Initiation
Overweight

IRWD, IRWD US
Price: $12.91

Price Target: $18.00

Ironwood Pharmaceuticals

Initiating at Overweight; A Potential Blockbuster in the GI Market

We are initiating coverage of Ironwood Pharmaceuticals with an Overweight rating and an $18 price target. Ironwood's key value driver is linaclotide, a phase 3 drug that we think has $3B peak potential in the US in the chronic constipation (CC) and irritable bowel syndrome with constipation (IBS-C) markets. OTC meds are quite common in these GI markets; however, our physician feedback and market analysis reveals a major unmet medical need. Our Overweight rating is supported by commercial success in CC and IBS-C, but with significant upside potential primarily from a better than expected clinical profile with IBS-C phase 3 data in 4Q10 and new indications such as opioid-induced or post-surgical constipation.

- **CC indication largely de-risked; IBS-C data is a key catalyst this year.** Linaclotide's phase 3 data in CC met all primary and secondary endpoints and showed a differentiated clinical profile with a rapid onset of action and a sustained benefit. The second piece to the linaclotide profile is in IBS-C, where phase 2b data are robust in a large trial (419 patients) and should be predictive of phase 3 success with data likely coming in 4Q10. We like the risk / reward profile in IRWD shares ahead of the IBS-C data. In our view, linaclotide is likely to see a benefit on pain, which should complete the picture of a unique, best-in-class drug with dual indications (CC and IBS-C) and multi-billion dollar peak potential.

- **Partnerships offset commercial risk with good economics.** The CC and IBS-C markets are large and underserved with more than 17M Americans seeking care from a physician. The commercial effort for linaclotide will require significant resources, but we think that Ironwood's US partner (Forest Labs) is an ideal one that will leverage up to 1,000 sales reps targeting GI specialists and primary care physicians. In our view, the 50/50 profit split with Forest allows upside participation without excessive SG&A spend. In the US, our forecasts assume a 2012 launch ($29M in sales), accelerating to almost $700M by 2015, which we think could prove to be conservative. Economics from EU linaclotide sales through partner Almirall are assumed in our forecasts, but any economics from Asian linaclotide sales through partner Astellas are excluded from our model.

- **Valuation attractive.** Our Dec 2010 PT is $18 (implying 39% upside potential) based on a conservative NPV analysis. We value US linaclotide at $11/sh, EU linaclotide at $4/sh, and have added $3/sh in cash. Our model assumes profitability in 2014 with EPS of $0.17 and acceleration in 2015 with EPS of $1.45.

US Biotechnology

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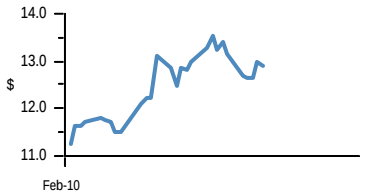
Price Performance



	YTD	1m	3m	12m
Abs	14.8%	12.3%	14.8%	14.8%

Ironwood Pharmaceuticals, Inc. (IRWD;IRWD US)

	2009E	2010E	2011E	2012E
EPS - Recurring ($)				
Q1 (Mar)		(0.23)		
Q2 (Jun)		(0.22)		
Q3 (Sep)		(0.20)		
Q4 (Dec)		(0.18)		
FY	(0.83)	(0.83)	(0.28)	(0.74)

Source: Company data, Bloomberg, J.P. Morgan estimates.

Company Data	
Price ($)	12.91
Date Of Price	12 Mar 10
52-week Range ($)	13.58 - 11.20
Mkt Cap ($ mn)	1,257.43
Fiscal Year End	Dec
Shares O/S (mn)	97
Price Target ($)	18.00
Price Target End Date	31 Dec 10

See page 33 for analyst certification and important disclosures, including non-US analyst disclosures.

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Table of Contents

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Key Investment Points

Ironwood Pharmaceuticals (IRWD)

Overweight

Linaclotide: A phase 3 candidate with $3B peak potential in the US
Ironwood's key value driver is linaclotide, a novel, once daily, oral drug currently in phase 3 development for chronic constipation (CC) and irritable bowel syndrome with constipation (IBS-C). Our research on these markets and our discussions with GI specialists reveals a significant unmet medical need with an addressable combined population of 17M patients who seek care in the US. Despite the broad use of OTC medications in these markets, the patient population is motivated, the drug is differentiated in our view, the management team from Ironwood has significant expertise in the therapeutic area, and the partnership with Forest is value-add. Our peak forecast of $3B in the US assumes penetration rates in the 25-35% range, which could prove to be conservative.

Phase 3 data for CC is robust; IBS-C data is a key catalyst in 4Q10
Linaclotide's phase 3 data in CC met all primary and secondary endpoints in large trials (~1,300 patients). The safety profile looked quite good, and the efficacy profile demonstrated a rapid onset of action and a sustained clinical benefit. Additional data could be seen at the DDW meeting (May 1-5; New Orleans), which should be a key catalyst for IRWD shares. The second indication for linaclotide is IBS-C where phase 2b data are robust in a large trial of 419 patients, which should be predictive of phase 3 success. We expect phase 3 data from two large trials in IBS-C (800 patients each) in 4Q10. A key finding would be a clinical benefit on abdominal pain, a hallmark of IBS-C, and based on our discussions with GI specialists, linaclotide is likely to show a pain benefit. In our view, the IBS-C data should complete the profile of a best-in-class drug with the dual indications of CC and IBS-C.

