INITIATION **REPORT**

Synergy Pharmaceuticals (SGYP/NASDAQ)

March 29, 2012

BREAN MURRAY CARRET & CO.

Jonathan Aschoff, 212-702-6652 Jonathan.Aschoff@bmur.com

Second To Start, But Not To Finish Second – Initiating Coverage of Synergy Pharmaceuticals with A Buy And $13 Target Price

Initiating Coverage at Buy
Target Price: $13

Investment Summary

- We are initiating coverage of Synergy Pharmaceuticals, Inc. with a Buy rating and 12-month target price of $13. Synergy is focused on developing drugs for gastrointestinal disease, and its lead drug plecanatide, a guanylate cyclase receptor agonist, is in Phase 2/3 for chronic idiopathic constipation (CIC) and a Phase 2b trial in IBS-C should start in 3Q12. A key investment catalyst is the 4Q12 release of Phase 2/3 plecanatide results in CIC, a significant de-risking event. Another important positive catalyst is the 2Q12 PDUFA date for competing drug linaclotide, which we expect to result in an approval that formally validates the mechanism, driving Synergy shares higher.

- Close peer drug linaclotide has completed extensive clinical testing in CIC and IBS-C. If approved, we expect Ironwood and partners Forest and Almirall to demonstrate the significant, unmet need that exists in these indications. Our plecanatide optimism draws from the positive Phase 2a results, the clear lack of an effective therapy in CIC or IBS-C, and the well-validated mechanism of action. (FRX, $34.62, Not Rated) (IRWD, $13.23, Not Rated)

- Should Synergy's Phase 2/3 succeed, we note the company's large discount to Ironwood (about 15% of the valuation), but we believe that even before data are available, the mere approval of linaclotide in June should increase interest in Synergy and its differentiated drug. It is important to note that Forest and Almirall both signed their linaclotide agreements prior to the release of any pivotal results in CIC or IBS-C. Given that a drug like plecanatide would be best marketed broadly to general practitioners, we would not expect Synergy to go the distance itself, and view any clear, differentiating success in the Phase 2/3 trial as likely sufficient to attract the attention of an acquirer. As a company with fewer than a dozen employees, a possible acquisition to us sounds far more likely than a commercialization partnership.

- We believe that being three years behind linaclotide is advantageous because the constipation market must be developed for this new class of drugs, and why not leave that heavy lifting up to linaclotide. More importantly, we believe that the diarrhea differential between the two drugs will persist after pivotal plecanatide trials, thus allowing Synergy to benefit out of the gate from a reservoir of constipated patients motivated enough to seek linaclotide, but unable to tolerate its chief diarrhea side effect. Being second to the market with a clear competitive advantage is no disadvantage at all, in our view.

- Synergy is also in late preclinical stage with SP-333, its next-generation GC-C receptor agonist that has been further optimized to have a longer half-life within the gut due to its resistance to proteolysis. We anticipate an IND filing in 3Q12, initiation of a Phase 1 trial safety trial in healthy volunteers by YE12, and further development in ulcerative colitis.

Price	$3.99
52-Week High/Low	$5.24 - 1.86
Shares Outstanding (000)	50,274
Market Cap. (000)	$200,593
Average Daily Volume	46,921

EPS	**FY11A**	**FY12E**	**FY13E**
Mar	$(0.08)	$(0.16)	-
Jun	$(0.10)	$(0.16)	-
Sep	$(0.01)	$(0.16)	-
Dec	$(0.11)	$(0.16)	-
FY	**$(0.30)**	**$(0.64)**	**$(0.71)**
Prior	-	-	-
Consensus	-	$(0.75)	NA
P/E	NM	NM	NM
FY Rev.	-	-	-

Source: BigCharts.com

Investment summary

We are initiating coverage of Synergy Pharmaceuticals, Inc. with a Buy rating and 12-month target price of $13. Our target price is supported by a DCF analysis that utilizes a 40% discount rate and a 5x multiple of the projected 2019 EBITDA as the terminal value. New York-based Synergy is focused on developing drugs for gastrointestinal disease. Plecanatide, a guanylate cyclase (GC-C) receptor agonist and the company's lead compound, is currently in a Phase 2/3 trial for chronic idiopathic constipation (CIC). In 3Q12, we also anticipate Synergy to initiate a randomized, placebo-controlled Phase 2b trial in constipation-predominant irritable bowel syndrome (IBS-C) with plecanatide, with the potential to release results a year later. We are projecting approval of plecanatide in the U.S. in 2015, in the E.U. in 2016, and in Asia starting in 2017. Our financial model incorporates only revenue from plecanatide in CIC and IBS-C.

The key investment catalyst for Synergy is the anticipated 4Q12 release of Phase 2/3 plecanatide results from 880 CIC patients; trial enrollment should complete in 2Q12. Success in this trial would constitute a significant de-risking event for the company. Given that a drug like plecanatide would be best marketed broadly to general practitioners, we would not expect Synergy to go the distance itself, and view any clear, differentiating success in even the ongoing Phase 2/3 trial as likely sufficient to attract the attention of an acquirer. As a company with fewer than a dozen employees, an acquisition to us sounds far more likely than a commercialization partnership. For valuation purposes, however, we borrow from Ironwood's path and model Synergy as being similarly partnered in the future, participating in the U.S. commercialization, and receiving ex-U.S. royalties.

A close peer drug, linaclotide has completed extensive clinical testing in CIC and IBS-C, and is awaiting a June 9, 2012, PDUFA date. If approved, we expect Ironwood and partners Forest Laboratories and Almirall to demonstrate the significant, unmet need that still exists in these indications. Our plecanatide optimism draws from the positive Phase 2a results released at the 4Q11 ACG conference, the clear lack of an effective therapy in CIC or IBS-C, and the well-validated mechanism of action.

Should Synergy's Phase 2/3 succeed, we must point out the company's large discount to Ironwood (about 15% of the valuation), but we believe that even before data are available, the mere approval of linaclotide in June should increase interest in Synergy and its differentiated drug. To give a sense of the economics already driven by linaclotide, its three partners have already paid a total of $207 million in upfront fees and milestone payments and purchased $40 million worth of Ironwood shares. Remaining milestones total to $250 million more, and ex-U.S. royalties are conservatively estimated to be in the 15-25% range (Ironwood and Forest to jointly commercialize and share profits in the U.S.). It is important to note that Forest and Almirall both signed their linaclotide agreements prior to the release of any pivotal results in CIC or IBS-C.

We believe that being about three years behind linaclotide is advantageous because the constipation market needs to be developed for this new class of compounds, and why not leave that heavy lifting up to Ironwood and its partners. More importantly, we believe that the diarrhea differential between the two closely related drugs will persist after pivotal plecanatide trials have been conducted, thereby allowing Synergy to benefit out of the gate from a reservoir of severely constipated patients motivated enough to seek linaclotide, but unable to tolerate its chief diarrhea side effect. Being second to the market with a clear competitive advantage is no disadvantage at all, in our view.

Synergy is also in late preclinical stage with SP-333, its second drug candidate and next-generation GC-C receptor agonist that has been further optimized to have a longer half-life within the gut due to its resistance to proteolysis. We anticipate an IND filing in 3Q12, initiation of a Phase 1 trial safety trial in healthy volunteers by YE12 that carefully assesses any systemic absorption, and ultimately further development in ulcerative colitis.

Plecanatide is protected by composition of matter patents that expire in 2022 and 2023 in the U.S. and in Europe. These issued patents not only cover composition, but also describe a method-of-use, covering selective application of GC-C receptor agonists to treat gastrointestinal disorders, thereby providing even stronger coverage. The issued composition of matter patent covering SP-333 for ulcerative colitis and Crohn's disease expires in 2028. There is also the potential for added patent protection through patent term extension and Hatch-Waxman term extensions.

Exhibit 1: Product Pipeline

Source: Company documents

Exhibit 2: Catalyst Calendar

Timing	Compound	Event	Indication
2Q12	plecanatide	Complete enrollment in Phase 2/3 trial	CIC
3Q12	plecanatide	Initiate Phase 2b trial	IBS-C
3Q12	SP-333	File IND	Ulcerative colitis
4Q12	plecanatide	Top-line results from Phase 2/3 trial	CIC
3Q13	plecanatide	Top-line results from Phase 2b trial	IBS-C

Source: Company documents and Brean Murray Carret & Co estimates

Valuation

We derive our target price of $13 through a DCF analysis, assuming a 40% discount rate that is applied to all cash flows and the terminal value, which is based on a 5x multiple of the projected 2019 EBITDA. We view our valuation as conservative in that our revenue build assumes that only 20% of the potential patients will seek any kind of medication for either CIC or IBS-C that goes beyond laxatives and stool softeners. With such a large market potential, and given our view that plecanatide is a differentiated product, we are highly optimistic that there will be a large demand for the drug. We forecast a market penetration for plecanatide that is less than one fourth of our estimated population seeking advanced treatments like plecanatide's primary competition, with ex-U.S. markets peaking at 18% adoption. Our valuation assumes approval in the U.S. in 2015, approval in the E.U. in 2016, and 2017 approvals in Asian markets. Additionally, our valuation does not include any collaborative revenue – a potential source of non-dilutive funding that could easily amount to the company's current market value – given the linaclotide experience. We also believe we are being conservative by completely ignoring the pipeline value behind plecanatide, although we expect to be shown otherwise in due time.

