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Company Update

EQUITY RESEARCH

November 2, 2011

Synergy Pharmaceuticals, Inc.

Rating: Buy

Synergy Data Wows At ACG Meeting - Reiterate Buy

Key Metrics

SGYP - OTC BB	$2.19
Pricing Date	Nov 1 2011
Price Target	$15.00
52-Week Range	$6.99 - $1.90
Shares Outstanding (mm)	94.5
Market Capitalization ($mm)	$206.9
3-Mo Average Daily Volume	52,608
Institutional Ownership	0%
Debt/Total Capital	NA
ROE	NA
Book Value/Share	$(0.04)
Price/Book	(54.8)x
Dividend Yield	NA
LTM EBITDA Margin	NA

EPS($) FY: December

	2010A	Prior 2011E	Curr. 2011E	Prior 2012E	Curr. 2012E
1Q-Mar	(0.03)	--	(0.04)A	--	(0.08)E
2Q-Jun	(0.07)	--	(0.05)A	--	(0.10)E
3Q-Sep	(0.04)	--	(0.03)E	--	(0.11)E
4Q-Dec	(0.04)	--	(0.06)E	--	(0.13)E
FY	(0.17)	--	(0.18)E	--	(0.42)E
P/E	NM		NM		NM

Revenue($mm)

	2010A	Prior 2011E	Curr. 2011E	Prior 2012E	Curr. 2012E
1Q-Mar	NA	--	NA	--	NA
2Q-Jun	NA	--	NA	--	NA
3Q-Sep	NA	--	NA	--	NA
4Q-Dec	NA	--	NA	--	NA
FY	NA	--	NA	--	NA

Company Description:

Synergy Pharmaceuticals, Inc., a development-stage biopharmaceutical company, focuses on the development of drugs to treat gastrointestinal (GI) disorders and diseases. It is developing SP-304, a guanylyl cyclase C (GC-C) receptor agonist, to treat GI disorders, primarily chronic constipation and IBS-C; and has SP-333, a second-generation GC-C receptor agonist in pre-clinical development stage to treat gastrointestinal inflammatory diseases. The firm is headquartered in New York, New York; the company's website is www.synergypharma.com.

Investment Highlights:

- **American College of Gastroenterology (ACG) Meeting Impact.** We draw investors' attention to Synergy Pharmaceuticals' data presentations at the ACG meeting in Washington, D.C., where the firm presented clinical data on plecanatide in constipation and preclinical data on both plecanatide and its follow-on candidate, SP-333, in models of inflammatory bowel disease. In addition, and perhaps most excitingly, Synergy and its collaborators presented groundbreaking preclinical data showing that plecanatide and other GC-C receptor agonists could have efficacy in treating colon cancer. In the wake of these data presentations, we are reiterating our Buy rating and 12-month price target of $15 on Synergy shares.
- **Highly Innovative Platform.** In our view, Synergy is the leader in the GC-C receptor modulator space, and its ability to target conditions such as colon cancer make the firm a significant value proposition. The firm presented preclinical data at the ACG Meeting indicating that the frequency of colonic tumors in a well-respected and widely-utilized mouse model could be reduced via the administration of plecanatide. The company also showed data indicating that the mechanism of the drug involved reduction in the rate of cell division in tumor tissues and an increase in programmed cell death, downstream of impact on various cytokines. Synergy's ability to deploy its candidates in high-value areas like colon cancer could enable the company to develop highly-priced, innovative medications to address significant unmet needs.
- **Plecanatide Phase 3 Program Advancing.** Synergy recently initiated a Phase 3 trial of plecanatide, enrolling over 800 patients. This trial is expected to yield positive efficacy data on plecanatide in chronic constipation, which could lead to a transformative partnership on plecanatide or a wholesale acquisition.
- **Stealing A March On Linaclotide.** We consider the GC-C receptor space to be a hot domain following the positive Phase 3 data reported with linaclotide and the successful submission of the drug to the FDA. Plecanatide may have a superior safety profile with similar efficacy to linaclotide. We believe that the results at ACG clearly show Synergy's leadership in the GC-C receptor field, and underscore the firm's unique ability to deploy its platform to develop peptide-based therapeutics spanning an entire gamut of GI tract disorders. These include chronic constipation, irritable bowel syndrome of the constipation-predominant subtype (IBS-C), ulcerative colitis, inflammatory bowel disease (IBD), Crohn's disease, and even colon cancer.

The Disclosure section may be found on pages 14 - 16 of this report.
The Valuation section may be found on page 14 of this report.

Valuation

Free Cash Flow: We believe Synergy could be free cash flow-negative for the foreseeable future. We define free cash flow as operating cash flow minus capital expenditures and dividend payments. We utilize a discounted cash flow analysis supporting a risk-adjusted Net Present Value (rNPV) framework to derive our $15 price target.

Risk-Adjusted Net Present Value Analysis

We have projected peak annual global sales for plecanatide (SP-304) – formerly known as guanilib – to be approximately $4.4 billion in 2021, prior to projected patent expirations in the 2022 time frame. This estimate includes only sales for treatment of chronic constipation and constipation-predominant irritable bowel syndrome. We estimate that, at a peak market share of 24% of all patients seeking therapy, there would be 3.4 million patients receiving plecanatide to treat constipation-related conditions. In valuing this drug candidate, we have assessed the probability of success at 60% – since the molecule recently successfully completed a Phase 2a trial, has also shown proof-of-concept efficacy in animal models, and employs a validated mechanism of action – as is evidenced by the clinical success of linaclotide, a similar agent. Our risk-adjusted base case NPV calculation yields a value of $1.5 billion, or around $13 per share, for this drug candidate, assuming a partnership with an established pharmaceutical firm that would provide Synergy with 30% royalties on net sales globally. We assume that Synergy or a potential partner could file for approval of plecanatide by late 2013. The drug could be launched in early 2015, in our view, assuming a standard 10-month review period.