Partnerships mitigate commercial risk and have good economics
Tapping an underserved and frustrated CC and IBS-C market will be a challenge, but we think that Ironwood's US partner (Forest Labs) is an ideal one that mitigates commercial risk. Forest and Ironwood could have up to 1,000 sales reps targeting GI specialists and primary care physicians, which we see as a robust effort for a differentiated drug. The 50/50 profit split with Forest allows Ironwood to participate significantly in the linaclotide launch but mitigates the risk of excessive commercial spend. In Europe, Almirall is an attractive partner for Ironwood that provides strong pan-European commercial expertise and is incentivized for success. Our model assumes a 23% royalty on linaclotide sales at launch (increasing to 35%, though this could prove conservative), with EU royalties representing more than 15% of total Ironwood revenues in 2015. In Asia, Ironwood is partnered with Astellas, which is a strong partner for the IBS-C market, but we've excluded all economics from Astellas from our Ironwood model.

Valuation attractive, leverage starts to play out a few years into the launch
Our Dec 2010 price target is $18, which is based on a conservative NPV analysis of the sum of the parts (US linaclotide at $11/sh, EU linaclotide at $4/sh, cash at $3/sh). We assume a 2012 launch in the US ($29M in sales), growing to almost $700M by 2015. Conservatively, we assume an EU launch in 2013, which could be 2012. Our model assumes profitability in 2014 with EPS of $0.17 with significant earnings acceleration in 2015 with EPS of $1.45.

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Investment Risks

Commercial risk
The IBS-C and CC markets are still undeveloped for branded pharmaceuticals and in our view require a significant marketing effort to increase disease awareness. We believe that to maximize this opportunity, Ironwood and its partners will need a presence among primary care physicians, which could in turn lead to significant sales and marketing expense. Further, other agents have struggled to see meaningful uptake in the IBS-C and CC markets, and linaclotide could face similar challenges. We view commercial risk as the most significant risk to our Overweight rating.

Clinical risk
Late-stage clinical trials are very difficult to predict, and it could be difficult for linaclotide to show similar data in phase 3 IBS-C studies to what it showed in phase 2 studies. In addition, a clinical benefit on abdominal pain has been cited to us as a key point of product differentiation; hence, failure to show a pain benefit is a key source of clinical risk and a risk to our Overweight rating.

Regulatory risk
In the event of successful clinical programs for linaclotide in IBS-C, Ironwood would then face regulatory risk for both the IBS-C and CC indications, where there may be uncertainty as to whether the clinical data are supportive of FDA approval. Given that linaclotide could be used in a large number of patients, this could lead to increased scrutiny by the FDA, particularly with regard to safety.

Financing risk
Following completion of its initial public offering, Ironwood had ~$320M in cash on hand. We forecast a burn of around $200M from 2010 to 2013 and a turn to profitability by 2014. That said, the company may still need to raise capital in the public markets, diluting current shareholders. We have not assumed further financings in our model, but financing is a risk that would effectively lower our forecasts through dilution.

Legal risk
Inability to defend linaclotide patents in the US or Europe could substantially limit the commercial opportunity. Ironwood holds composition of matter patents that typically defend intellectual property in the US and Europe expiring in 2025 and 2024, with the US patents being eligible for Hatch-Waxman extension to 2030.

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Company Description

Based in Cambridge, MA, Ironwood is a late-stage biotech company focused on the development and commercialization of innovative therapeutics initially aimed at the gastrointestinal (GI) disease market. Ironwood completed its initial public offering on February 2, 2010; J.P. Morgan acted as a joint book-running manager for the offering. The company's key value driver is linaclotide, a novel agonist of guanylate cyclase type-C, a receptor found in the lining of the intestine that has implications in several GI disorders. Ironwood has successfully completed a phase 3 study for linaclotide in chronic constipation (CC) and is conducting phase 3 studies in irritable bowel syndrome with constipation (IBS-C), with phase 3 data expected in 4Q10. Linaclotide has the potential to treat other GI disorders, but the pipeline behind linaclotide is relatively early stage.

Background

Ironwood completed an initial public offering in February 2010. The company has been primarily focused on maximizing the commercial opportunity for linaclotide and has no other late stage candidates currently in clinical development. Longer term, Ironwood sees commercial potential in other pipeline assets and label expansion with linaclotide, with the goal of becoming a fully integrated multiple-product biopharmaceutical company. Following its IPO, Ironwood's estimated cash/short-term investments total $320M, which should be enough runway to achieve profitability, which we project in 2014 in our model.

Clinical Pipeline

Ironwood is focusing on the development of linaclotide for indications in the lower intestine, including CC and IBS-C. The company has successfully completed two phase 3 studies for linaclotide in CC and is in the process of completing two phase 3 studies in IBS-C, with data expected in 4Q10. Together with a safety database, the CC and IBS-C studies will form the basis of an NDA filing that is expected in early 1H11 for both indications. Looking beyond CC and IBS-C, linaclotide has potential label expansion opportunities in pediatric patients as well as in other GI disorders such as opioid-induced constipation and/or post-surgical constipation, none of which are assumed in our current Ironwood model.