Constipation Market Opportunity

Looking at both CIC and IBS-C, we estimate that about 100 million patients exist, a sizeable minority (about 20%) that suffer from severe enough forms to aggressively seek treatment. Chronic idiopathic constipation (CIC) is a widespread and often debilitating disorder. Constipated patients can be divided into three distinct groups: (1) patients with primary constipation (without underlying diseases and not caused by the use of medication); (2) patients constipated as a result of their regular use of opioids; and (3) patients with severe constipation due to neurodegenerative disorders like multiple sclerosis and Parkinson's disease. CIC is characterized by infrequent and difficult passage of stool over a prolonged period. Other symptoms include infrequent bowel movements, bloating, straining, abdominal discomfort, pain, incomplete evacuation, and unsuccessful attempts at evacuation. CIC is defined by the widely accepted Rome III criteria based on the type and duration of symptoms. CIC is seen as a persistent disease with approximately 70% of patients having more than three symptomatic episodes per week. According to an article from 2007 in *Alimentary Pharmacology and Therapeutics*, it is believed that 40% of patients with CIC are not satisfied with their current medication. We have modeled an approximate average rate of 11% of CIC in North American, European, and Asian populations, and our fraction modeled as attainable by plecanatide peaks out at almost 20% prior to expiry of its patents in 2022 and 2023. We also believe that we are being extremely conservative with a daily pill price of about $5 in the U.S., less than $3.33 in the E.U., and about $2.50 in Asia.

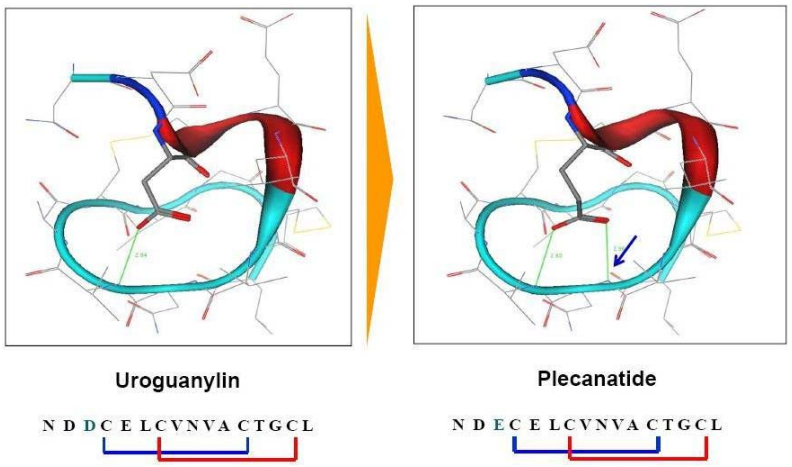
IBS-C is another chronic gastrointestinal disorder that we have modeled as affecting an average of 5% of the North American, European, and Asian populations, but these patients also have more severe pain associated with their condition compared to CIC patients, so the interest in trying new therapies is high. Thus far, in IBS-C in the U.S., there is only Amitiza, but it is marginally effective for constipation, ineffective for pain, carries with it about a 30% rate of nausea, and is a twice daily oral, which likely explains its 2011 sales growth rate of about 3% over 2010. Perhaps a better indicator of what an effective drug can do is where Zelnorm was headed in terms of revenue prior to its withdrawal from the U.S. market in 2007 due to cardiovascular toxicity. Zelnorm sales accounted for $560 million in 2006 for Novartis, with most of that revenue coming from the U.S. market, a clear sign to us that a safe and effective drug will sell. Most drugs used for IBS-C are targeting the constipation more than the pain, and there is clearly a need for drugs that can usefully address both symptoms. Drugs like stool softeners and laxatives are used for IBS-C, but hardly address the pain. Synergy has the benefit of linaclotide, however, not only to develop a market, but also to create and feed a pool of patients that respond to the mechanism, but for whom linaclotide's diarrhea is too severe.

Plecanatide Background

Uroguanylin (UG) is an endogenous natriuretic peptide hormone that is secreted into the gastrointestinal lumen, where it binds to the GC-C receptor and stimulates intracellular production of cyclic guanosine monophosphate (cGMP). Increased cGMP production activates cystic fibrosis transmembrane conductance regulator (CFTR), thereby enhancing the transepithelial efflux of sodium, potassium, chloride, as well as the influx of calcium. Via regulation of this ion transportation – fluid transport in the gastrointestinal tract – increases and thus, most importantly, bowel movements increase in frequency as a result. Plecanatide (formerly referred to as SP-304 and earlier as guanilib) is a synthetic analog of uroguanylin, and belongs to a novel class of non-systemically absorbed drugs designed to treat CIC, IBS-C, and other gastrointestinal diseases. Plecanatide is an oral drug that, like uroguanylin, activates the GC-C receptor that is expressed on the epithelial cells lining the gastrointestinal mucosa, ultimately resulting in the facilitation of bowel movement. Oral plecanatide has also been shown in animal models to promote intestinal secretion and reduce gastrointestinal inflammation.

Given the high homology and similarity in mechanism of action among the hormone uroguanylin (N-D-**D**-C-E-L-C-V-N-V-A-C-T-G-C-L), and drug candidates plecanatide (N-D-**E**-C-E-L-C-V-N-V-A-C-T-G-C-L) and linaclotide (**C**-C-E-**Y**-C-**C**-N-**P**-A-C-T-G-C-**Y**; forms 3 di-sulfide bridges versus the two formed in plecanatide and uroguanylin) – and the proven activity of the hormone and the competing drug to induce bowel movements – we believe that plecanatide has a strong chance of being a meaningful player in the potentially multibillion constipation market. The bold amino acids above emphasize the single, conservative difference between plecanatide and native uroguanylin, as well as the more striking difference between linaclotide and the other two, which explains linaclotide's potency, but also its propensity to cause severe diarrhea. Most importantly, plecanatide's likely ability to differentiate itself from linaclotide through a low incidence of diarrhea should make the drug a valuable asset in the fight against constipation. We believe that the potency of linaclotide is easy to explain due to its bacterial derivation – and therefore structural similarity to enterotoxin ST – which is a superagonist with wide pH optima for binding the GC-C receptor. A swift exit from the host is all that bacteria are trying to achieve with enterotoxin ST, but clearly severe diarrhea, as with a case of traveler's diarrhea, results as well. We believe that plecanatide is very safe, and provided the drug demonstrates enough efficacy in Phase 2/3, substantial value creation should occur.

Exhibit 3: Similarity of Plecanatide to Uroguanylin



Source: Company documents

Competitive Landscape for CIC and IBS-C Therapies

The constipation market is filled with numerous products such as fiber, laxatives, probiotic agents, and antibiotics, but for patients that are severely constipated and therefore for whom these products do not work, the primary plecanatide competition consists of chloride C-2 channel activators, 5-HT4 receptor agonists, and the mechanistically alike linaclotide. Takeda and Sucampo Pharmaceuticals have commercialized Amitiza (lubiprostone; chloride C-2 channel activator), Shire Pharmaceuticals markets Resolor (prucalopride; a selective, high-affinity selective 5-HT4 receptor agonist), and Forest Laboratories and Ironwood intend to market plecanatide's closest peer drug, linaclotide, in 2H12.

Amitiza

Amitiza's efficacy is not exactly a barrier to entry in the field, with only a 12-13% rate of overall symptom improvement (double that of its placebo arm), yet it causes nausea in about 30% of patients. This is the only FDA approved drug for IBS-C, and it is also approved for CIC. In August 2011, Sucampo submitted an MAA in the U.K. for Amitiza for CIC, which should be approved there in 2012. Net sales of Amitiza increased 2.9%, to $226 million, in 2011, from $220 million in 2010.

Resolor

After an extensive Phase 3 program involving three trials enrolling more than 3,000 patients, the once daily oral drug Resolor was approved in several European countries for women with CIC, and its European patent expires in November 2015. Resolor's efficacy is impressive, with bowel function normalized in 25-30% of patients, and the most frequent side effects being transient headache, diarrhea, and nausea. In January 2012, Shire announced that it acquired the rights to develop and market Resolor in the U.S., in an agreement with Janssen Pharmaceutica. Resolor is Phase 3-ready in the U.S., and definitive plans will be implemented following discussions with the FDA. As of YE11, Resolor was available in 6 E.U. countries ($6.1 million in sales), with launches in additional European countries planned this year. The mechanistically related drug Zelnorm was withdrawn by the FDA in 2007, mainly due to its increased risk of heart attack and stroke, and was rejected outright in the E.U.