Table 1: Plecanatide (SP-304) Market Metrics

Plecanatide - Global	
Total constipation patients[1]	164MM
Patients seeking treatment[2]	14.6MM
Peak market share[3]	24%
Treatment revenue/prescription/course of therapy[4]	$1,275
Peak sales[5]	$4.4B
Launch[6]	2015
Peak sales year	2021
Protection expires[7]	2022
Discount rate	15%
Probability of success[8]	60%
Risk-adjusted NPV[9]	$1.5B
NPV per share	$12.84
Estimated Net Cash Position ($MM; end-2Q 2012)	$72MM
Additional Value Drivers (peptide pipeline, including SP-333)	$150MM
Total enterprise value	$1.7B
Shares Outstanding (MM; end-2Q 2012)	117MM
Present value-derived price target	$15.00

Notes on assumptions:

[1] Constipation patients - worldwide (only includes US and European Union)
(Source: National Institute of Health, American Gastroenterological Association)

[2] Patients with moderate-to-severe chronic constipation and constipation-predominant irritable bowel syndrome (IBS-C)
(Source: Morgan Joseph TriArtisan estimates)

[3] Peak market share - blended; factoring in competition from laxatives, lubiprostone, prokinetics and linaclotide

[4] Revenue/year/prescription - estimated to be similar to linaclotide (wholesale acquisition cost)

[5] Peak sales - treatment revenue/year x treated patients x peak market share

[6] Launch in 2015 (US) / 2016 (EU)

[7] Patent expiry starting in 2022

[8] Probability of success - plecanatide has completed proof-of-concept development and is entering Phase 3

[9] Cash flow fully taxed at 35% following launch; upfront payments and milestones cancel out operating loss carry-forwards

Source: Company reports; Morgan Joseph TriArtisan estimates

American College of Gastroenterology Data

We would draw investors' attention to the American College of Gastroenterology (ACG) 2011 Annual Meeting, which has been taking place in Washington, D.C. The conference began on October 29 (Saturday) and ends on November 2 (Wednesday), 2011. This is one of the premier events on the conference calendar for the gastroenterology space, leading up to Digestive Disease Week next year. Several firms have been presenting data at this conference, including Ironwood Pharmaceuticals and its partner Forest Laboratories, along with Synergy Pharmaceuticals. We had therefore recommended that investors take note of the following poster presentations:

Ironwood Pharmaceuticals / Forest Laboratories

- Poster P765 describes a pooled analysis from the two pivotal Phase 3 IBS-C trials. This poster is authored by Dr. William D. Chey and was presented on Monday, October 31, from 10:30 a.m. – 4:30 p.m. ET.
- Poster P764 describes patients with at least moderate bloating from the two pivotal Phase 3 CC trials. This poster is authored by Dr. Anthony Lembo and was presented on Monday, October 31, from 10:30 a.m. – 4:30 p.m. ET.
- Poster P1170 provides an assessment of endpoints used in evaluating treatments for IBS-C and is based on the Phase 2b IBS-C clinical study of linaclotide. This poster is authored by Dr. Jeff Johnston and was presented on Tuesday, November 1, from 10:30 a.m. – 4:30 p.m. ET.

Synergy Pharmaceuticals

- Poster P409 discusses a preclinical study assessing the ability of GCC receptor agonists to delay the progression of colitis to colonic tumors in $Apc^{min}/+$ mice, a special genetic strain, which have a mutation in the same gene that causes familial adenomatous polyposis (FAP) and – like individuals with FAP – develop large numbers of intestinal tumors at an early age. $Apc^{min}/+$ mice have been useful for testing pharmaceuticals that may be beneficial for the treatment of FAP. In our view, this poster is exciting because it shows the potential utility of Synergy's platform in delaying or preventing development of colorectal cancer in susceptible individuals. This poster was presented on Sunday, October 30, from 10:30 a.m. – 4:30 p.m. ET. The data were generated via collaboration between Synergy Pharmaceuticals and the Institute of Hepatitis Virus Research in Doylestown, PA, and Fox Chase Cancer Center in Philadelphia, PA.
- Poster P1174 describes the Phase 2 clinical data generated with plecanatide, Synergy's Phase 3 agent to treat irritable bowel syndrome of the constipation-predominant subtype (IBS-C) and chronic constipation (CC). The poster was presented on Tuesday, November 1, from 10:30 a.m. – 4:30 p.m. ET.
- Poster P1124 describes novel guanylate cyclase C (GCC) receptor agonists for the treatment of inflammatory bowel disease. This lead author is Dr. Kunwar Shailubhai, Synergy's Chief Scientific Officer. The poster was presented on Tuesday, November 1, from 10:30 a.m. – 4:30 p.m. ET.

The ACG meeting has drawn interest from key opinion leaders, and the data presented therein confirms our view that linaclotide is a highly effective agent with a favorable risk/benefit profile, particularly when compared to existing marketed drugs. In addition, we believe that the presentations made at the ACG meeting have not only shown that plecanatide is also a highly effective drug with potentially significant safety advantages (notably the absence of diarrhea), but also indicate that Synergy possesses a much broader platform with the ability to target inflammatory bowel disease (including ulcerative colitis) and colon cancer.

Plecanatide Clinical Data

At the American College of Gastroenterology Meeting in Washington, D.C., Synergy researchers and their collaborators presented the Phase 2a data set from a clinical trial conducted with multiple doses of Synergy's lead drug candidate, plecanatide. This was a Phase 2a, randomized, double-blind, placebo-controlled, 14-day repeat, oral, dose-ranging study. There were four dose cohorts in this trial: plecanatide (0.3 mg, 1.0 mg, 3.0 mg, or 9.0 mg) and matching placebo. The study was designed with a 3:1 randomization (plecanatide: matching placebo) scheme, involving 20 subjects per dose cohort (15 plecanatide: 5 matching placebo). Subjects took one daily dose in the morning for 14 days. Blood samples for pharmacokinetic (PK) analysis were drawn prior to dosing on days 1 and 14 and at 0.5, 1.0, and 2 hours post-dosing.

This data was presented in Poster 1174 on Tuesday, November 1, 2011. The drug demonstrated an exemplary safety profile in the Phase 2a study, in which no deaths were reported. In addition, there were no serious adverse events (SAE) reported in subjects receiving plecanatide. Among individuals receiving placebo, 10% (2/20) reported adverse events, while among those receiving plecanatide, 17.2% (10/58) reported AEs. However, among the individuals who reported GI-related AEs (related or unrelated to treatment), the percentage of subjects receiving placebo was 10% (2/20), while the percentage on plecanatide was only 8.6% (5/58). The majority of adverse events (AE) were mild / moderate and transient in nature. Perhaps most important, no diarrhea was reported for any subject receiving plecanatide. One subject on placebo discontinued from the study due to diarrhea. We note that, in our opinion, this is a particularly favorable result considering that 4% of patients with chronic constipation receiving the Ironwood drug linaclotide in Phase 3 trials withdrew from those studies due to diarrhea. While the Phase 2a trial was a small study, it nevertheless provides promising hints that plecanatide is a safe and effective therapeutic agent.