Table 1: Ironwood Pipeline: Linaclotide Indications

Indication	Pre-clinical	Ph I	Ph II	Ph III	NDA	Market
CC						
IBS-C						

Source: Company reports.

Catalysts and Milestones

Ironwood has significant, value-driving near-term catalysts in 2010 highlighted by the 4Q10 results for the two phase 3 studies of linaclotide in IBS-C. The IBS-C trials are critical to the longer term opportunity, in our view. We expect these data, along with the already completed phase 3 studies in CC, to form the basis of an NDA filing in 1H11 and EU regulatory filings following shortly thereafter. Given the unmet need

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in IBS-C, linaclotide may qualify for Priority Review, which could point to potential approval by YE11, though we formally model approval in mid-2012 (see Table 2 for details).

Table 2: Ironwood Pharmaceuticals: Clinical Catalysts and Expected Events

Est Timing	Drug	Indication	Event	Significance
May 1-5	Linaclotide	CC	Presentation of data at DDW meeting	Medium
4Q10e	Linaclotide	IBS-C	Phase 3 data from MCP-103-302 study	High
4Q10e	Linaclotide	IBS-C	Phase 3 data from LIN-MD-31 study	High
2011	Linaclotide	Other indications	Explore additional indications	Low
1H11	Linaclotide	IBS-C / CC	US filing	Medium
2H11	Linaclotide	IBS-C / CC	EU filing	Medium
2H11	Linaclotide	IBS-C / CC	Potential FDA AdComm	High
Mid-2012	Linaclotide	IBS-C / CC	FDA approval	High
2H12	Linaclotide	IBS-C	EU approval	Medium

Source: Company data and J.P. Morgan estimates.

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Linaclotide: Market Background

Ironwood's key value driver is linaclotide, a first-in-class compound currently in phase 3 development for the treatment of irritable bowel syndrome with constipation (IBS-C) and chronic constipation (CC). In Nov 2009 the company announced positive top-line results from two phase 3 studies evaluating linaclotide in CC. Ironwood is expected to have data from its two phase 3 IBS-C trials in 4Q10. With a novel mechanism targeting a major unmet need with limited competition in its core markets, we believe that linaclotide has significant blockbuster potential. Assuming a peak penetration of 25-35% in CC and IBS-C, respectively, we think that linaclotide has almost $3B peak potential in the US alone. From an IP perspective, Ironwood holds composition of matter patents in the US that expire in 2025 before potential Hatch-Waxman IP extension. Ironwood also holds European Union composition of matter patents, which expire in 2024. A patent application is pending in Japan, and if issued, this would expire in 2024.

A Quick Overview: CC and IBS-C

To understand the long-term value of linaclotide, we think it is worth reviewing the disease dynamics of the IBS-C and CC markets. CC and IBS-C are quite common gastrointestinal disorders that collectively affect over 45 million people in the US alone, and far more people worldwide. CC is normally characterized by constipation, or infrequent bowel movement, and as a result of the constipation patients often times experience bloating and abdominal discomfort. IBS-C is also characterized by constipation, but the key factor that differentiates it from CC is that patients also have abdominal pain, which is often severe. In IBS-C, this pain is not normally relieved with evacuation, implying that it is not a direct result of constipation.

Chronic Constipation (CC)

Prevalence

The estimated prevalence of chronic constipation in the US varies between 2% and 28%, although most studies estimate the prevalence at 10–15%.[1] Differences in the reported prevalence of CC probably reflect differences in the underlying design of the studies (e.g., mailed surveys versus face-to-face interviews) or variation in the symptom-based definitions of CC. Similar to other chronic conditions, there is a trend toward increased prevalence with aging. Additionally, women appear to be affected more often than men (estimated prevalence ratio of 2.2:1).[1]Of the total ~35M CC sufferers, only 25% or approximately 8.8M seek medical care.[2]

Symptoms, Diagnosis, and Pathophysiology

Patients with constipation often describe a constellation of symptoms that include hard or lumpy stools, infrequent stools, straining, and the feeling of incomplete evacuation. Despite an attempt to standardize the definition of constipation within the Rome criteria, there remains a lack of consensus, which can serve as a barrier to treatment (see Table 3 for Rome III criteria details). Pathophysiologically, constipation is generally classified as either primary (idiopathic) or secondary in nature. Secondary constipation can often times be seen in patients with neurologic, metabolic, or systemic disorders, and in patients with colorectal cancer. Also,

[1] McCrea *et al., J Pain Symptom Manage;* 37:737-745 (2009)
[2] Johanson and Kralstein, *Aliment Pharmacol Ther;* 25: 599-608 (2007)

secondary constipation can be caused by medications, most notably opioids, which can relax the GI tract. Most pharmacologic therapies target the idiopathic form of constipation. However, it is possible that these therapies could also work in secondary constipation as well, and in practice, physicians could use an idiopathic therapy off label in secondary constipation patients if there is evidence of activity and favorable safety data.

