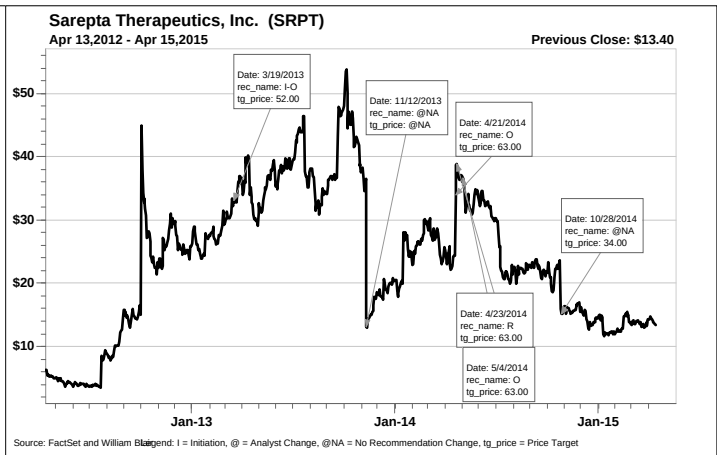
DOW JONES: 18,058.69
S&P 500: 2,112.93
NASDAQ: 5,056.06





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Market Perform (Hold)	33	Market Perform (Hold)	3
Underperform (Sell)	2	Underperform (Sell)	0

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