Table 2: Plecanatide Phase 2a Safety Data – GI Adverse Events

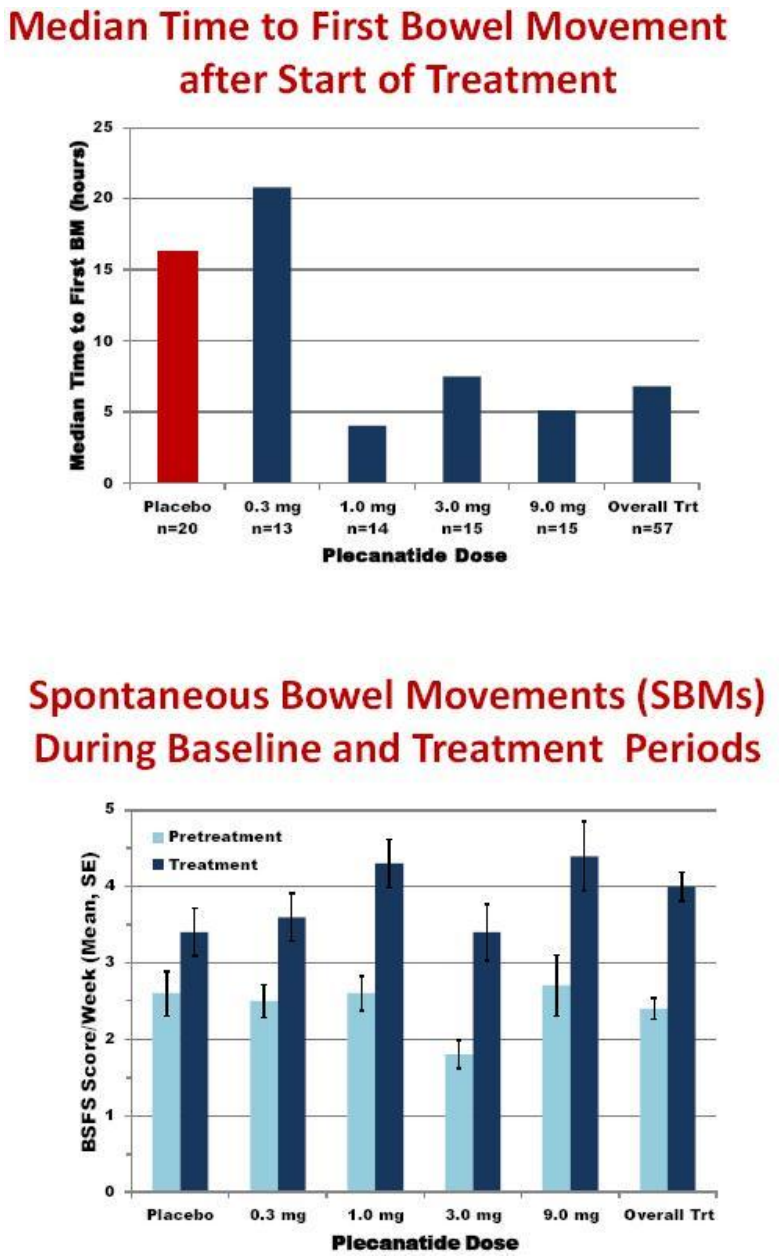
AE	Placebo	0.3 mg	1.0 mg	3.0 mg	9.0 mg
Ab Cramping	1 (5.0%)	0	0	0	0
Ab Pain	1 (5.0%)	0	0	0	0
Bloating	0	0	0	0	1 (6.7%)
Diarrhea	1 (5.0%)	0	0	0	0
Flatulence	2 (10.0%)	0	0	0	0
Nausea	0	1 (7.1%)	0	0	
Upset Stomach	0	0	0	1 (6.7%)	0

Source: Synergy Pharmaceuticals

While the primary endpoint in this trial was safety and tolerability, several secondary assessments were used to determine pharmacodynamic activity (efficacy). These were summarized by descriptive statistics for the patients who received at least one post-baseline pharmacodynamic assessment [modified intent-to-treat population (equivalent to the safety population)]. The endpoints comprised: time to first bowel movement after first daily dose; stool frequency (spontaneous bowel movements, SBMs); completeness of evacuation (complete spontaneous bowel movements, CSBMs); stool consistency (Bristol stool form scale, BSFS); straining (7-category scale); and global assessments of abdominal discomfort, constipation severity, and overall relief (6-category scales).

The results of the secondary endpoint analyses – as depicted in the charts below – indicate that plecanatide induced a reproducible, robust, and dose-dependent effect on constipation symptoms. The drug was clearly effective in the dosage range from 1.0mg/day up to 9.0mg/day, with no clear dose-dependent signal on the safety front. The 0.3mg/day dose appeared to be inactive.