Table 3: Rome III Diagnostic Criteria for Chronic Constipation

Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis
1. Must include 2 or more of the following: • Fewer than 3 defecations per week • Straining during at least 25% of defecations • Lumpy or hard stools in at least 25% of defecations • Sensation of incomplete evacuation for at least 25% of defecations • Sensation of anorectal obstruction/blockage for at least 25% of defecations • Manual maneuvers to facilitate at least 25% of defecations
2. Loose stools rarely present without the use of laxatives
3. Insufficient criteria for IBS

Source: Longstreth et al., Gastroenterology; 13:1480-1491 (2006)

Irritable Bowel Syndrome with Constipation (IBS-C)

Prevalence

The prevalence of IBS in the US is estimated to be 9-22%, and similar to CC most studies suggest the prevalence is between 10% and 15%.[3] Also similar to CC, women are more likely than men to be diagnosed with IBS. IBS is clinically categorized into 3 subtypes based on the patient's typical bowel habits: IBS-C (IBS with predominant constipation), IBS-D (IBS with predominant diarrhea) and IBS-A (IBS with alternating constipation and diarrhea or mixed IBS). Estimates of IBS subgroup prevalence vary substantially among studies, but most have reported a fairly even distribution among IBS-C, IBS-D, and IBS-A.[4], [5] These statistics imply that approximately 12M people in the US suffer from symptoms associated with IBS-C.

Diagnosis

The Rome III criteria define IBS as a chronic disorder characterized by abdominal pain or discomfort associated with disordered defecation (see Table 3). Abdominal pain has been suggested to be the key discriminating characteristic between IBS-C and chronic constipation. IBS is sub-classified on the basis of severity with most of IBS patients falling under moderate category (48%) followed by mild (31%) and severe (20%).[6]

Table 4: Rome III Diagnostic Criteria for Irritable Bowel Syndrome

Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis
Recurrent abdominal pain or discomfort at least 3 days per month in the last 3 months associated with *2 or more* of the following:
1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form (appearance) of stool

Source: Longstreth et al., Gastroenterology; 13:1480-1491 (2006)

[3] Drossman *et al., Gastroenterology;* 123(6):2108-2131 (2002)
[4] Tillisch *et al., Am J. Gastroenterol;* 100: 896-904 (2005)
[5] Saito *et al., Am J. Gastroenterol;* 97: 1910-1915 (2002)
[6] Drossman *et al., J. Clin Gastroenterology* (2009)

Assessing the Market: Barriers to Treatment

Under-diagnosis

IBS is often under-recognized, even among patients being seen for other medical conditions. Of those who experience IBS symptoms in the US, the majority are undiagnosed (76.6%).[7] Delayed diagnosis is another big concern as shown in a study conducted by the International Foundation of Functional Gastrointestinal Disorders in 2007, where patients reported an IBS diagnosis typically 6.6 years after the symptoms began.[7]

Communication barriers

Despite formal Rome criteria, there is a significant overlap among GI disorders and symptoms, including dyspepsia, GERD, CC, and IBS. Patients often discuss the predominate symptom making it difficult for physicians to effectively diagnose and treat the underlying disease. One of the key issues in diagnosing and treating CC and IBS-C is that patients are often embarrassed to discuss in detail their symptoms. Instead of pinpointing the issue right away, for many patients it takes several years of new treatments for other ailments that have no impact on the underlying issues before the patient and physician definitively make a CC or IBS-C diagnosis.

Assessing the Market: Current Treatment Options

Lifestyle modifications, dietary advice, patient reassurance, and education are frequently recommended by health care providers as the first step in therapy for patients with mild symptoms. The positive about the first step in the treatment paradigm is that it is safe and well tolerated. The negative is that these options are usually ineffective, and ultimately the more severe patients could require a more complex approach that includes pharmacotherapy combined with behavior modification. Over-the-counter (OTC) medications are generally used next, and these include bulking agents and osmotic or secretory laxatives. Osmotic laxatives (e.g., lactulose or miralax) are usually less effective in more severe forms of constipation and may lead to a worsening of symptoms such as bloating, flatulence, and distension. In clinical practice, physicians also use antispasmodic agents (e.g., buscopan, bentyl) and anti-depressants, but none of these therapies are associated with a consistent or sustained clinical benefit.

Patients Are Unsatisfied with Current Treatment Options

Pharmacologic treatment of constipation has been traditionally based on osmotic or secretory laxatives and bulking agents. However, these therapies often fail, especially in the more severe forms of constipation, and induce side-effects such as bloating or abdominal cramps. Patient satisfaction with current treatment options is clearly not high, which was noted by all of the GI specialists we spoke with. In a US population-based survey of constipation sufferers, nearly half (47%) were not satisfied with their current treatment, citing efficacy (82%) and safety (16%) for their dissatisfaction.[8] In another study on IBS-C patients, 92% of patients reported that they are not fully satisfied with their treatments.[9]

[7] Hungin *et al*., *Aliment Pharmacol Ther; 21:1365-1375* (2005)
[8] Johanson and Kralstein, *Aliment Pharmacol Ther;* 25: 599-608 (2007)
[9] Drossman *et al., J. Clin Gastroenterology* (2009)

Pain in IBS-C Is Most Troublesome for Patients

As we mentioned above, the key differentiating factor for IBS-C compared with CC is pain, where 80% of patients cite abdominal pain as the most frequent factor that makes IBS-C severe. Additionally, 29% of patients cite pain as the number one most troubling aspect of IBS-C, with 78% of patients having continuous of frequent recurring pain in the last six months. It is not surprising then that 69% of patients indicated that pain needs to be improved for a medication to be used.[10]

Pharmacologic Therapies

Table 5 summarizes the key drugs either approved or in development for the pharmacologic treatment of CC and IBS-C, focusing on chloride channel activators, selective 5-HT4 agonists, and investigational drugs. Only two drugs have been formally approved by FDA for IBS-C and CC: Zelnorm (Novartis) and Amitiza (Takeda).

