Summer Street RESEARCH PARTNERS

Synergy Pharmaceuticals (SGYP)

Reiterate Buy Ahead of the Pivotal Data of Plecanatide

November 26, 2012

SUMMARY

We reiterate our Buy rating and target price of $9 ahead of the top-line data release from the plecanatide phase II/III CIC trial expected in the first week of January 2013. The outcome of the phase II/III CIC trial is highly binary. We believe the chances for this phase II/III trial to report positive data are high. Our optimism on the trial is based on the validated mechanism of action by competing drug linaclotide (IRWD, NR), and preliminary but competitive positive efficacy and safety of plecanatide observed in a prior randomized placebo-controlled phase IIa trial in CIC patients. If the side effect profile of plecanatide is confirmed in the phase II/II trial, the absence of diarrhea could represent a key advantage of plecanatide over linaclotide.

EVENT

SGYP expects to report top-line data from the phase II/III CIC trial of plecanatide in the first week of January 2013. We expect the data to be positive. In this note, we review the phase II/III trial design and prior data supporting the trial.

INTERPRETATION

The outcome of the phase II/III CIC trial is highly binary. Based on the validated mechanism of action by competing drug linaclotide, a first-in-class GC-C receptor agonist recently obtained FDA approval for CIC and IBS-C, and preliminary but competitive positive efficacy and safety of plecanatide observed in a prior randomized placebo-controlled phase IIa trial in CIC patients, we believe the chances for the phase II/III trial to report positive data are relatively high. If the side effect profile of plecanatide is confirmed in the phase II/II trial, the absence of diarrhea could represent a key advantage of plecanatide over linaclotide.

ACTION

We reiterate our Buy rating and target price of $9 ahead of the top-line data release from the phase II/III CIC trial.

SGYP
Rating: BUY
Price Target: $9

Market Data	
Price:	$4.24
52-week high:	$7.08
52-week low:	$2.05
Shares out:	66.11M
Shares short:	1.99M
Average volume (10-day):	453,786

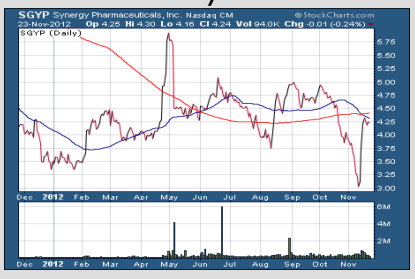
Valuation Metrics	
Market cap:	$280.29M
Enterprise value:	$242.92M
Book value/share:	$0.48

Financial Highlights	
Cash/equivalents:	$37.4MM
Debt:	$0.00

REV ($MM)	2011A	2012E	2013E
Q1	0	0A	-
Q2	0	0A	-
Q3	0	0A	-
Q4	0	0E	-
FY	0	0E	0

EPS ($)	2011A	2012E	2013E
Q1	(0.08)	(0.13)A	-
Q2	(0.10)	(0.17)A	-
Q3	(0.01)	(0.15)A	-
Q4	(0.12)	(0.15)E	-
FY	(0.30)	(0.61)E	(0.52)

One-Year History



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Biotechnology — Company Update

INVESTMENT THESIS

SGYP's lead compound, plecanatide, has great potential to become the second, but best-in-class, guanylate cyclase-C (GC-C) receptor agonist for treating chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C). We expect potentially positive top-line data from an ongoing phase II/III CIC trial, which is expected in early January 2013, to provide significant upside in the near term. Additionally, we expect potentially successful proof of concept of plecanatide in IBS-C (phase IIb trial planned in 4Q12) to significantly expand plecanatide's market opportunity. Assuming success, we expect plecanatide to potentially become a best-in-class oral treatment for both CIC and IBS-C, two large unmet medical needs that are not sufficiently served with available therapies. Although linaclotide, a first-in-class GC-C receptor agonist, is likely two to three years ahead of plecanatide, we believe the market is big enough to allow room for several players. Additionally, plecanatide's potential side effect advantage of causing less diarrhea might offer it a significant competitive advantage. While not our main thesis, we believe SGYP is an attractive acquisition target with plecanatide as a potential best-in-class compound targeting the large unmet medical needs of CIC and IBS-C.

DISCUSSIONS

We believe the phase II/III Plecanatide in CIC trial has a high probability of success

SGYP initiated a repeat-dose, oral, dose-ranging, randomized, double-blind, and placebo-controlled phase II/III trial evaluating plecanatide in CIC patients in October 2011. The trial completed the enrollment of 951 patients by the end of August 2012. Based on the anticipated dropout rate, management is very confident that the trial should obtain the targeted 880 randomized patients for data analysis. The trial expects to complete its last patient visits by December 7th and release the top-line data during the first week of January 2013.