Figure 1: Plecanatide Phase 2a Efficacy Data

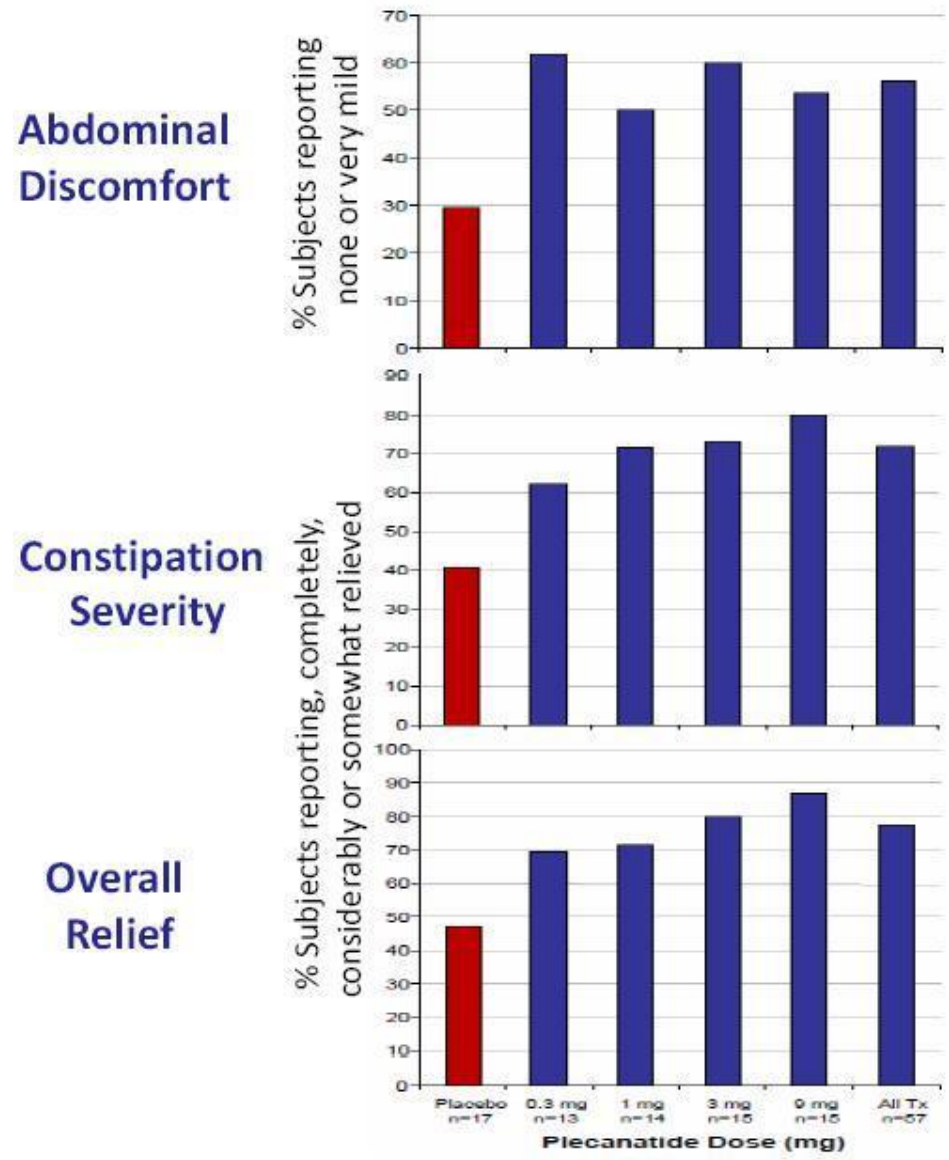


Source: Synergy Pharmaceuticals

As can be seen from the above data, the most substantial impact of plecanatide therapy over the course of this two-week trial was on the time to first bowel movement, where a clear and statistically significant decrease was observed following administration of plecanatide at all doses above the 0.3mg/day dose. However, there were sustained improvements on other efficacy endpoints as well, including the global assessment scores. Plecanatide improved stool consistency, reduced straining, and ameliorated

abdominal discomfort. In our view, the data on the global assessment scales is particularly noteworthy because it demonstrates that the drug made a substantial impact on patient wellbeing after a very short period of time. We would expect that in a three-month setting (the typical time period for pivotal studies), the impact of plecanatide therapy would be even more pronounced. The assessment scale data are shown below:

Figure 2: Plecanatide Phase 2a Global Assessment Scale Data



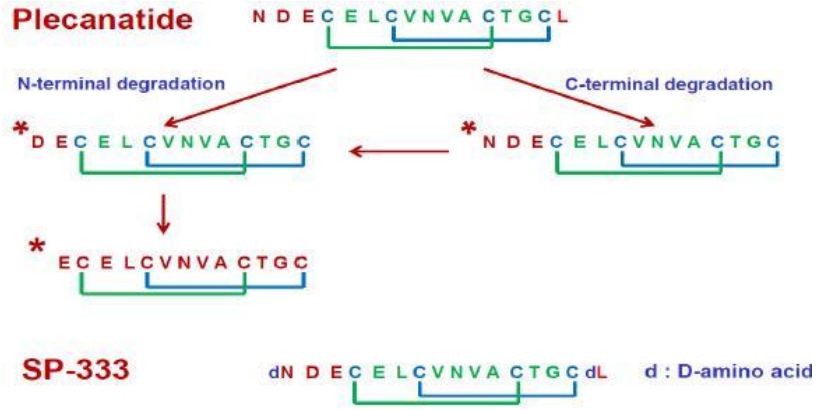
Source: Synergy Pharmaceuticals

There was no detectable absorption of plecanatide at any dose up to 9mg/day (assay sensitivity of 10ng/ml). In our view, this is a key advantage of the guanylyl cyclase C (GC-C) receptor agonist peptide class, exemplified by both plecanatide and linaclotide, in that these agents mimic the mechanism of action of the endogenous human hormone uroguanylin. We would note that the doses of linaclotide typically administered (145 µg or 290 µg) are significantly lower than those of plecanatide utilized in this Phase 2a study; however, we believe this is due to the differential binding affinity of plecanatide for the GC-C receptor.

SP-333 / Plecanatide Anti-Inflammatory Data

Synergy researchers and their collaborators also revealed preclinical activity data on their follow-on candidate to plecanatide, SP-333, at the American College of Gastroenterology (ACG) Meeting in Washington, D.C. Poster 1124 detailed the results obtained with SP-333 and provided background on this molecule's genesis as a metabolite of plecanatide. The amino acid composition of both SP-333 and plecanatide is shown below:

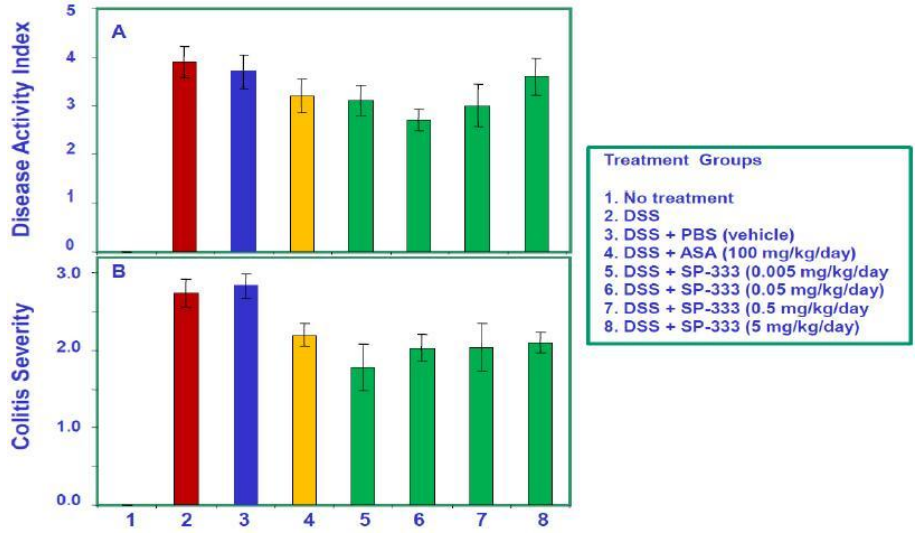
Figure 3: Plecanatide Metabolism



Source: Synergy Pharmaceuticals

As a known metabolite of plecanatide, generated via digestion of this peptide by the intestinal fluid, SP-333 forms an important component of Synergy's proprietary technology platform focusing on novel agonists of the GC-C receptor. Interestingly, these peptides have varying modes of action and appear to possess both motility-inducing and anti-inflammatory properties. Shown below is an example of SP-333 activity in a model of ulcerative colitis in mice. The model in question involves the use of dextran sulfate sodium (DSS), a well-known gastrointestinal irritant that causes weight loss and bloody diarrhea when administered in solution to animals. As indicated below, SP-333 reproducibly reduced colitis severity in this model, even at extremely low doses.