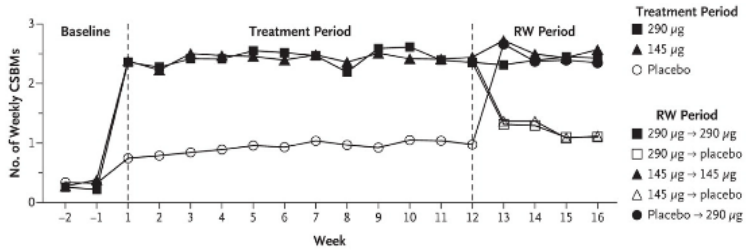
Linaclotide – the Closest Competitor

Ironwood submitted its linaclotide (GC-C receptor agonist) NDA in October 2011 in the U.S. for IBS-C and CIC after about 6,000 patients were examined in 6 Phase 3 trials, and we fully expect the product to launch in 2H12 after a positive June 9, 2012, PDUFA date outcome for both indications. Almirall submitted an MAA in the E.U. in September 2011 for linaclotide for IBS-C, which should be approved in 2H12. GC-C agonists are likely to offer potent efficacy, but with a more favorable safety profile, given that they are not systemically absorbed. Although linaclotide is a potent and close peer of plecanatide, its high incidence of diarrhea is likely to offer plecanatide a clear window of opportunity.

Linaclotide in CIC

Linaclotide was successful in two Phase 3 CIC trials (3 arms per trial, total enrollment of 1,276, total randomization of 1,272 patients), where responder rate was used as the primary endpoint (percentage of patients having at least 3 CSBMs/week who also showed an increase of at least 1 CSBM/week from baseline for at least 9 weeks of the 12-week treatment period (similarly rigorous to the plecanatide Phase 2/3 primary endpoint). Linaclotide was tested at 145ug and 290ug, and the responder rate for the lower dose was 21.2% and 16%, for the higher dose was 19.4% and 21.3%, and for placebo was 3.3% and 6% (for trials 303 and 01, respectively; p<0.01 for any linaclotide group versus placebo), given the rigor of the endpoint. Mean weekly SBM and CSBM frequency was also increased by each dose of linaclotide (only disclosed as pooled data for each dose), notably up to 5.1 and 5.6 SBMs/week and to 2.2 and 2.9 CSBMs/week with linaclotide, for the 145ug and 290ug doses, respectively, versus 3 and 3.2 SBMs/week, and 0.9 and 0.9 CSBMs/week in each trial's placebo group.

Exhibit 4: Mean Number of Weekly CSBMs in Trial 303



Source: N Engl J Med 2011; 365:527-536, August 11, 2011

Linaclotide also achieved all pre-specified secondary endpoints in both Phase 3 trials, including stool consistency, straining, and abdominal symptoms (bloating and discomfort). Other specifics measured were physical discomfort, satisfaction, psychosocial discomfort, worries/concerns, and overall PAC-QOL.

The incidence of adverse events was similar among all study groups, with the exception of diarrhea, which importantly for Synergy, led to an average discontinuation of treatment in 4.2% of patients for the combined linaclotide-dose groups. Discontinuation of treatment due to adverse events was higher for linaclotide-treated patients (7.9% for 145µg and 7.3% for 290µg), versus 4.2% for placebo, mainly due to the increased diarrhea rate on drug. More specifically, 4.7% and 3.8% of linaclotide patients (145µg and 290µg, respectively), versus 0.5% of placebo patients, discontinued due to diarrhea, a difference of 4.2%.

Exhibit 5: Adverse Events During Treatment – Combined Safety Populations for Trials 303 and 01

Table 3. Adverse Events during Treatment (Combined Safety Populations in Trials 303 and 01).*

Adverse Event	Placebo (N=424)	Linaclotide	
		145-μg Dose (N=430)	290-μg Dose (N=422)
		no. of patients (%)	
Any event	221 (52.1)	260 (60.5)	235 (55.7)
Diarrhea	20 (4.7)	69 (16.0)	60 (14.2)
Flatulence	22 (5.2)	24 (5.6)	21 (5.0)
Abdominal pain	13 (3.1)	17 (4.0)	20 (4.7)
Abdominal distention	10 (2.4)	15 (3.5)	15 (3.6)
Upper respiratory infection	17 (4.0)	22 (5.1)	13 (3.1)
Nasopharyngitis	13 (3.1)	9 (2.1)	17 (4.0)
Sinusitis	8 (1.9)	13 (3.0)	11 (2.6)
Upper abdominal pain	7 (1.7)	13 (3.0)	5 (1.2)

* Data are shown for adverse events that were reported in at least 3% of patients in either linaclotide group and for events that were reported in a higher proportion of patients in either linaclotide group than in the placebo group.

Source: N Engl J Med 2011; 365:527-536, August 11, 2011

Linaclotide in IBS-C (Trial LIN-MD-31)

Linaclotide achieved all 4 primary endpoints and all pre-specified secondary endpoints (p≤0.0014 for all secondary endpoints) in its first 12-week Phase 3 trial (two composite responder endpoints for abdominal pain and CSBMs, and individual responder endpoints for abdominal pain and CSBMs) in patients meeting modified Rome II criteria for IBS-C. Secondary endpoints included abdominal pain/discomfort, bloating, and bowel symptoms, and safety was consistent with that observed in earlier trials (i.e., diarrhea again being linaclotide's most distinguishing and common adverse event). In the 803-patient LIN-MD-31 trial, only the 290ug dose was tested, and the complete responder endpoint #1 (abdominal pain and CSBM) favored drug (12.1% versus 5.1%; p=0.0004), as did the CSBM responder endpoint (19.5% versus 6.3%; p<0.0001), the abdominal pain responder endpoint (34.3% versus 27.1%; p=0.0262), and the composite responder endpoint #2 (also abdominal pain and CSBM) 33.6% versus 21%; (p<0.0001). All secondary endpoints measured in the LIN-MD 31 trial demonstrated statistically significant improvements for linaclotide, such as the abdominal pain component of composite responder #2 (50.1% versus 37.5%; p=0.0003), and the CSBM component of same (48.6% versus 29.6%; p<0.0001). Diarrhea was 19% versus 4%, flatulence was 5% versus 2%, and abdominal pain was 5% versus 3%, for linaclotide and placebo, respectively. More importantly, overall discontinuation rates due to adverse events were 8% on drug versus 3% on placebo, and most likely due to diarrhea.

Phase 3 IBS-C Trial MCP-103-302

The primary and secondary analysis period for the 805-patient, MCP-103-302 trial was designed identically to the first IBS-C trial, and it too achieved all 4 of its primary endpoints (p<0.0001). The complete responder endpoint #1 (abdominal pain and CSBM) favored drug (12.7% versus 3%), as did the CSBM responder endpoint (18% versus 5%), the abdominal pain responder endpoint (38.9% versus 19.6%), and the composite responder endpoint #2 (33.7% versus 13.9%). All secondary endpoints were also met (p<0.001; abdominal pain/discomfort, bloating, percent pain-free days, CSBM frequency, SBM frequency, stool consistency, straining). Key secondary endpoints were positive, including the abdominal pain component of composite responder #2 (48.9% versus 34.5%; p=0.0001), and the CSBM component of same (47.6% versus 22.6%; p<0.0001). Diarrhea was 19.7% versus 2.5% for linaclotide and placebo, respectively. Most importantly for Synergy, overall discontinuation rates due to adverse events were 10.2% on linaclotide versus 2.5% on placebo, due to the 4.5% diarrhea dropout rate on drug versus 0.2% for placebo, underscoring again the opportunity for Synergy's plecanatide.

There are also other CIC and IBS-C programs underway at ARYx Therapeutics (naronapride; 5-HT4 receptor agonist; in Phase 2 in CIC and IBS-C), Theravance (TD-5108 and TD-8954; 5-HT4 receptor agonists; Phase 1 and 2 in GI motility, but seem to be progressing slowly), and Albireo (elobixibat; IBAT inhibitor; Phase 3 in CIC to start in 2012, Phase 2 to start in IBS-C). (THRX, $19.91, Buy)

Exhibit 6: Competitive Landscape

Drug	Mechanism	Efficacy	Safety	Trial % discontinuation
SP-304 (plecanatide)	GC-C receptor agonist	>50% of patients had an SBM within 5 hours. Achieve 4 CSBM/week	Bloating, nausea (mild)	No Phase 2a discontinuations in the drug arm
Resolor (prucalopride)	5-HT4 receptor agonist	30% of patients had normalized bowel function	Diarrhea, headache, nausea (mild)	17.5% overall, and 10.1% (due to AE's)
ASP0456 (linaclotide)	GC-C receptor agonist	21.3% improvement in bowel function	Diarrhea (severe)	7.9% overall, and 4.7% (due to diarrhea)
Amitiza (lubiprostone)	C-2 chloride channel activator	13% symptom improvement	Nausea (30% of pts)	12.9% overall, and 9.7% (due to AE's)

Source: Company documents, Brean Murray, Carret & Co. research

Valuation Disconnect Between Synergy and Ironwood

A key point is that Synergy is valued at a large discount to Ironwood, which has linaclotide for CIC and IBS-C (June 9, 2012 PDUFA) and is partnered with Forest Laboratories in North America, Almirall S.A. in the E.U., and Astellas in most of Asia. To give a sense of the economics already driven by linaclotide, for North American rights, Forest already paid Ironwood $120 million in upfront fees and milestone payments, and purchased $25 million of Ironwood shares. The remaining precommercial milestones total to $85 million, and potential sales milestones total to $100 million more. Forest and Ironwood are to share equally in development and commercialization costs, as well as in any profits and losses, in the U.S., with Ironwood slated to receive an approximate a 15% royalty in Canada and Mexico. For European rights, Almirall S.A. paid Ironwood $57 million in upfront fees and milestone payments and bought $15 million of Ironwood shares. The remaining precommercial milestones could bring in $20 million more, and Almirall is funding the full development and commercialization of linaclotide in Europe. Royalty rates from Almirall start above 20%, minus the transfer price paid for the active pharmaceutical ingredient. For Asian rights outside of China, Astellas paid Ironwood a $30 million upfront fee and precommercial milestones could add up to $45 million. Astellas is funding the full development and commercialization of linaclotide in those Asian regions. Royalty rates from Astellas start above 20%, minus the transfer price paid for the active pharmaceutical ingredient. Linaclotide is covered by composition of matter patents in the U.S. until 2025, and in Europe and Japan until 2024.