Based on the validated mechanism of action by competing drug linaclotide (which succeeded in two phase III CIC trials and two phase III IBS-C trials and obtained regulatory approval earlier this year) and preliminary positive efficacy and safety of plecanatide demonstrated in a prior randomized placebo-controlled phase IIa trial in CIC patients, we believe the chances for this phase II/III trial to report positive data are relatively high.

Rigorous phase II/III CIC trial design is similar to the linaclotide phase III trials

The phase II/III trial of plecanatide targets to enroll ~880 evaluable patients who are randomized 1:1:1:1 to receive oral, once-daily plecanatide at 0.3 mg, 1.0 mg, 3.0 mg, or placebo for 12 consecutive weeks. Patients are screened against the enrollment criteria and first enter a two-week pre-treatment screening period. Patients need to have <=3 complete spontaneous bowel movements (CSBM) per week in order to be randomized. The primary endpoint is responder rate in terms of CSBMs. The trial is powered at 90% to detect at least a 10% difference in overall CSBM responders between plecanatide 1.0 mg versus placebo separately with plecanatide 3.0 mg versus placebo, while the 0.3 mg dose was considered the minimally effective dose. Responders are defined as the following criteria: >=3 CSBMs a week for nine of 12 weeks of the study; increase of at least one CSBM on weekly basis over baseline; >=3 of the CSBMs need to be in the last four weeks within the 12-week treatment period. Secondary endpoints include reduction in straining and abdominal symptoms such as pain, discomfort, and bloating at the end of 12 weeks (as measured by patient reported outcome [PRO] measures collected via an interactive voice response system [IVRS]); an improvement in the hardness of stool; the frequency of spontaneous movements; a reduction in time to first bowel movement; and treatment-emergent adverse events (AE).

The plecanatide phase II/III trial was designed as a pivotal trial, with the endpoints essentially the same as linaclotide's phase III trials in CIC. Management plans to schedule a post-phase II meeting with the FDA to discuss the regulatory requirement for plecanatide for treating CIC. Depending on the data from this phase II/III trial, we anticipate the FDA will require one or more phase III trials to confirm plecanatide's efficacy and safety in CIC patients.

Promising preliminary phase IIa data bodes well for the phase II/III CIC trial

SGYP previously completed a randomized, double-blind, placebo-controlled, 14-day repeat dosing, and dose-ranging phase IIa trial evaluating the safety, PD, and efficacy of multiple dosing of plecanatide. Patients were randomized 3:1 to receive either plecanatide at 0.3, 1.0, 3.0, or 9.0 mg QD, or placebo in the morning for 14 days. There were 20 patients per dose cohort, in which 15 patients received drug treatment and five patients received placebo. The trial enrolled 84 patients at 14 medical centers in the US. Eighty patients were randomized and 78 patients were evaluable. Based on the data

presentation in 2010 American College of Gastroenterology (ACG) annual scientific meeting and in the 2011 ACG conference, Plecanatide showed impressive preliminary efficacy. Patients on plecanatide (doses of 1 mg, 3 mg, and 9 mg) reported significant decreases in time to first bowel movement after dosing as compared to placebo patients. Additionally, patients treated with plecanatide also reported increases in both the average number of SBMs and CSBMs per week. Although the numerical number of improvement in weekly SBMs and CSBMs as compared to baseline was not reported, we believe the efficacy of plecanatide was highly impressive since the average number of SBMs exceeded four times a week and the average number of CSBMs exceeded three times a week at 1 mg and 9 mg, respectively. The treatment delta in weekly SBM frequency (over baseline, over placebo) was roughly in the range of 0 to 1.3, and for weekly CSBM frequency was roughly in the range of 0 to 1.3 across the four dosing cohorts. Of note, the treatment delta in terms of weekly CSBM frequency (over baseline, over placebo) for linaclotide was roughly in the range of 1 to 1.6 for its effective and tolerable doses. In addition to increasing bowel movement frequency, plecanatide also improved other efficacy measures including improving stool consistency, reducing straining during bowel movements and improving abdominal discomfort, constipation severity, and overall relief after treatment as compared to patients receiving placebo.

Low incidence of diarrhea could be a key differentiating factor for plecanatide

Plecanatide also showed a favorable side effect profile in the phase IIa trial, with most AEs being mild/moderate and transient. There was no detectable systemic absorption of plecanatide in patients at any of the dose levels tested in the trial and maximum tolerated dose (MTD) was not reached. There were no serious adverse events (SAE) and no deaths reported in the trial. Approximately 10% (2/20) of placebo patients versus 17.2% (10/58) of patients treated with plecanatide had reported AEs, respectively. Plecanatide was associated with minimal GI-related AEs (8.6% and 10% for plecanatide and placebo patients, respectively). More impressively, there was no diarrhea observed in any patient treated with plecanatide in the phase IIa trial as compared to one placebo patient who discontinued treatment due to diarrhea.