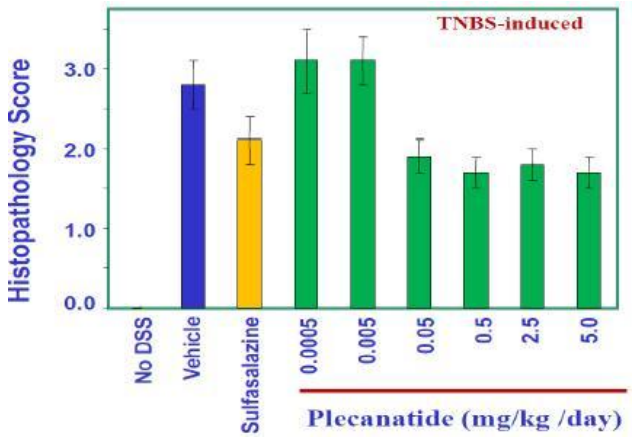
Figure 4: SP-333 Colitis Model Activity



Source: Synergy Pharmaceuticals

The poster on SP-333 included activity data generated with plecanatide, showing that this agent also has anti-inflammatory properties. Plecanatide demonstrates amelioration of colitis induced by administration of 2,4,6-trinitrobenzene-sulfonic acid (TNBS), a sensitizing allergen, in BDF1 hybrid mice. This strain is generated by crossing female C57BL/6 mice with male Dilute Brown Agouti (DBA/2) mice. The TNBS-induced colitis model is widely utilized in the testing of anti-inflammatory agents that impact the pro-inflammatory cytokine signaling network, which has been linked to the development of chronic gastrointestinal inflammation and fibrosis. The graph below shows that sustained, statistically significant reduction in colitis damage, as measured via histopathological scoring, could be achieved through the oral administration of plecanatide, even at relatively low doses. This, in our view, demonstrates the broad applicability of the drug in inflammation-related gastrointestinal disorders.

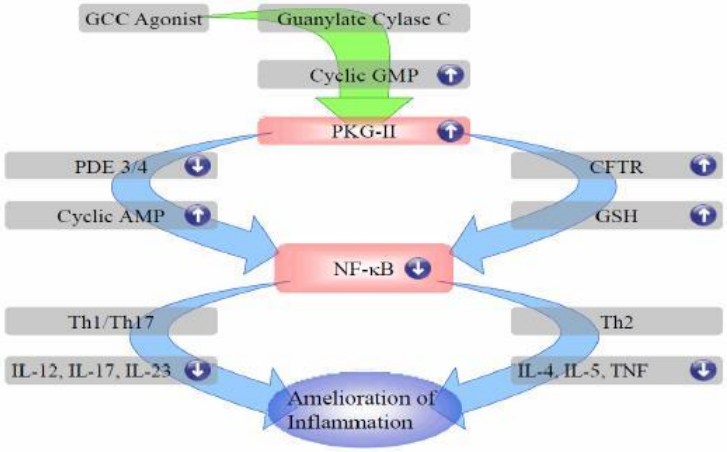
Figure 5: Plecanatide Colitis Model Activity



Source: Synergy Pharmaceuticals

The mechanism of action for plecanatide and SP-333 is hypothesized to lie in these agents' ability to regulate the levels of pro-inflammatory cytokines. This signaling pathway is delineated in the schema below. Stimulation of cyclic GMP secretion through stimulation of the GC-C receptor leads to down-modulation of the NFκB pathway, which in turns reduces levels of the pro-inflammatory Th1/Th17 cytokines IL-12, IL-17, and IL-23. The Th2 cytokines IL-4, IL-5, and tumor necrosis factor (TNF) are also decreased.

Figure 6: Plecanatide / SP-333 Anti-Inflammatory Mechanism

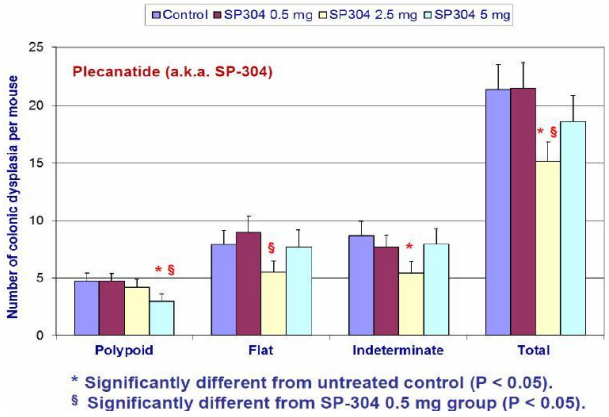


Source: Synergy Pharmaceuticals

Plecanatide Anti-Tumor Impact Unveiled

Perhaps the most groundbreaking work unveiled by Synergy researchers and their collaborators at the American College of Gastroenterology, in our view, was the striking impact of plecanatide on the multiplicity of colonic tumors in a mouse model of familial adenomatous polyposis (FAP), a genetic condition that in humans is linked to the development of colon cancer. The model in question involves a genetic strain known as the $Apc^{Min/+}$ mouse. In this model, plecanatide given orally at the dose of 2.5mg/kg reduced the multiplicity of tumors within the colon. The expression of uroguanylin, which had previously been shown to be reduced within human colon tumors, and which was reduced in the mice upon exposure to DSS, was partially restored in the intestinal tissues of these animals following treatment with plecanatide. The efficacy of plecanatide (SP-304) in the DSS-treated $Apc^{Min/+}$ mouse model is shown below:

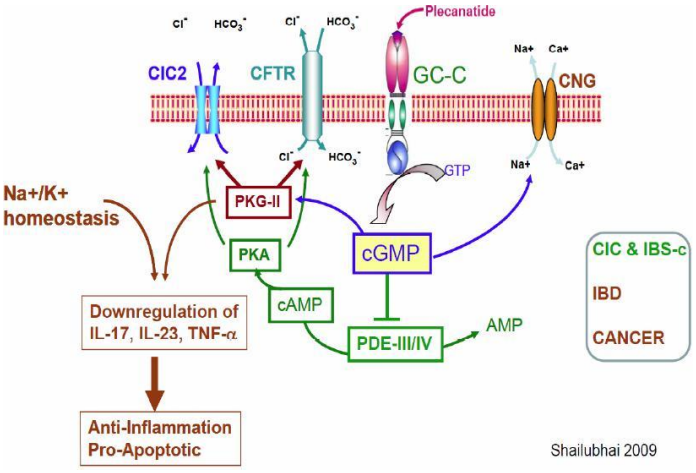
Figure 7: SP-304 Antitumor Impact in DSS-Treated $Apc^{Min/+}$ Mice



Source: Synergy Pharmaceuticals

The mechanism of action for plecanatide and related GC-C receptor agonists was postulated to involve a complex cytokine signaling network, depicted in the schema below. The investigators hypothesized that plecanatide and related peptides could selectively reduce the number of actively dividing cells within tumors as well as increase the proportion of cells undergoing apoptosis. This hypothesis was confirmed with Ki67 (a cell division marker) and caspase-3 (a protein associated with the apoptosis pathway).