Table 5: Compounds available or under development for CC and IBS-C

Name	Indication	Company	Development stage
Guanylate cyclase activators			
Linaclotide	CC, IBS-C	Ironwood	Phase 3
Chloride channel activators			
Amitiza	CC, IBS-C	Sucampo/Takeda	Launched 2006 (CC)/2008 (IBS-C)
5-HT4 receptor agonists			
Zelnorm	CC, IBS-C	Novartis	Withdrawn (2007)
Resolor	CC	Movetis	Launched 2010 (EU only)
TD-5108	CC	Theravance	Phase 2
ATI-7505	CC	ARYx	Phase 2

Source: Company reports

Assessing the Market: The Zelnorm History

Zelnorm (tegaserod), a partial agonist at the 5-hydroxy-tryptamin-4 (5-HT4) receptor, was approved in 2002 by the FDA for the treatment of women with IBS-C for up to 12 weeks. In August 2004, Zelnorm's label was expanded to include the chronic treatment of both men and women below the age of 65 who have chronic idiopathic constipation. In 2006, Zelnorm recorded WW sales of $561M, with the bulk of this coming from the US. At that time Zelnorm was seeing strong annual volume growth, and it was expected to exceed $1B in sales by the end of the decade.

Safety Led to Zelnorm's Downfall

In March 2007, a meta-analysis of 29 short-term (1 to 3 month) randomized, controlled trials found an increased number of cardiovascular adverse events in patients treated with Zelnorm, with 13 confirmed events in Zelnorm treated patients and 1 confirmed event for placebo (0.1% vs. 0.01%). Novartis withdrew the compound from the market at the FDA's request.[11] Currently, Zelnorm is only available through the FDA under an emergency investigational drug protocol.

Absorption Likely Played a Role

Zelnorm was well absorbed systemically (i.e., not specific to the gut). This was not initially obvious as a safety risk, but 5-HT4 receptors are located in various regions of the body including the central nervous system, the entire digestive system, the

[10] Drossman *et al., J. Clin Gastroenterology* (2009)
[11] http://www.fda.gov/Drugs/DrugSafety/PublicHealthAdvisories/ucm051284.html

bladder, and, importantly, the heart. Hence, it appears likely that the broad systemic absorption of Zelnorm played a role in the cardiovascular events seen in the meta-analysis.

Physicians and Patients Generally Liked Zelnorm

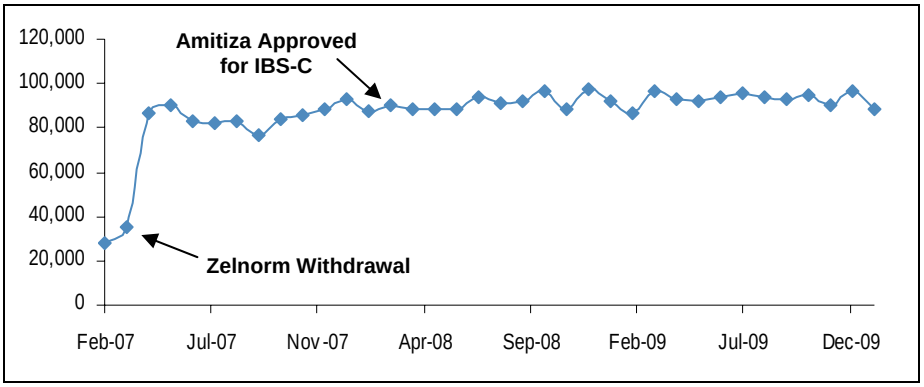
Physicians and patients were generally pleased with Zelnorm's efficacy, with one physician indicating that "20% of patients wished they could still take it, even with the cardiovascular risks." Importantly, Zelnorm established the market for IBS-C and CC and showed that with the right agent and the right strategy, the market opportunity could be quite large. However, it is important to point out that physicians indicated to us that the high profile withdrawal of Zelnorm "could slow down the PCP evolution" for linaclotide, though we believe that over time as experience and the safety database grow, PCPs will become a key component of linaclotide utilization.

Assessing the Market: Amitiza Today

Amitiza, a type-2-chloride channel (ClC) activator, was approved in January 2006 by the FDA for the treatment of chronic constipation in men and women at doses of 24 mcg BID. In April 2008, the FDA subsequently approved Amitiza at a dose of 8 mcg BID for the treatment of women who have irritable bowel syndrome with constipation (IBS-C). Although efficacious in treating chronic constipation, Amitiza has not been received well by IBS-C patients. In fact, abdominal discomfort/pain improved only transiently and it has been associated with many other adverse reactions such as abdominal distension/pain, diarrhea, and nausea.

So far, the sales trajectory of Amitiza has been disappointing. By way of comparison, Amitiza US sales in 2007 were $146M (this does not reflect the product's approval for IBS-C in 2008), and only $210M in 2008. Amitiza prescriptions accelerated following the Zelnorm withdrawal but remained almost steady thereafter, even after the subsequent approval in IBS-C (see Figure 1).