Linaclotide will likely prove to be more potent, in our view, but chronic non-life threatening indications like CIC and IBS-C require a high degree of drug safety; therefore, there should be ample room for both drugs to benefit from wide use. Although only Phase 2a data are available, plecanatide has demonstrated a clean safety profile relative to key competitor linaclotide. The cleaner safety stems from plecanatide being derived from natural human uroguanylin, which is present in the gastrointestinal tract, versus linaclotide's bacterial peptide derivation. Plecanatide has close structural homology to the natural human hormone, as only one conservative amino acid change (D to E) was made among its 16 amino acids, and thus it binds the GC-C receptor in a highly similar and natural way.

Phase 2a Plecanatide Trial Design

At the 2010 and 2011 American College of Gastroenterology (ACG), Synergy presented positive Phase 2a plecanatide results in chronic constipation from the same trial. The original 2010 poster statistically assessed for efficacy in patients that received at least 5 doses of either plecanatide or placebo and had corresponding diary data for daily bowel habits (per protocol population). The updated 2011 poster differed in that it statistically analyzed for efficacy in only the 78 patients (of 84 total enrolled) that received at least one dose of either plecanatide or placebo and that received at least one post-baseline pharmacodynamic assessment (a modified intent-to-treat population). The trial was a randomized, double-blind, placebo-controlled, 14-day QD dose-ranging. There were 4 plecanatide dose cohorts (0.3mg, 1mg, 3mg, and 9mg), with each cohort comprising 15 plecanatide patients and 5 matching placebo patients. After each cohort was completed, a safety review was conducted prior to initiating the next cohort. Safety was the primary endpoint, with secondary endpoints as follows: (1) time to first bowel movement after first daily dose; (2) stool frequency (spontaneous bowel movements, SBMs); (3) completeness of evacuation (complete spontaneous bowel movements, CSBMs); (4) stool consistency (Bristol stool form scale, BSFS); (5) straining (7-category scale); and (6) abdominal discomfort (6-category scale).

Exhibit 7: Phase 2a Trial Design

		Treatment		
Screening	Pre-Treatment	Week 1	Week 2	Follow-Up
Days -28 to -14	Days -14 to -1	Days 1 to 7 (+/- 1 Day)	Days 8 to 14	Day 21 (+/- 3 Days)

Source: Company documents

Phase 2a Plecanatide Trial Results

In the Phase 2a trial, no plecanatide was detected systemically (assay sensitivity = 10ng/mL), no serious adverse events (SAEs) occurred in the plecanatide groups, and no diarrhea was reported in the plecanatide groups, with 1 placebo patient discontinuing due to diarrhea, the only SAE in the trial. We therefore expect to see no diarrhea in Synergy's pivotal trials, a necessary differentiation between plecanatide and linaclotide for Synergy to significantly penetrate the market. By contrast, linaclotide caused diarrhea in 13% of Phase 2a patients and in 12-18% of Phase 3 patients. About 8.6% (5/58) of plecanatide patients reported GI-related adverse events (whether considered to be related or not related to therapy) versus 10% (2/20) of placebo patients, and the percentage of those who reported adverse events of any kind considered related to treatment were 17.2% (10/58) for plecanatide and 10% (2/20) for placebo. Adverse events of any kind, considered to be related or unrelated to therapy, occurred in about 29% (17/58) of plecanatide patients and in 20% (4/20) of placebo patients. Severe adverse events, not to be confused with the more worrisome SAEs, occurred in about 8.6% (5/58) of plecanatide patients and in no placebo patients. Adverse event "severity" is a point on an arbitrary scale of intensity for the adverse event in question, whereas "seriousness" includes things like death, life-threatening events, hospitalization (initial or prolonged), permanent disability, congenital anomaly, or requiring intervention to prevent permanent damage.

Exhibit 8: Summary of All Adverse Events

Event	Placebo n=20	0.3 mg n=14	1.0 mg n=14	3.0 mg n=15	9.0 mg n=15
Total AE	4 (20.0%)	3 (21.4%)	6 (42.9%)	2 (13.3%)	6 (40.0%)
Treatment Emergent AE	4 (20.0%)	3 (21.4%)	6 (42.9%)	2 (13.3%)	6 (40.0%)
Severe AEs	0	1 (7.1%)	0	1 (6.7%)	3 (5.2%)
Serious AEs	1 (5.0%)	0	0	0	0
Related AEs	2 (10.0%)	2 (14.3%)	2 (14.3%)	1 (6.7%)	5 (33.3%)
AEs Leading to Discontinuation	1 (5.0%)	0	0	0	0

Source: Company documents

Exhibit 9: Gastrointestinal-Related Adverse Event Summary With Relationship to Treatment

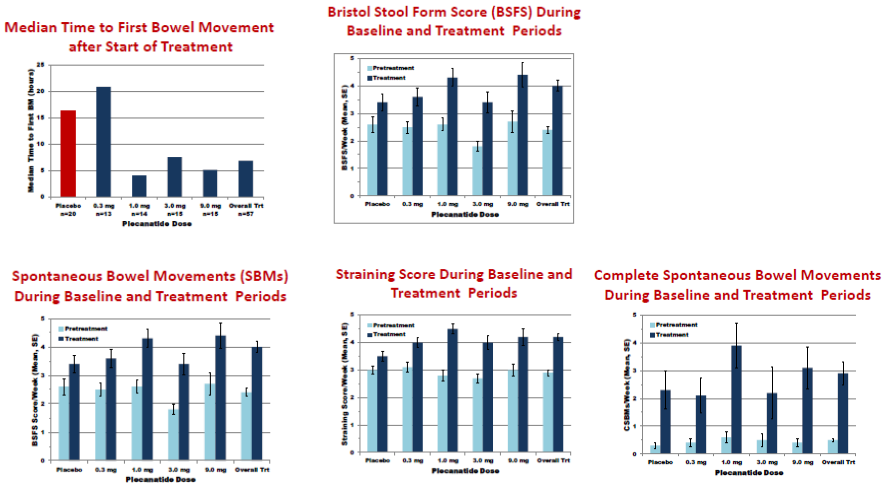
AE	Placebo	0.3 mg	1.0 mg	3.0 mg	9.0 mg
Ab Cramping	1 (5.0%)	0	0	0	0
Ab Pain	1 (5.0%)	0	0	0	0
Bloating	0	0	0	0	1 (6.7%)
Diarrhea	1 (5.0%)	0	0	0	0
Flatulence	2 (10.0%)	0	0	0	0
Nausea	0	1 (7.1%)	0	0	
Upset Stomach	0	0	0	1 (6.7%)	0

Ab = Abdominal

Source: Company documents

The 3 highest doses substantially decreased the median time to first bowel movement. Plecanatide also demonstrated increases in mean stool frequency (SBM and CSBM), improvements in stool consistency, less straining and less abdominal discomfort. For all 4 plecanatide-dose groups combined, the drug reduced the median time to first bowel movement to about 7 hours compared to placebo of approximately 17 hours. Plecanatide demonstrated a mean stool frequency of about 4.5 SBM/week (compared with a mean of about 2.5 SBM/week at baseline) at the 1mg dose, versus placebo in which a mean of 2.5 SBM/week at baseline increased to about a mean of about 3.5 SBM/week. Plecanatide also demonstrated a mean stool frequency of 4 CSBM/week (compared with <1/week at baseline) at the 1mg dose, versus placebo in which <1 CSBM/week at baseline increased to a mean of about 2 CSBM/week. Plecanatide also improved stool consistency as measured by the average weekly Bristol Stool Form Score (BSFS), with an average BSFS of almost 4.5 post-treatment for the 1mg group versus about 3.5 for placebo-post treatment. For some helpful context, the weekly CSBM frequency delta in the linaclotide CIC Phase 3 trials was 1.3 and 2.0 for the 145ug and 290ug doses, respectively, but again, with notable amounts of diarrhea.

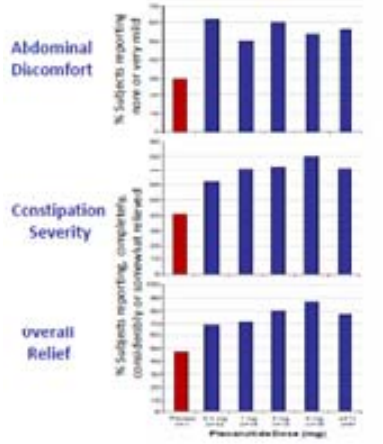
Exhibit 10: Various Phase 2a Efficacy Measurements



Source: Company documents

Perhaps a solid indicator of usage if approved can be found in the analysis of patients' accounts of abdominal discomfort, constipation severity and overall relief, even when only considering the lower 3 doses from Phase 2a that were selected for Phase 2/3. Plecanatide reduced abdominal discomfort to "none or very mild" in about 57% of patients versus 30% for placebo. Also, constipation severity was "completely, considerably, or somewhat relieved" by plecanatide in about 70% of patients versus about 40% of placebo patients. Lastly, about nearly 73% of plecanatide patients reported overall relief as being "completely, considerably, or somewhat relieved" after treatment compared with about 47% of placebo patients.