Figure 8: Plecanatide Mechanism of Action

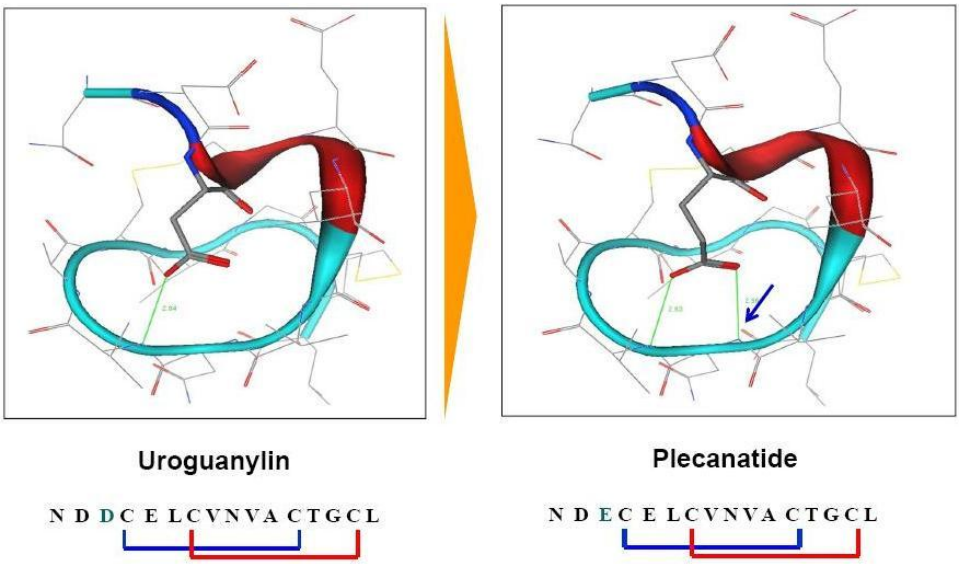


Source: Synergy Pharmaceuticals

Plecanatide vs. Linaclotide

We believe that one of the most important advantages Synergy holds is the fact that its primary asset, plecanatide, is based on an endogenous hormone with a well-established mechanism of action. As shown in the figure below, plecanatide is identical to the sequence of uroguanylin, which is produced endogenously except for a single crucial amino acid change. At the third position, an aspartic acid residue (D) is changed to glutamic acid (E). This makes the overall conformation of the plecanatide peptide substantially more stable. The formation of inter-converting isomers is also attenuated.

Figure 9: Plecanatide Conformation



Source: Synergy Pharmaceuticals

In our view, the safety profile of plecanatide has a substantial likelihood of being more favorable than that of linaclotide in the long term, since plecanatide is virtually identical to the native uroguanylin sequence, with the exception of a single amino acid residue. Linaclotide, by contrast, is homologous with uroguanylin but is actually derived from a bacterial enterotoxin (derived from *E. coli*). We must note here that we are not disputing the efficacy of linaclotide. It is clearly a highly potent and effective agent. Nevertheless, we believe the mechanism of action shared by linaclotide and plecanatide permits plecanatide to have the advantage of being a "fast follower," with the added potential advantage of an improved side effect profile and the possibility of better tolerability (unlike linaclotide, the Synergy agent is based on the native uroguanylin sequence). However, only further large-scale studies assessing the long-term impact of plecanatide therapy are likely to provide conclusive evidence of plecanatide's relative efficacy.

While we do not currently believe that the FDA would require head-to-head trials vs. linaclotide, this may not be the case once plecanatide has completed initial pivotal trials. If linaclotide were approved and considered the standard-of-care in chronic constipation or IBS-C, it is conceivable that head-to-head trials might be necessary. However, there is likely to be room for both agents in the GI disorders market, although if all other attributes are equal, we believe that, over time, plecanatide might begin to take the upper hand because of its safety advantages. The strategic advantage that Synergy might hold over Ironwood may only become apparent in the case of SP-333, which is intended to target ulcerative colitis – an area Ironwood and its partners do not intend to pursue with linaclotide. However, the UC market may prove more competitive given the presence of other potently anti-inflammatory agents both on the market and in development.

Plecanatide Market Model

We have modeled sales of plecanatide in select indications within the gastrointestinal (GI) disorders market. These are as follows:

- Chronic constipation, wherein the drug has already demonstrated positive and statistically significant therapeutic impact, and which represents a logical choice for deploying plecanatide given the mechanism that it shares with linaclotide and uroguanylin.
- Constipation-predominant irritable bowel syndrome (IBS-C), wherein the drug has not yet been tested but where we believe it would – in keeping with its activity profile in chronic constipation – show statistically significant activity in patients suffering from this condition. Again, our expectations are driven by the efficacy data that has already been demonstrated with linaclotide in this indication.

Both of the above are extremely large commercial opportunities within the healthcare space, in our view. Chronic constipation results from a lack of an adequate number of bowel movements (typically less than three per week) over an extended period of time (usually defined as greater than six months). When suffering from chronic constipation, patients often try laxatives and fiber supplements prior to physician prescribed therapy. Due to limitations in existing treatments, a significant need exists for a safe and effective chronic constipation therapy. Based on a 2004 epidemiology review, it is estimated that between 36 and 57 million people in the U.S. have chronic constipation and that approximately 33% of them see a physician for this condition. Other estimates have placed the number of chronic constipation sufferers in the U.S. as high as 80 million.

IBS is a set of chronic symptoms associated with the lower GI tract, particularly the colon, and is usually experienced as abdominal pain, bloating, and discomfort. This can include constipation with difficult or painful bowel movements or diarrhea due to excess fluid in the colon. While the etiology of IBS remains unclear, lack of colonic motility may be a significant contributory factor. As with chronic constipation, patients need an effective motility agent when other remedies, such as change in diet, reduction of stress, or consumption of laxatives or fibers, do not relieve the IBS symptoms. Plecanatide is targeted for use among IBS patients who have constipation-predominant disease. According to a 2005 article in the *Alimentary Pharmacology and Therapeutics* journal, an estimated 5.5 million adults in the U.S. suffer from IBS with constipation, and a further 28 million adults suffer from IBS with intermittent constipation.

We have modeled sales of plecanatide in the treatment of IBS-C and chronic constipation as shown overleaf (see Table 3). According to our assumptions, we believe plecanatide could reach peak worldwide annual sales of ~$6.3 billion in 2018. This peak sales figure represents ~2.2 million patients on therapy. We assume penetration would be highest among those ~10 million patients in the U.S. who currently are classified with severe constipation and who actively seek treatment for the condition. Furthermore, we also expect substantial use of the drug in severe IBS-C. We do not assume substantial penetration of the patient population segment suffering from IBS with intermittent constipation. In addition, we do not currently model sales of SP-333 in any indication at this juncture, since this agent has yet to begin human clinical testing. Although we fully expect linaclotide to reach the market prior to plecanatide, with a lead time of approximately 24 months or more, we believe the market presence of linaclotide would likely have a positive impact on receptivity for plecanatide among patients and physicians, since linaclotide would serve as a trailblazer for a completely new class of anti-constipation therapies and thus could facilitate understanding of plecanatide and its attributes. We believe the likelihood of approval of linaclotide is very high, since the NDA has now been accepted and the drug met all its endpoints in four Phase 3 trials.