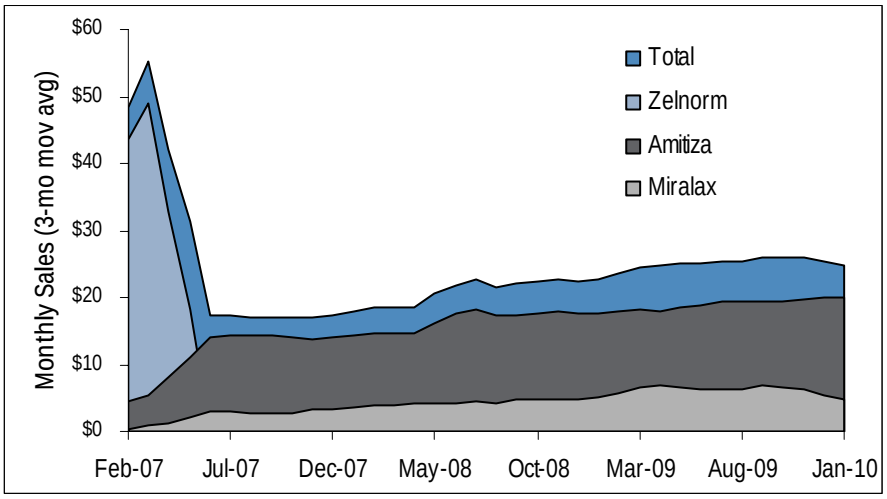
Figure 1: Amitiza Monthly TRx Trends (2007A-2009A)



Source: IMS Health

The 2007 withdrawal of Zelnorm from the US market created a significant void for patients and physicians. The total US sales of CC/IBS drugs declined from $48M per month in February 2007 to $25M per month in January 2010 (see Figure 4).

Figure 2: IMS Monthly Sales for CC and IBS-C Products (2007-2009A)
$ in millions



Source: IMS Health.

Linaclotide Differentiation

Linaclotide demonstrated favorable efficacy and safety results in phase 3 CC trials with statistically significant improvements across all endpoints. Importantly, in the IBS-C studies linaclotide showed a robust improvement in abdominal pain, an important unmet need in IBS-C. In our view, the clinical profile of linaclotide looks strong, and we expect positive phase 3 data in IBS-C in 4Q10. In light of the market opportunity and the clinical profile thus far for linaclotide, below we highlight what we believe are the key drivers of linaclotide differentiation.

Novel mechanism of action
Linaclotide binds specifically to GC-C receptor, a transmembrane protein located in intestinal epithelial cells. Its action is localized to the gut with minimal systemic exposure, meaning less potential for off-target toxicity. Linaclotide has no effect on the serotonin system, unlike Zelnorm, Propulsid, or Lotronex, each of which work through serotonin receptors in the intestine that are also implicated in various other organs of the body, which consequently resulted in serious safety issues.

Unmet need
There is a significant unmet need for better treatments for IBS-C and CC. Amitiza is the only FDA approved treatment available, and it has had minimal commercial success, particularly in IBS-C patients. Amitiza is associated with various adverse events (shortness of breath, nausea, worsening upper GI symptoms) and is not very helpful in reducing pain. Currently, physicians indicate that “Amitiza is used mostly just to manage flares, but even there it is not very effective.” Hence, physicians and patients still seek new treatment options that are effective.

Multi-symptom improvement and well tolerated
In phase 2b and phase 3 studies linaclotide showed compelling trends for improvement across all endpoints including abdominal pain, discomfort, bloating, and constipation symptoms. Importantly, linaclotide looks quite safe and well

tolerated, which could drive broad adoption in both the gastroenterology and primary care settings. In the two recent phase 3 CC trials, the most common treatment-emergent adverse event was diarrhea (12% to 20% of patients vs. 3% to 7% for placebo).

Pain arguably the most important differentiator
Given that pain is the biggest unmet need in IBS-C, we think the pain benefit seen with linaclotide in the phase 2b IBS-C studies could be a key point of differentiation. Notably, Amitiza and Zelnorm both showed a benefit on pain, but Amitiza only showed a modest improvement over placebo at week 12 on a larger 7 point severity scale (-0.45 vs. -0.36, p=0.028), and according to physicians this is not clinically meaningful. As a comparator, in phase 2b linaclotide IBS-C trials, the 300 mcg linaclotide arm demonstrated a highly significant reduction in abdominal pain on a smaller 5 point severity scale (-0.90 vs. -0.49, p<0.001). Even Zelnorm, which had much better commercial success than Amitiza has seen, only saw a pain benefit (defined as a 1 point reduction from baseline to week 12) in 1-10% of patients in phase 3 studies. We would expect linaclotide to see a much greater improvement considering it showed a mean reduction of -0.90 on a smaller scale at 12 weeks.

Rapid treatment effect . . .
Linaclotide showed a clinical response within 1-3 days and a sustained benefit throughout the treatment period (12 weeks plus the 4 week randomized withdrawal period) without any evidence of rebound below baseline after discontinuation in the 4-week follow-up period. This is important because our talks with physicians have indicated that one of the disappointments with Amitiza is that it fails to show immediate relief, which leads to a lack of compliance.