Exhibit 11: Global Assessment Scores After Treatment



Source: Company documents

Plecanatide Phase 1 trial in Healthy Volunteers

The Phase 1 trial characterized the safety, tolerability, pharmacokinetic (PK), and pharmacodynamic (PD) effects of plecanatide in healthy volunteers. It was double-blind, placebo-controlled, and randomized, and a single, oral, ascending dose (0.1mg, 0.3mg, 0.9mg, 2.7mg, 5.4mg, 8.1mg, 16.2mg, 24.3mg, and 48.6 mg) was given to each of 71 healthy volunteers. PD effects were evaluated by the time to first stool and by the 7-point Bristol Stool Form Scale (BSFS) to examine stool consistency.

All doses of plecanatide were well tolerated and most importantly no SAEs were observed. Equally important and consistent with a clean safety profile, there was no measurable systemic absorption of the drug regardless of dose (assay sensitivity=10ng/mL). The trial was not powered for statistical significance, but there were clear signs of efficacy, evidenced by observed decreases in the time to first bowel movement and increases in the post-dose BSFS, versus placebo. Clearly, the Phase 1 results were supportive of further investigation in CIC and IBS-C.

Common Terminology Criteria for Adverse Events version 3.0 was used to assess all adverse events and 19% (12/63) subjects experienced mild adverse events, all of which resolved within 2 hours of dosing. Of critical differentiating importance relative to close peer linaclotide, plecanatide did not cause any severe diarrhea even at the highest doses.

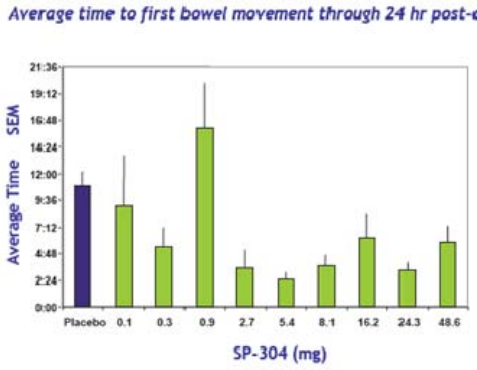
Exhibit 12: Number of Adverse Event Reported With an Assigned Relationship to Plecanatide

Adverse Event Term	Number Reported	%
Diarrhea *	8	12.70%
Abdominal Discomfort	3	4.76%
Nausea	2	3.17%
Emesis	1	1.59%
Headache	1	1.59%

*** Diarrhea is defined as an increase in the number of bowel movements per day compared to baseline**

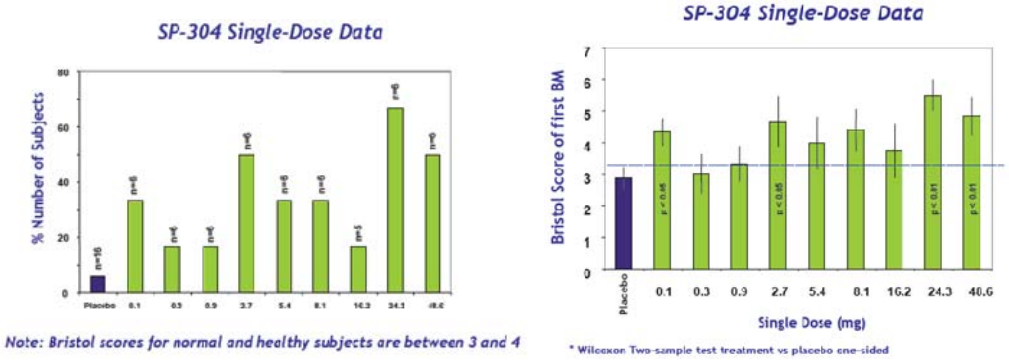
Source: Company documents

Exhibit 13: Average Time to First Bowel Movement Through 24 Hours Post Dose



Source: Company documents

Exhibit 14: Plecanatide Improves Stool Consistency



Source: Company documents

Phase 2/3 Plecanatide CIC Trial (SP304-20210; http://clinicaltrials.gov/ct2/show/NCT01429987?term=plecanatide&rank=1)

The ongoing randomized, double-blind, placebo-controlled Phase 2/3 is a 12-week QD oral dose-ranging trial evaluating plecanatide in CIC, and its powering should enable Synergy to use it as one of its registrational trials if FDA agrees to that. Trial enrollment began in October 2011, and enrollment completion should occur in 2Q12, by our estimation. The primary endpoint is CSBM, and a responder analysis will be utilized. The trial is 90%-powered to detect at least a 10% difference in overall CSBM responders between each dose of plecanatide and placebo. A complete spontaneous bowel movement occurs 24 hours away from laxative use and the patient reports a feeling of complete evacuation. A weekly responder will have 3 or more CSBM and an increase of at least one CSBM from baseline within a week. A monthly responder achieves this for 3 of the 4 weeks in a month. Most importantly for success, an overall CSBM responder must achieve the monthly response in 2 of the 3 months of treatment, with one of those months being the final (i.e., the 3rd) month.

Synergy will also evaluate secondary endpoints of spontaneous bowel movements (SBMs), disease-specific quality-of-life measures, and daily constipation symptoms such as straining, stool consistency, and abdominal discomfort. The more subjective secondary endpoints will be assessed by patient-reported outcome measures gathered via an interactive voice response system. The 4-arm (placebo, 0.3mg, 1mg, or 3mg) trial is being conducted at 110 U.S. sites, with a planned enrollment of 880 CIC patients. Synergy is utilizing PAREXEL International as its Contract Research Organization. We are anticipating positive trial results in 4Q12 in at least the 1mg-dose group versus placebo – given the standout performance of that dose group in the Phase 2a trial – and given that linaclotide already has established the utility of employing this mechanism of action. If the FDA agrees that the ongoing trial counts as an initial registrational trial, then we expect that at most two additional trials will be required for approval.

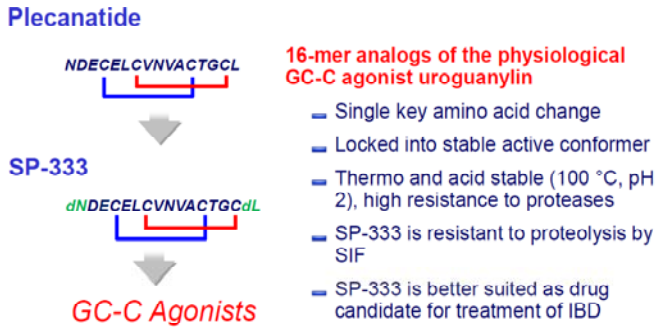
Phase 2b IBS-C Trial Intentions

In 3Q12, Synergy intends to initiate a randomized Phase 2b trial to explore the potential of plecanatide to treat IBS-C patients with IBS-C. We believe that top-line results from the trial could be available in 3Q13. Synergy will include 3 doses of plecanatide in this trial with treatment groups equally powered (1:1:1:1 randomization including placebo). There will be 12 weeks of treatment, preceded by 2 weeks of pre-treatment to establish a baseline, and 4 weeks of withdrawal. The trial's efficacy endpoints (like the pivotal linaclotide IBS-C trials) are aligned with FDA guidance on Clinical Evaluation of Products for the Treatment of IBS-C, issued in March 2010. The trial will be conducted exclusively in the U.S., and many of the centers will be those that are participating in the ongoing Phase 2/3 CIC trial. We estimate the trial cost to be about $12 million.

SP-333 – A Next-Generation GC-C Receptor Agonist for IBS-C

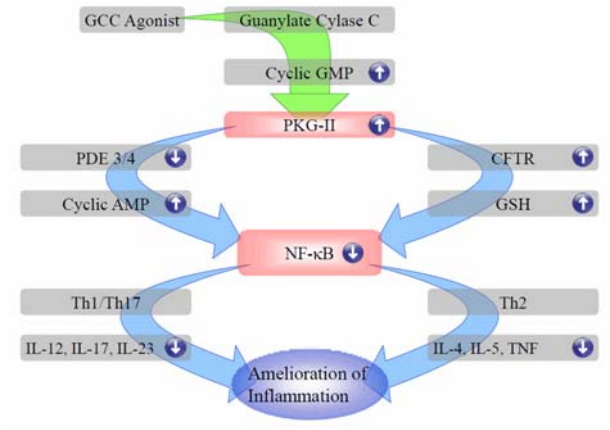
Given that Synergy has shown oral treatment with UG inhibits polyp formation in ApcMin/+ mice, and that the anti-cancer and anti-inflammatory activities of GC-C agonists are achieved through downregulation of certain pro-inflammatory cytokines, the company sought to understand if other oral GC-C agonists would reduce inflammation in murine colitis models. Synergy already showed that oral plecanatide ameliorated DSS- and TNBS-induced gastrointestinal inflammation in mice, and the company has since discovered SP-333, a highly potent and proteolysis-resistant peptide orally administered analog of UG. We describe below a study showing how SP-333 can reduce gastrointestinal inflammation through the downregulation of pro-inflammatory cytokines such as IL-4, IL-5, IL-17, IL-23, and TNF-a, thereby supporting the view that SP-333 has the potential to treat ulcerative colitis and Crohn's Disease.