While there is no direct comparison, and plecanatide clinical data have been obtained only in early stage trials so far, it appears linaclotide is associated with much higher levels of diarrhea. Combined analysis of the two pivotal phase III trials showed linaclotide is associated with ~15% of diarrhea versus ~1.2% for placebo. If the absence of diarrhea is confirmed in the phase II/III trial, we believe it represents a key advantage of plecanatide over linaclotide.

VALUATION

We use a sum-of-the parts analysis to value SGYP shares. Our 12-month target price of $9 is derived by summing up SGYP's development programs: the risk-adjusted NPV of plecanatide at ~$477MM, SP-333 at $35MM, and the company's technology and discovery engine at $80MM (Figure 1).

Figure 1. Sum-of-the-Parts Analysis

Plenacatide	$	476,984
SP-333	$	35,000
Technology	$	80,000
Fair value	**$**	**591,984**
Fair value / share	**$**	**9.2**

INVESTMENT RISKS

- Clinical risks associated with plecanatide: We assign a significant proportion of our projected value to plecanatide. Therefore, if the ongoing phase II/III trial in CIC or future clinical trials in CIC or IBS-C fail to deliver positive results, it would have a negative impact on our projections and target price.
- Regulatory risks associated with plecanatide: Plecanatide may not obtain regulatory approval even if it demonstrates positive clinical data. Our model factors in the risk-adjusted sales of plecanatide in CIC and IBS-C. If the drug does not obtain regulatory approval, it will negatively impact our target price.
- Liquidity and financing risk: We estimate SGYP's cash position should be sufficient to fund operations through 2013. There are risks associated with obtaining sufficient funding to sustain operations. The company may need to raise additional capital via equity financing, potentially causing dilution.
- Commercialization risk: The market potential of plecanatide in CIC and IBS-C may not be as large as we project.

• High stock price volatility: High stock price volatility is common among developmental companies in the biotechnology sector.

CATALYSTS/UPCOMING MILESTONES

- ✓ Complete patient enrollment in the pivotal phase II/III trial of plecanatide in CIC (3Q12)
- ✓ File an IND for SP-333 in patients with ulcerative colitis (3Q12)
- ✓ Potential for competitor linaclotide to obtain regulatory approval for CIC and IBS-C in the US (3Q12/September PDUFA date)
- ✓ Potential to initiate a phase I trial evaluating SP-333 in healthy volunteer (4Q12)
- Potential to initiate a randomized, placebo-controlled phase IIb trial evaluating plecanatide in patients with IBS-C (4Q12)
- Report topline results from a phase II/III trial of plecanatide in CIC (1Q13/first week of January)
- Potential to initiate a trial to evaluate multi-dose SP-333 in healthy volunteer (1Q13)
- Potential to report top-line data from the phase IIb trial of plecanatide in patients with IBS-C (3Q13)

COMPANY DESCRIPTION

Synergy Pharmaceuticals, Inc., is a New York-based biopharmaceutical company focusing on the development of drugs to treat gastrointestinal disorders and diseases. Its leading compound, plecanatide, is being evaluated in a phase II/III trial (ongoing) in patients with chronic idiopathic constipation and in patients with constipation-predominant irritable bowel syndrome (phase IIb planned). The second compound, SP-333, a second-generation GC-C receptor analog, recently has an IND submitted for treating ulcerative colitis. SGYP also recently acquired FV-100, an orally available nucleoside analogue, for the treatment of shingles, from BMS.