Table 3: Plecanatide GI Tract Disorders Market Size Model

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
US Population	311,000,000	314,887,500	318,823,594	322,808,889	326,844,000	330,929,550	335,066,169	339,254,496	343,495,177	347,788,867	352,136,228	356,537,931	360,994,655	365,507,088	370,075,927
Patients with chronic constipation	62,200,000	62,977,500	63,764,719	64,561,778	65,368,800	66,185,910	67,013,234	67,850,899	68,699,035	69,557,773	70,427,246	71,307,586	72,198,931	73,101,418	74,015,185
Patients seeking treatment for constipation	6,220,000	6,297,750	6,376,472	6,456,178	6,536,880	6,618,591	6,701,323	6,785,090	6,869,904	6,955,777	7,042,725	7,130,759	7,219,893	7,310,142	7,401,519
Patients with constipation-predominant irritable bowel syndrome (IBS-C)	15,550,000	15,744,375	15,941,180	16,140,444	16,342,200	16,546,477	16,753,308	16,962,725	17,174,759	17,389,443	17,606,811	17,826,897	18,049,733	18,275,354	18,503,796
Patients seeking treatment for IBS-C	2,332,500	2,361,656	2,391,177	2,421,067	2,451,330	2,481,972	2,512,996	2,544,409	2,576,214	2,608,417	2,641,022	2,674,034	2,707,460	2,741,303	2,775,569
Plecanatide Penetration Rates															
Chronic constipation					2.5%	7%	11%	15%	19%	22%	25%	21%	17%	11%	9%
Constipation-predominant irritable bowel syndrome (IBS-C)					6%	11%	18%	25%	29%	31%	35%	30%	24%	18%	11%
Patients on plecanatide (SP-304)					310,502	736,318	1,189,485	1,653,866	2,052,384	2,338,880	2,685,039	2,299,670	1,877,172	1,297,550	971,449
Average cost per chronic constipation patient ($)					180	495	916	1,145	1,259	1,322	1,362	1,403	1,445	1,488	1,533
Average cost per IBS-C patient ($)					350	788	1,378	1,516	1,592	1,639	1,689	1,739	1,792	1,845	1,901
US plecanatide (SP-304) sales ($ MM)					**81**	**444**	**1,298**	**2,129**	**2,833**	**3,349**	**3,959**	**3,496**	**2,937**	**2,107**	**1,601**
European Population	395,000,000	399,937,500	404,936,719	409,998,428	415,123,408	420,312,451	425,566,356	430,885,936	436,272,010	441,725,410	447,246,978	452,837,565	458,498,035	464,229,260	470,032,126
Patients with chronic constipation	47,400,000	47,992,500	48,592,406	49,199,811	49,814,809	50,437,494	51,067,963	51,706,312	52,352,641	53,007,049	53,669,637	54,340,508	55,019,764	55,707,511	56,403,855
Patients seeking treatment for constipation	2,370,000	2,399,625	2,429,620	2,459,991	2,490,740	2,521,875	2,553,398	2,585,316	2,617,632	2,650,352	2,683,482	2,717,025	2,750,988	2,785,376	2,820,193
Patients with constipation-predominant irritable bowel syndrome (IBS-C)	19,750,000	19,996,875	20,246,836	20,499,921	20,756,170	21,015,623	21,278,318	21,544,297	21,813,600	22,086,271	22,362,349	22,641,878	22,924,902	23,211,463	23,501,606
Patients seeking treatment for IBS-C	1,975,000	1,999,688	2,024,684	2,049,992	2,075,617	2,101,562	2,127,832	2,154,430	2,181,360	2,208,627	2,236,235	2,264,188	2,292,490	2,321,146	2,350,161
Plecanatide Penetration Rates															
Chronic constipation						0.5%	2%	6%	9%	11%	13%	14%	15%	16%	14%
Constipation-predominant irritable bowel syndrome (IBS-C)						2%	5%	8%	12%	15%	18%	21%	23%	25%	22%
Patients on plecanatide (SP-304)						54,641	157,460	327,473	497,350	622,833	751,375	855,863	939,921	1,025,947	911,862
Average cost per chronic constipation patient ($)						120	288	432	475	499	514	529	545	562	578
Average cost per IBS-C patient ($)						230	403	543	571	588	605	623	642	661	681
European plecanatide (SP-304) sales ($ MM)						**11**	**58**	**161**	**261**	**340**	**423**	**498**	**564**	**634**	**581**
Total plecanatide (SP-304) sales ($ MM)					**81**	**456**	**1,356**	**2,290**	**3,094**	**3,689**	**4,382**	**3,993**	**3,501**	**2,741**	**2,182**

Source: Company Reports and Morgan Joseph TriArtisan estimates

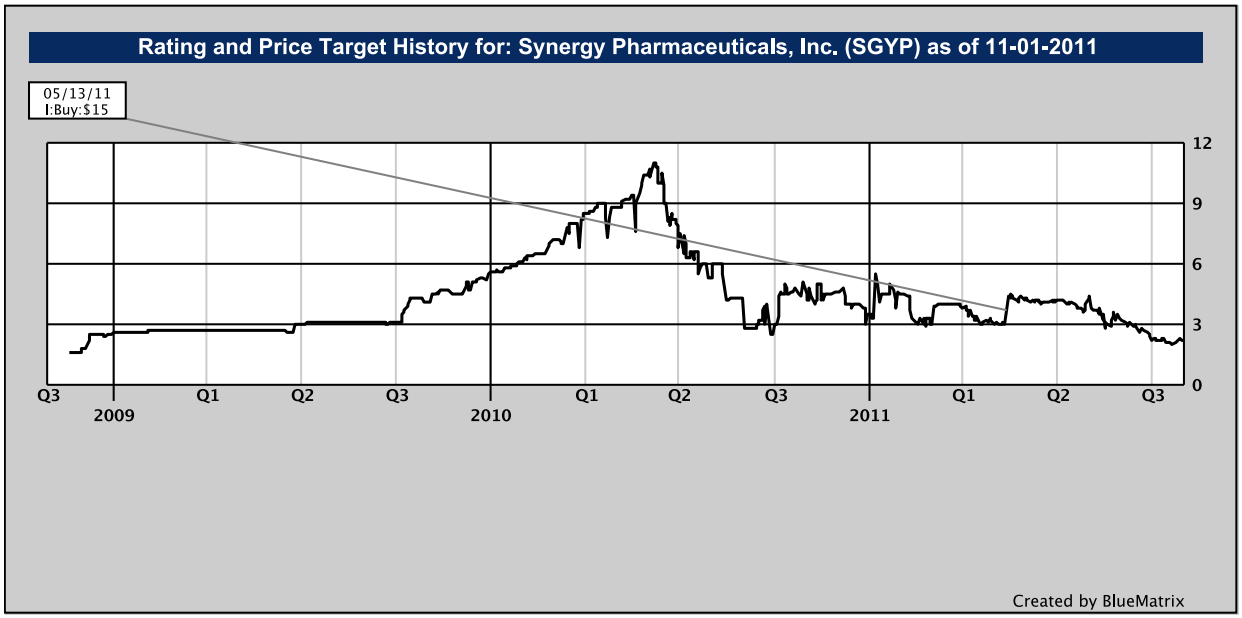
Table 4: Synergy Pharmaceuticals, Inc. (SGYP.PK) – Historical Income Statements, Financial Projections