Exhibit 15: Similarity of SP-333 and Plecanatide



Source: Company documents

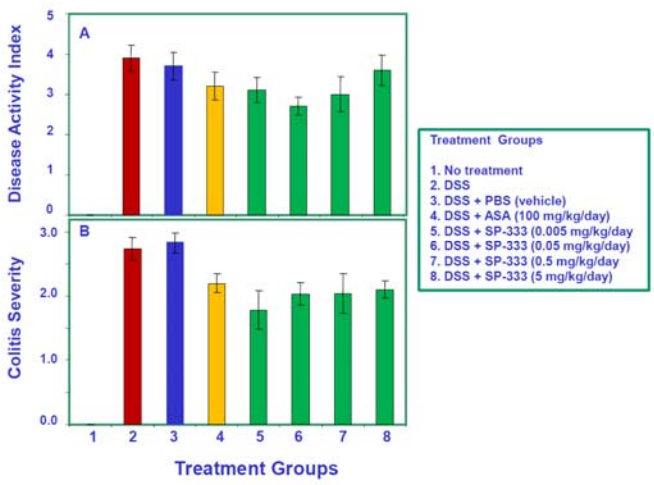
Exhibit 16: Mechanism of Anti-Inflammatory Action of GC-C Agonists



Source: Company documents

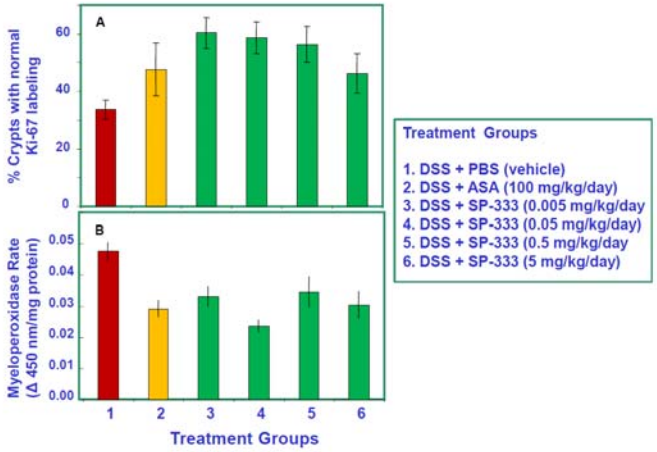
Inflammation was induced in BDF1 and BALB/c mice via dextran sulfate sodium (DSS) or trinitrobenzene sulfonic acid (TNBS) to simulate ulcerative colitis. GC-C agonists or vehicle control were administered once daily by oral gavage, then the mice were euthanized for analysis. Body weight, stool consistency, presence of rectal bleeding or blood in stool, colon weight, and colon histology was read by investigators blind to treatment. Explants of colon tissue were cultured to measure cytokine production. We note that the data with SP-333 in mice demonstrate that the compound has the potential to treat gastrointestinal inflammation via inhibiting the synthesis of several pro-inflammatory cytokines. We believe that Synergy will be able to file an IND for SP-333 for ulcerative colitis in 3Q12.

Exhibit 17: SP-333 Ameliorates DSS-Induced Colitis in BDF1 Mice



Source: Company documents

Exhibit 18: SP-333 Improves Symptoms of DSS-Induced Colitis in BDF1 Mice



Source: Company documents

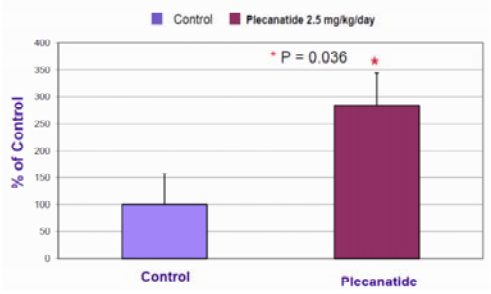
GC-C Receptor Agonists in Colon Cancer

Near term at the AACR 2012 conference, Synergy will present preclinical results from studies in which enhancement of cyclic GMP production by GC-C agonists has been shown to delay progression of colitis into colorectal cancer though the downregulation of pro-inflammatory cytokines. There are an estimated 875,000 cases of colorectal cancer diagnosed annually worldwide, accounting for 8.5% of all new cancers, and patients with ulcerative colitis and Crohn's disease are at increased risk of developing colorectal cancer. Persistent gastrointestinal inflammation may contribute to colorectal malignancies, and thus Synergy is exploring the role of GC-C agonists in reducing disease incidence. Since cGMP signaling mediates the anti-inflammatory effects of nitric oxide and hemeoxygenase-1, drugs that increase cyclic GMP and cyclic AMP levels by inhibiting their degradation (like phosphodiesterase inhibitors) are effective in mouse models of ulcerative colitis. Natural activation of GC-C by the peptide hormone uroguanylin (UG) results in enhanced production of cyclic GMP, and it has been shown by Synergy that UG expression is suppressed in human colon tumors and that the oral treatment with UG inhibited polyp growth in mice via a cGMP-mediated mechanism. Synergy then showed that its own GC-C agonists (UG analogs plecanatide and SP-333) also reduced gastrointestinal inflammation in murine colitis models via downregulation of pro-inflammatory cytokines. Therefore, Synergy has sound reason to investigate whether GC-C agonists may delay progression of colitis into colorectal tumors.

In the present study, ApcMin/+mice were randomized to receive either powdered diet supplemented with or without plecanatide. DSS (4%) was administered in the drinking water for two cycles on 3 or 4 days of the 21 day cycles. Tumors per animal was assessed for each segment of the colon, and mRNA levels of UG, GC-C, Ki-67 and protein levels of β-catenin within the colon were measured, as was the expression of cytokines in explant colon cultures. Synergy showed that plecanatide and SP-333 were both as effective as sulfasalazine or 5-ASA in inhibiting DSS-induced inflammation in mice. Treatment with plecanatide also reduced the number of tumors within the colon, increased expression of protein kinase G-II (PKG-II) and decreased the levels of Ki-67 and β-catenin. DSS treatment lowered expression of UG, but UG levels were partially restored by plecanatide. In explant colon cultures, plecanatide reduced production of the pro-inflammatory cytokines IL-6, IL-17, and IL-23. Taken together, all of these results suggest that the anti-inflammatory and anti-cancer effects of plecanatide occur via downregulation of pro-inflammatory cytokines. The study provides the basis for further development of GC-C agonists as potential orally-delivered, mucosally active drugs for gastrointestinal inflammatory diseases and IBD-associated colon cancer. We look forward to updating investors when the full results come out next week and suspect that the results will be at least as positive as what was presented at ACG in 2011 (described immediately below).

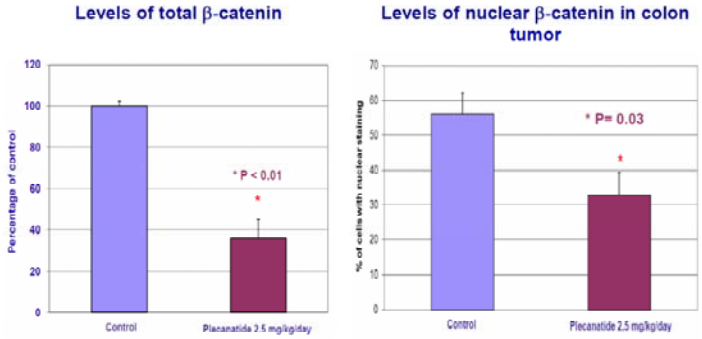
A highly similar preclinical study to the above-mentioned study that is soon to be presented at AACR was also presented at ACG 2011, in which only oral plecanatide was examined for its ability to delay progression of colitis to colonic tumors in ApcMin/+mice through the downregulation of pro-inflammatory cytokines. Below we show the ability of plecanatide to regulate some of those cytokines, specifically activating PKG-II, reducing expression of β-catenin and Ki-67, and increasing the number of caspase-3 positive cells (indicating apoptosis).