. . . But also likely to be used chronically
Ironwood is seeking a label for chronic use in IBS-C and CC patients. This should be supported by the longer duration 26 week '302 study in IBS-C patients as well as long-term safety data. This will be an important area of differentiation from Amitiza, which is generally used sporadically with poor compliance. Even Zelnorm was generally only used for 3-month durations. Hence, a critical upside lever to linaclotide estimates could come from longer treatment duration.

Summary of Physician Feedback

In order to assess the sentiment toward linaclotide, we spoke to many physicians in high volume CC and IBS-C practices, including linaclotide investigators as well as GI specialists in the community who were less familiar with linaclotide. Overall, the gastroenterologists with whom we spoke were encouraged with the overall benefit-risk profile of linaclotide and expect to use it in patients as soon as it is approved. The commentary appears quite encouraging and supportive of the assumptions in our US market model. Below are a few of the quotes that we thought were interesting:

- **"The phase 2b data in IBS-C are a good start since there is a significant improvement in pain symptoms and bloating. I would expect linaclotide to show a pain benefit in phase 3 as well."**
- "GI disorders have many overlapping symptoms. Sometimes I am not even able to pin down a diagnosis in 6 months. Abdominal pain/discomfort is the major differentiator between IBS and CC, but not the only one."

- **"There is a great unmet need, especially in moderate to severe patients; 50% of my IBS-C patients are not satisfied with current treatment options.** We desperately need a drug; there are just no good medications available."
- "The 4 week follow up data suggest that linaclotide is efficacious and safe enough to use and can be prescribed for long term use."
- "Although I am disappointed that linaclotide doesn't work in the upper GI tract, it does not worsen the upper GI symptoms either, unlike Amitiza. It is kind of neutral; no benefit, no deterioration. Moreover, we can't expect these drugs to work for both upper and lower GI disorders."
- **"It's hard to comprehend the atrial fibrillation SAEs observed in linaclotide studies; it could not be a drug related side effect.** The incidence is very low across treatment arms. I am not concerned,"
- **"The therapeutic gain is very low with Amitiza.** Lots of patients complain of pain; compliance is poor and there is no immediate relief."
- **"As a drug, Amitiza fails.** Acute shortness of breath is a serious side effect with it and patients are literally scared of using it. Nausea and diarrhea are other concerns. **I would switch 90-95% of my Amitiza patients to linaclotide, once available."**
- **"Linaclotide is safe enough to use even if it is mis-prescribed, at the worst the patient will get diarrhea."**
- "It will be wonderful if linaclotide works for both IBS-C and CC, but if not there is no reason to believe that it is a bad drug. Ideally, I believe, there is 80% probability that linaclotide will work well in IBS-C.**"**

Linaclotide: MOA and Clinical Data

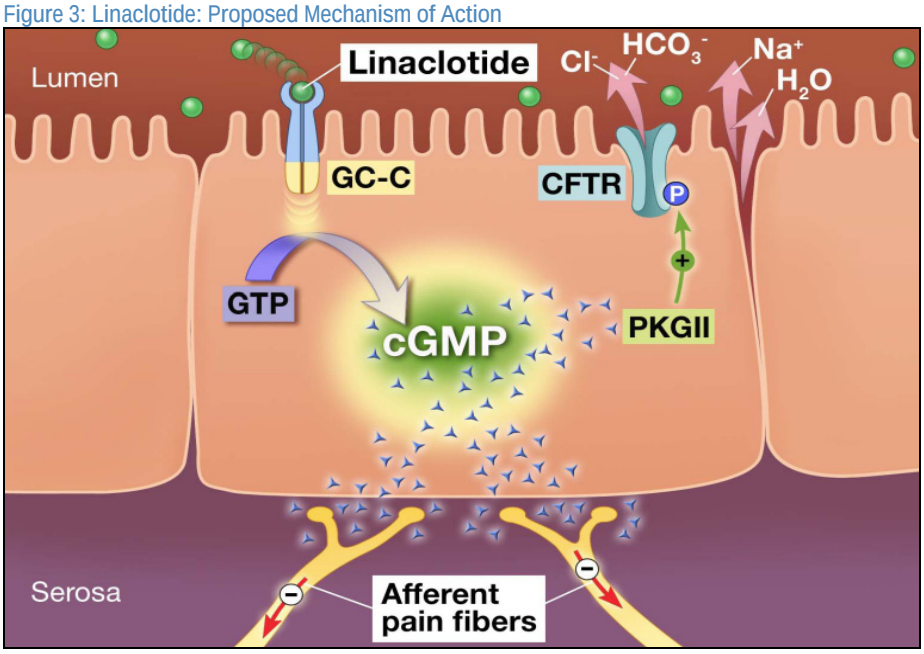
Mechanism of Action

Linaclotide is a 14 amino acid peptide agonist of guanylate cyclase type-C (GC-C). Linaclotide is minimally absorbed, which could be key for its safety profile as it implies localized activity in the intestine but not systemic exposure that could lead to a broad range of treatment-emergent adverse events. Preclinical studies validate that linaclotide's MOA is mediated through the GC-C receptor as the effects of the drug were lost in knock-out mice that lack the receptor. Importantly, GC-C is found only on the epithelial cells that line the intestine, which explains why, mechanistically, linaclotide is minimally absorbed and should be safe for gastrointestinal disorders without fear of off-target toxicity.