FY end December 31
$ in thousands, except per share data

			2011E					
	2009A	2010A	1QA	2QA	3QE	4QE	2011E	2012E
Revenue								
Total revenue	-	-	-	-	-	-	-	-
Expenses								
Cost of product and service revenue	-	-	-	-	-	-	-	-
Research & development	4,257	9,559	1,478	2,354	1,500	3,000	8,333	30,000
Selling and marketing	-	-	-	-	-	-	-	-
General and administrative	3,943	6,563	1,898	1,524	1,300	2,500	7,222	17,000
Total expenses	8,200	16,121	3,376	3,879	2,800	5,500	15,555	47,000
Gain (loss) from operations	(8,200)	(16,121)	(3,376)	(3,879)	(2,800)	(5,500)	(15,555)	(47,000)
Other income/expense								
Interest income/expense	75	109	12	20	-	-	32	-
Change in fair value of derivative instruments-warrants	-	297	(339)	(698)	-	-	(1,036)	-
Other income/expense	-	494	-	-	-	-	-	-
Total investment income and other	75	900	(327)	(678)	-	-	(1,004)	-
Loss before provision for income taxes	(8,125)	(15,221)	(3,702)	(4,557)	(2,800)	(5,500)	(16,559)	(47,000)
Deferred income tax benefit	-	-	-	-	-	-	-	-
Net loss/income	(8,125)	(15,221)	(3,702)	(4,557)	(2,800)	(5,500)	(16,559)	(47,000)
Net loss per share (basic)	(0.11)	(0.17)	(0.04)	(0.05)	(0.03)	(0.06)	(0.18)	(0.42)
Net loss per share (diluted)	(0.11)	(0.17)	(0.04)	(0.05)	(0.03)	(0.06)	(0.18)	(0.42)
Weighted average number of shares outstanding (basic)	73,281	89,751	92,335	93,286	93,237	95,162	93,505	111,668
Weighted average number of shares outstanding (diluted)	73,281	89,751	92,335	93,286	93,237	95,162	93,505	111,668

Source: Company Reports and Morgan Joseph TriArtisan estimates

Required Disclosures



Price Target

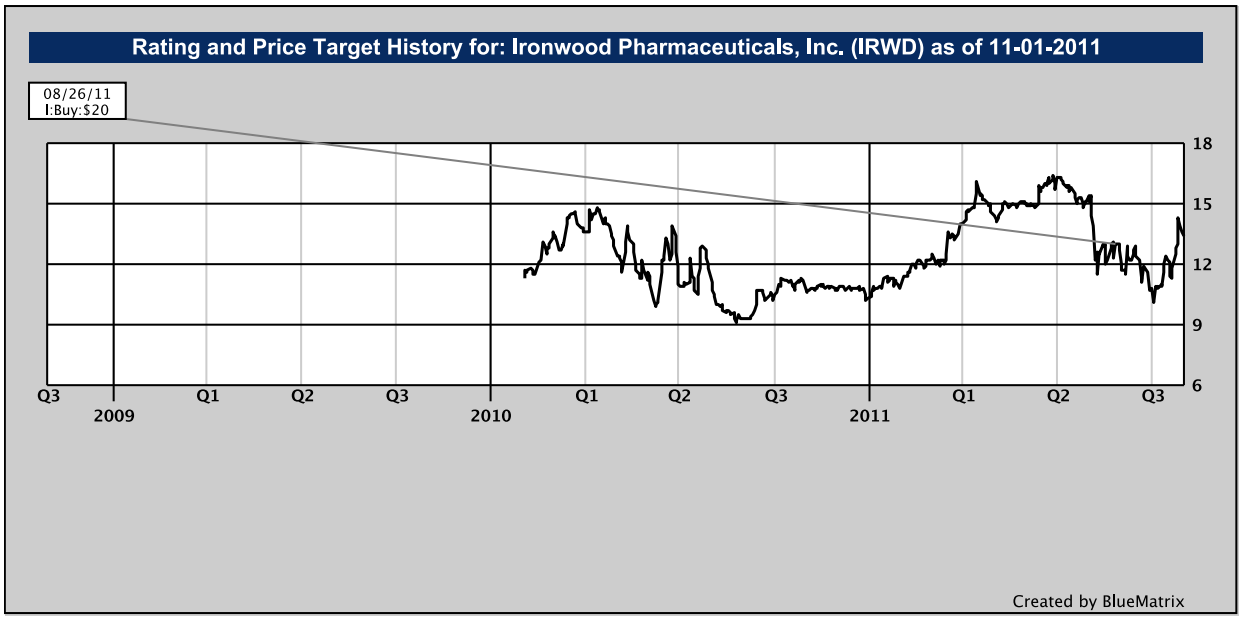
Our price target is $15.00.

Valuation Methodology

We use a risk-adjusted Net Present Value (rNPV) methodology to calculate the price target. Intrinsic value for the company's drug candidates is derived based on the size of the market opportunity and probability of approval, among other factors, using a discounted cash flow approach. Intrinsic values are then added to derive our $15 price target.

Risk Factors

Issues that could prevent the achievement of our price objective include, but are not limited to, clinical, regulatory, competitive, reimbursement and financial risks. Drugs in clinical development may not advance due to inadequate safety, efficacy, or tolerability. Regulatory agencies may decline to approve regulatory submissions in a timely manner, or may not approve a drug candidate at all. The firm may require substantial funding to advance the clinical progress of its candidates, which could be dilutive to current shareholders. We expect competition for the company's drugs from several public and private companies developing pharmaceuticals. Sales of the firm's drugs could depend upon reimbursement from private, as well as public, reimbursement agencies.



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Rating	Percent	Investment Banking Services/Past 12 Mos. Percent
BUY [B]	68.80	11.63
HOLD [H]	31.20	5.13
SELL [S]	0.00	0.00

Meaning of Ratings

A) A Buy rating is assigned when we do not believe the stock price adequately reflects a company's prospects over 12-18 months.
B) A Hold rating is assigned when we believe the stock price adequately reflects a company's prospects over 12-18 months.
C) A Sell rating is assigned when we believe the stock price more than adequately reflects a company's prospects over 12-18 months.

Other Disclosures

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