Exhibit 19: Effect of Plecanatide on Activation of PKG-II in Colon Tissues



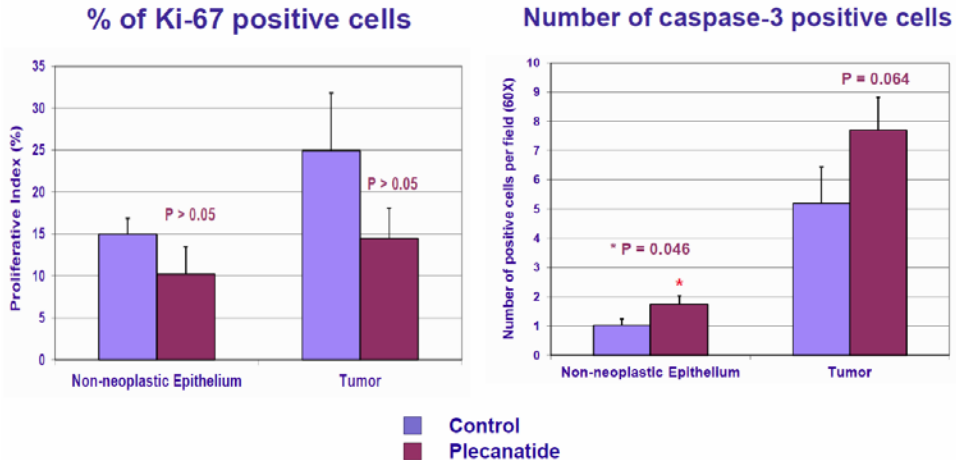
Source: Company documents

Exhibit 20: Oral Treatment With Plecanatide Reduces β-catenin Levels in Colon



Source: Company documents

Exhibit 21. Effect of Treatment With Plecanatide on Levels of Ki-67 and caspase-3 in Colon Tissue



Source: Company documents

Intellectual property

Plecanatide is protected by composition of matter patents that expire in 2022 and 2023. More specifically, one U.S. patent (issued in May 2006 and expiring in March 2023: USPTO # 7,041,786) protects plecanatide itself, whereas another U.S. patent (issued in September 2010 and expiring in June 2022: USPTO # 7,799,897) protects plecanatide and derivatives thereof. There is also the potential for added patent protection through patent term extension and Hatch-Waxman term extensions. New chemical entities also receive 5 years of market exclusivity after product launch in the U.S.

Furthermore, there is an issued European composition of matter patent (expiring in 2023: EP 1 379 224 B1) covering plecanatide, as well as two other issued foreign patents that cover composition-of-matter of plecanatide and expire in 2022. In April 2010, two parties filed an opposition to Synergy's issued European patent, which could take several years to clarify. New chemical entities also receive up to 10 years of market exclusivity after launch in Europe.

In February 2011, the USPTO issued a composition of matter patent for SP-333 (USPTO # 7,879,802), Synergy's second-generation GC-C receptor agonist for inflammatory bowel disease such as ulcerative colitis and Crohn's disease, which expires in 2028. There is also the potential for added patent protection through patent term extension and Hatch-Waxman term extensions.

The aforementioned issued patents not only cover composition, but also describe a method-of-use, covering selective application of GC-C receptor agonists to treat gastrointestinal disorders.

Regarding unissued intellectual property, Synergy has filed 11 pending U.S. patent applications, and 29 pending foreign patent applications. These applications cover a range of plecanatide and SP-333 derivatives and analogs.

Financials

Revenue. All projected revenue is due to plecanatide sales in the CIC and the IBS-C indications only, and we are conservatively not even including any future upfront license fees and milestones payments, although it would be reasonable to do so using Ironwood's deals as a commercialization proxy in our projections. We are projecting plecanatide to begin selling in both indications in 2015 in the U.S. (off label in IBS-C initially), in the E.U. in 2016, and in 2017 for the Asian markets. Both indications involve large markets of under-diagnosed patient populations, and thus these indications could surprise to the upside. We are projecting plecanatide to generate $1 billion from royalties and profit sharing worldwide in 2019. We expect the majority of this revenue to be generated from the U.S. profit-sharing relationship that we anticipate will occur, given the anticipated safety advantages – and, therefore, extended usability – of plecanatide.

Expenses. We project the COGS for plecanatide to range between 2-4%, depending on the price in the country in question, given that it is a 16 amino acid-long biologic that is not at all complicated to synthesize. We are modeling that Synergy will be supplying plecanatide to potential partners, and will be reimbursed in all territories except in the U.S., where we anticipate a profit-sharing agreement. In this case, we anticipate that Synergy will be responsible for 50% of all the U.S. COGS in both indications.

We project G&A expense to transition to SG&A expense in 2015, as Synergy ramps up for the launch of plecanatide. We have therefore projected 100% annual growth in SG&A in 2014-2016. The salesforce should be large, given that we anticipate Synergy and a potential partner to market to both gastroenterologists and general practitioners. We project significant SG&A growth from the $7 million in 2011 to $103 million in 2017 to be reasonable for Synergy's portion of the marketing expenses. We are also projecting R&D expense to grow 30% in 2013 and 20% in 2014, due to the several anticipated Phase 3 trials ahead. Beyond 2014, we do not project a decrease in R&D, as we anticipate future development to continue, led by trials with SP-333.

Bottom Line. We project Synergy to be profitable in 2015, due to plecanatide sales in the U.S. The 2015 diluted shares take into consideration the warrants and options, which we project to be in the money by 2015. Finally, due to tax loss carry forwards, we are not projecting a full 35% tax rate until 2018.

Balance Sheet. Synergy ended YE11 with $13.2 million in cash and will likely need to raise capital this year to fund its operations. We expect significant stock price appreciation after release of the Phase 2/3 CIC data in 4Q12. There are 5.6 million outstanding warrants, with an average exercise price of about $5.60, which alone would bring in about $32 million. In addition, Synergy has no debt, which could give Synergy options for potential future capital.

Risks

- **Clinical risk.** Plecanatide may fail to deliver statistically significant results in late stage clinical trials, thus substantially reducing the value of Synergy and our target price.
- **Regulatory risk.** Plecanatide, even if successful in the clinic, could fail to be approvable by domestic and/or foreign regulatory bodies, which would reduce Synergy's value and our target price.
- **Financing risk.** Synergy does not have enough capital to fund its operations into 2013, and thus is reliant on obtaining additional outside funding, which may not occur or which could be substantially dilutive to existing investors.
- **Competitive risk.** Even if plecanatide is approved, it still may not be well adopted by the marketplace, which would adversely affect Synergy's value and our target price.
- **High stock price volatility.** This issue is common among small-cap biotechnology companies with relatively low trading volumes.

Synergy Pharmaceuticals, Inc.
Income Statement
Fiscal Year ends December
(in 000, except per share items)

	2009A	2010A	1Q11	2Q11	3Q11	4Q11	2011A	1Q12E	2Q12E	3Q12E	4Q12E	2012E	2013E	2014E	2015E	2016E	2017E
Plecanatide CIC revenue															84,591	192,296	361,243
Plecanatide IBS-C revenue															57,676	125,678	227,285
Total Revenue															**142,268**	**317,974**	**588,528**
COGS															7,904	22,126	48,967
R&D	3,733	9,559	1,478	2,354	3,883	5,704	13,419	5,989	6,288	6,603	6,933	25,812	32,266	38,719	44,527	46,753	49,091
SG&A	4,467	6,562	1,898	1,524	1,103	2,221	6,746	1,999	2,039	2,080	2,121	8,239	9,887	19,774	39,548	79,096	102,825
Total Operating Expenses	**8,200**	**16,121**	**3,376**	**3,879**	**4,986**	**7,925**	**20,165**	**7,988**	**8,327**	**8,682**	**9,054**	**34,052**	**42,153**	**58,493**	**91,978**	**147,975**	**200,882**
Operating Income	**(8,200)**	**(16,121)**	**(3,376)**	**(3,879)**	**(4,986)**	**(7,925)**	**(20,165)**	**(7,988)**	**(8,327)**	**(8,682)**	**(9,054)**	**(34,052)**	**(42,153)**	**(58,493)**	**50,289**	**169,999**	**387,646**
Interest income	75	108	24	20	20	26	90	27	29	30	32	117	121	125	128	132	136
Interest expense	0	0	(12)				(12)										
Other income (expense), net	0	494				363	363				200	200	190	181	171	163	155
Change in fair value of financial instrument	0	297	(339)	(698)	4,383	1,911	5,257	(500)	(515)	(530)	(546)	(2,092)	(2,155)	(2,219)	(2,286)	(2,354)	(2,425)
Pretax income	**(8,125)**	**(15,222)**	**(3,702)**	**(4,557)**	**(583)**	**(5,625)**	**(14,467)**	**(8,461)**	**(8,814)**	**(9,183)**	**(9,369)**	**(35,826)**	**(43,996)**	**(60,407)**	**48,303**	**167,940**	**385,512**
Provision for income tax (benefit)																5,038	96,378
Net Income	**(8,125)**	**(15,222)**	**(3,702)**	**(4,557)**	**(583)**	**(5,625)**	**(14,467)**	**(8,461)**	**(8,814)**	**(9,183)**	**(9,369)**	**(35,826)**	**(43,996)**	**(60,407)**	**48,303**	**162,902**	**289,134**
EPS	**(0.22)**	**(0.34)**	**(0.08)**	**(0.10)**	**(0.01)**	**(0.11)**	**(0.30)**	**(0.16)**	**(0.16)**	**(0.16)**	**(0.16)**	**(0.64)**	**(0.71)**	**(0.91)**	**0.69**	**2.29**	**4.01**
EPS diluted, GAAP	**(0.22)**	**(0.34)**	**(0.08)**	**(0.10)**	**(0.01)**	**(0.11)**	**(0.30)**	**(0.16)**	**(0.16)**	**(0.16)**	**(0.16)**	**(0.64)**	**(0.71)**	**(0.91)**	**0.64**	**2.11**	**3.69**
Shares Outstanding Basic/Diluted	36,641	44,875	46,167	46,643	47,309	50,274	47,598	51,782	55,407	57,069	58,781	55,760	62,308	66,046	70,009	71,059	72,125
Diluted shares outstanding	36,641	44,875	46,167	46,643	47,309	50,274	47,598	51,782	55,407	57,069	58,781	55,760	62,308	66,046	76,009	77,149	78,306