PIPELINE

Figure 2. SGYP's Pipeline

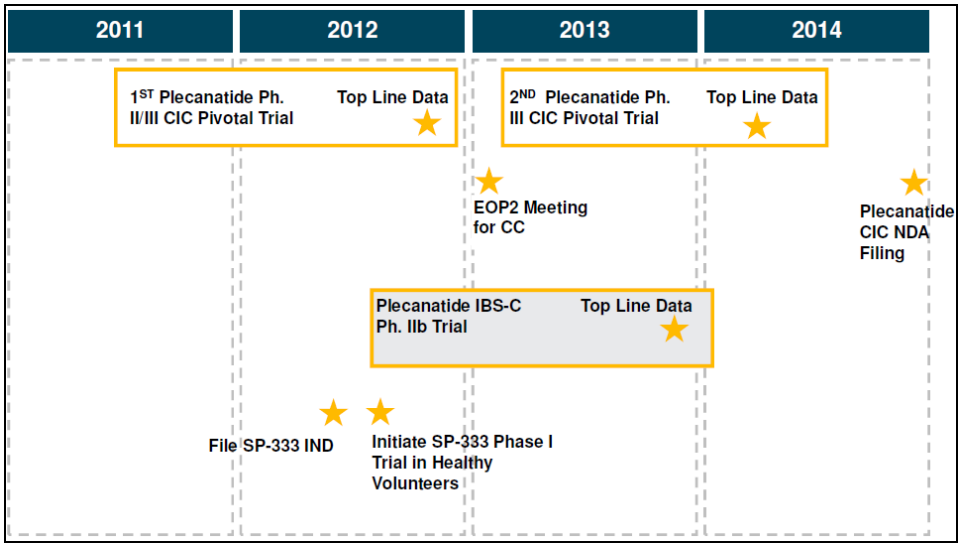

Figure 3. SGYP Income Statement

Synergy Pharmaceuticals, Inc.

Income Statement

Fiscal Year Ends December

(in 000, except per share amounts)

	2009A	2010A	1Q11A	2Q11A	3Q11A	4Q11A	2011A	1Q12A	2Q12A	3Q12A	4Q12E	2012E	2013E
Revenue	-	-											
Total Revenues	-	-	-	-	-	-	-	-	-	-	-	-	
Operating Expenses:													
Cost of goods sold	-	-	-	-	-	-	-	-	-	-	-	-	
Research and development	3,733	9,559	1,478	2,355	3,883	5,703	13,419	5,338	7,626	8,246	8,500	29,710	32,681
General and administrative	4,467	6,563	1,897	1,524	1,103	2,222	6,746	1,731	1,918	1,843	2,050	7,543	7,920
Total Operating Expenses	8,200	16,121	3,375	3,879	4,986	7,925	20,165	7,069	9,545	10,089	10,550	37,253	40,601
Loss from operations	(8,200)	(16,121)	(3,375)	(3,879)	(4,986)	(7,925)	(20,165)	(7,069)	(9,545)	(10,089)	(10,550)	(37,253)	(40,601)
Other income (expense):													
Interest and Investment Income	75	108	24	20	20	26	90	39	48	63	20	170	70
Interest expense			(12)				(12)						
Other income (expense):		494				362	363		256			256	
Change in fair value of derivative instruments - warrants		297	(339)	(698)	4,383	1,911	5,257	8	(1,317)	141		(1,168)	
Net loss before income taxes	(8,125)	(15,222)	(3,702)	(4,557)	(583)	(5,626)	(14,467)	(7,023)	(10,558)	(9,885)	(10,530)	(37,996)	(40,531)
Income tax benefit – principally from sale of New Jersey tax benefits in 2010 and 2008													
Net loss	(8,125)	(15,222)	(3,702)	(4,557)	(583)	(5,626)	(14,467)	(7,023)	(10,558)	(9,885)	(10,530)	(37,996)	(40,531)
Basic and diluted net loss per share	$ (0.22)	$ (0.34)	$ (0.08)	$ (0.10)	$ (0.01)	$ (0.12)	$ (0.30)	$ (0.13)	$ (0.17)	$ (0.15)	$ (0.15)	$ (0.61)	$ (0.52)
Weighted average number of shares outstanding – basic and diluted	36,641	44,875	46,167	46,643	47,309	48,657	47,587	54,298	60,416	65,806	70,506	62,757	77,557

Disclosures and Disclaimers — Fourth Quarter 2012

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Investment Rating Distribution for the Period 7/1/12 through 9/30/12:

Rating	Count	Percentage
BUY	35	80%
NEUTRAL	8	18%
SELL	1	2%
Companies under coverage at 9/30/12	**44**	**100%**

We have assigned an investment rating for at least one year for the following subject companies mentioned in this report:

SGYP

Ratings History

Date	Rating	Share Price	Price Target
3/22/12	BUY	$4.15	$9.00

SGYP Investment Risks

- **Clinical:** If the ongoing phase II/III trial of plecanatide in CIC or future clinical trials in CIC or IBS-C fail to deliver positive results, it would have a negative impact on our projections and target price.
- **Regulatory:** Plecanatide may not obtain regulatory approval even if it demonstrates positive clinical data.
- **Commercialization:** The market potential of plecanatide in CIC and IBS-C may not be as large as we project.
- **High stock price volatility:** High stock price volatility is common among developmental companies in the biotechnology sector.

Valuation Method for Price Target: Sum of the parts

Source: StockCharts.com