Source: Company reports, Brean Murray, Carret & Co. estimates

Synergy Pharmaceuticals, Inc.
Balance Sheet
Fiscal Year ends December
(All amounts are actual)

	2009A	2010A	1Q11	2Q11	3Q11	2011A	1Q12E	2Q12E	3Q12E	2012E
Current assets:										
Cash and cash equivalents	7,152,568	1,707,516	938,700	503,744	67,370	13,244,883	5,284,299	56,985,655	48,333,250	39,310,617
Prepaid expenses and other current assets / Rev	1,061,630	997,584	733,655	861,399	588,407	1,063,402	755,665	887,241	606,059	1,095,304
Total current assets	**8,214,198**	**2,705,100**	**1,672,355**	**1,365,143**	**655,777**	**14,308,285**	**6,039,963**	**57,872,896**	**48,939,309**	**40,405,921**
PPE fixed assets, net	9,725	7,749	7,255	6,761	6,267	5,773	5,279	4,785	4,291	3,797
Deposits and other assets	14,025	14,025	14,025	14,025	14,025	14,025	14,025	14,025	14,025	14,025
Note receivable (due from controlling shareholder)	972,552	1,674,087	1,554,067	1,378,473	1,427,181	1,541,456	1,587,700	1,635,331	1,684,391	1,734,922
Total assets	**9,210,500**	**4,400,961**	**3,247,702**	**2,764,402**	**2,103,250**	**15,869,539**	**7,646,967**	**59,527,037**	**50,642,016**	**42,158,666**
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)										-
Current liabilities:										-
Accounts payable	1,283,466	2,961,333	2,614,688	2,627,657	4,469,879	1,415,617	2,693,129	2,706,487	4,603,975	1,458,086
Other accrued liabilities	443,266	2,051,057	2,845,548	2,193,099	2,330,856	1,331,382	2,930,914	2,258,892	2,400,782	1,371,323
Total current liabilities	**1,726,732**	**5,012,390**	**5,460,236**	**4,820,756**	**6,800,735**	**2,746,999**	**5,624,043**	**4,965,379**	**7,004,757**	**2,829,409**
Long-term liabilities:										
Derivative financial instruments, at estimated fair value-warrants		3,487,959	5,139,347	7,958,506	386,838	3,325,114	3,657,625	4,023,388	4,425,727	4,868,299
Total long-term liabilities	-	3,487,959	5,139,347	7,958,506	386,838	3,325,114	3,657,625	4,023,388	4,425,727	4,868,299
Total liabilities	**1,726,732**	**8,500,349**	**10,599,583**	**12,779,262**	**7,187,573**	**6,072,113**	**9,281,668**	**8,988,767**	**11,430,484**	**7,697,708**
Stockholders' equity (deficit):										-
Common stock, par value $0.0001, 100,000,000 shares authorized, 54,279,906 shares outstanding at December 31, 2011. (No preferred issued)	8,844	4,610	9,280	9,418	9,493	5,429	5,592	5,983	6,163	6,348
Additional paid-in capital	47,395,465	51,037,984	51,483,101	53,376,493	55,415,806	79,401,015	76,429,309	137,415,533	135,271,470	139,889,707
Accumulated deficit	(39,920,541)	(55,141,982)	(58,844,262)	(63,400,771)	(63,983,622)	(69,609,018)	(78,069,602)	(86,883,246)	(96,066,101)	(105,435,097)
Total stockholders' equity (deficit)	**7,483,768**	**(4,099,388)**	**(7,351,881)**	**(10,014,860)**	**(5,084,323)**	**9,797,426**	**(1,634,702)**	**50,538,270**	**39,211,532**	**34,460,957**
Total liabilities and stockholders' equity (deficit)	**9,210,500**	**4,400,961**	**3,247,702**	**2,764,402**	**2,103,250**	**15,869,539**	**7,646,967**	**59,527,037**	**50,642,016**	**42,158,666**

Important Disclosures

Ratings and Target Price History

Priced as of market close 3/28/12.

At the time this report was published, Brean Murray, Carret & Co., LLC made a market in the securities of Synergy Pharmaceuticals and Theravance, Inc.

In the normal course of its business, Brean Murray, Carret & Co., LLC does and intends to seek compensation for investment banking and/or non-investment banking services from the companies in its coverage universe. As a result, investors should be aware that the Firm may have a conflict of interest that could affect the objectivity of this report. Investors should consider this report as only a single factor in making their investment decisions. Non-U.S. research analysts that may have contributed to this report are not registered/qualified as research analysts with the FINRA.

The research analyst(s) or research associate(s) principally responsible for the preparation of this research report has received compensation based upon various factors, including quality of research, investor client feedback, stock picking, competitive factors and firm revenues. The compensation is determined exclusively by research management and senior management (not including investment banking).

Brean Murray, Carret & Co. Stock Rating System

Buy - Expected to appreciate by at least 10% within the next 12 months.
Hold - Fully valued, not expected to appreciate or decline materially within the next 12 months.
Sell - Expected to decline by at least 10% within the next 12 months.

	# of Securities	% of Total Securities	# of IB-Related Securities in Past 12 mos.	% of Total Securities
BUY	132	60%	11	8.33%
HOLD	70	31.82%	2	2.86%
SELL	7	3.18%	0	0%
NOT RATED	11	5%	1	9.09%
TOTAL	**220**			

Note : Stock price volatility may cause temporary non-alignment of some ratings with some target prices.

Valuation Methodology and Risks

Synergy Pharmaceuticals (SGYP): We are initiating coverage of Synergy Pharmaceuticals with a Buy rating and 12-month target price of $13. Our target price is supported by a DCF analysis that utilizes a 40% discount rate and a 5x multiple of the projected 2019 EBITDA as the terminal value. Clinical risk – Plecanatide may fail to deliver statistically significant results in late stage clinical trials, substantially reducing the value of Synergy and our target price. Regulatory risk – Plecanatide, even if successful in the clinic, may fail to be approvable by domestic and/or foreign regulatory bodies, which would reduce Synergy's value and our target price. Financing risk – Synergy does not have enough capital to fund its operations into 2013, and thus is reliant on obtaining additional outside funding, which may not occur or which could be substantially dilutive to existing investors. Competitive risk – Even if plecanatide is approved, it still may not be well adopted by the marketplace, which would adversely affect Synergy's value and our target price. High stock price volatility. This issue is common among small cap biotechnology companies with relatively low trading volumes.

Theravance Inc (THRX): Our target price of $24 is derived from a probability adjusted scenario analysis of different sum-of-the-parts valuation models. Risks: Theravance is a development-stage company with no significant revenue stream. Clinical failure of Relovair, Zephyr, '081, or TD-2111 could result in a significant loss of value. Clinical success does not necessarily translate into higher valuation. The share price will also be susceptible to changes in the competitive landscape. Should Theravance's drugs receive approval, commercial success is not a given and failure to generate meaningful sales would also significantly impair the stock value. Theravance is unlikely to be profitable for a number of years, and the company's ongoing operating costs may require additional rounds of financing that would further dilute shareholders.

Analyst Certification

I, Jonathan Aschoff, hereby certify that the views expressed in this research report accurately reflect my personal views about any and all of the subject securities or issuers referred to in this document. The analyst and associate analyst further certify that they have not received and will not be receiving direct or indirect compensation in exchange for expressing the recommendation contained in this publication.

Disclaimers

Some companies that Brean Murray, Carret & Co., LLC follows are emerging growth companies whose securities typically involve a higher degree of risk and more volatility than the securities of more established companies. The securities discussed in Brean Murray, Carret & Co., LLC research reports may not be suitable for some investors. Investors must make their own determination as to the appropriateness of an investment in any securities referred to herein, based on their specific investment objectives, financial status and risk tolerance. This report may discuss numerous securities, some of which may not be qualified for sale in certain states and to certain categories of investors. Readers are advised that this analysis report is issued solely for informational purposes and is not to be construed as an offer to sell or the solicitation of an offer to buy. The information contained herein is based on sources which we believe to be reliable but is not guaranteed by us as being accurate and does not purport to be a complete statement or summary of the available data on the company, industry or security discussed in the report. Designated trademarks and brands are the property of their respective owners. Past performance is no guarantee of future results. Any opinions expressed herein are statements of our judgment as of the date of publication and are subject to change without notice. Entities including but not limited to the Firm, its officers, directors, employees, customers, affiliates may have a position, long or short, in the securities referred to herein, and/or other related securities, and from time to time may increase or decrease such position or take a contra position. The Firm (or persons related thereto) may make a market in the securities mentioned herein, and may from time to time perform investment banking or other services for, or solicit investment banking or other business from, and may have other relationships with any

company mentioned in this report. Brean Murray, Carret & Co., LLC is a member of SIPC, FINRA, licensed with various state securities regulatory authorities, and a registered U.S. Broker-Dealer. No part of this report may be reproduced in any form without the express permission of Brean Murray, Carret & Co., LLC. Additional information is available upon request.