Once the GC-C receptors are activated, cyclic guanosine monophosphate (cGMP) is increased, which then activates specific ion channels such as the cystic fibrosis transmembrane conductance regulator (CFTR). This drives increased fluid secretion in the intestinal lumen where digested food passes through. This essentially provides lubrication for the digestive process to continue to completion. Importantly, cGMP also can exit the epithelial cells and decrease visceral sensitivity by blocking the afferent pain fibers that connect the GI tract to the central nervous system. Hence, mechanistically it is logical that linaclotide should have a true impact on both CC and

IBS-C, with a potential impact on abdominal pain, which could differentiate it in the eyes of physicians.

Figure 3: Linaclotide: Proposed Mechanism of Action



Source: Company reports.

Linaclotide's role in reducing abdominal pain (the major component of IBS-C) has been further detailed in various preclinical studies. Linaclotide dose dependently stimulated intestinal secretion and accelerated intestinal transit in rats with no adverse effects noted in the therapeutic dose range. Moreover, linaclotide (0.3 mcg/kg) significantly reduced the abdominal contractile response to colorectal distension following trinitrobenzene sulphonic acid-induced colonic inflammation and induced stress.[12] These findings further suggest that linaclotide may influence visceral hypersensitivity.

Linaclotide Clinical Data Overview

Ironwood is conducting multiple trials for linaclotide in over 4,800 patients and healthy volunteers. The key completed, ongoing, and planned trials are listed in Table 5. Four of the phase 2 studies in IBS-C and CC, and two phase 3 studies in CC have been completed. Data is anticipated from the last two phase 3 studies in IBS-C in 4Q10. We are optimistic ahead of the phase 3 data in IBS-C in 4Q10 given the strong activity seen in prior phase 2 studies. Additionally, two long-term studies to assess the long-term safety profile of linaclotide over 6 to 12 months and longer are currently enrolling.

[12] Eutamene *et al., Neurogastroenterol Motil;* 22: 312-e84 (2010)

Table 5: Linaclotide Clinical Development

Trial	N	Setting	Phase	General Design	Geography	Status
MCP-103-004	42	CC	Ph 2a	Dose-finding study: tested 100, 300 and 1000mcg	US, Canada	Completed
MCP-103-201	310	CC	Ph 2b	Randomized, double blind pbo cont study for 12 wks: Pbo/75mcg/150mcg/300mcg/600mcg QD	US, Canada	Completed
MCP-103-005	36	IBS-C	Ph 2a	Dose-finding study: tested 100mcg and 1000mcg	US, Canada	Completed
MCP-103-202	419	IBS-C	Ph 2b	Randomized, double blind pbo cont study for 12 wks: Pbo/75mcg/150mcg/300mcg/600mcg QD	US, Canada	Completed
LIN-MD-01	633	CC	Ph 3	Randomized, double blind pbo cont study for 12 wks: Pbo/133mcg/266mcg QD (1:1:1)	US, Canada	Completed
MCP-103-303	643	CC	Ph 3	Randomized, double blind pbo cont study for 12 wks followed by 4 wk randomized withdrawal period: Pbo/133mcg/266mcg QD (1:1:1)	US, Canada	Completed
MCP-103-302	800	IBS-C	Ph 3	Randomized, double blind pbo cont study for 26 wks: Pbo/266mcg QD (1:1)	US, Canada	Data 4Q10e
LIN-MD-31	800	IBS-C	Ph 3	Randomized, double blind pbo cont study for 12 wks followed by 4 wk randomized withdrawal period: Pbo/266mcg QD (1:1)	US, Canada	Data 4Q10e
LIN-MD-02	1200	CC, IBS-C	Safety study	Non-randomized, open label, uncontrolled study	US, Canada	Enrolling
MCP-103-305	1300	CC, IBS-C	Safety study	Non-randomized, open label study	US, Canada	Enrolling

Source: Company reports, clinicaltrials.gov and J.P. Morgan estimates.

CC: Efficacy Data Quite Compelling

Phase 3 Trial Design

Ironwood carried out two phase 3 CC trials – '01 and '303 – that enrolled a total of 633 and 643 patients, respectively, all of which met the modified Rome II criteria for CC. The placebo-controlled, double-blind trials tested two doses in each trial (133mcg/d and 266mcg/d) across 200 centers in the US and Canada. Trial '01 included a two-week pretreatment baseline period and a 12-week treatment period. Trial '303 was identical to trial '01 in design except that it also included a four-week randomized withdrawal period. The baseline characteristics are highlighted in Table 6 below and indicate a moderate to severe CC population.

Table 6: Key Phase 3 Baseline Characteristics

Mean Values	Trial 303 (n=642)	Trial 01 (n=630)
CSBMs/ week	0.2 - 0.3	0.3
SBMs/ week	2.0 – 2.1	1.8 – 1.9
Stool Consistency^	2.4 – 2.5	2.3 – 2.4
Severity of Straining*	3.2 – 3.3	3.2 – 3.3
Abdominal Discomfort*	2.5	2.5 – 2.6
Bloating*	2.7 – 2.8	2.7 – 2.8
Constipation Severity*	3.2 – 3.3	3.3

Source: Company Reports ^ 7 point BSFS, * 5 point scale (none- very severe)

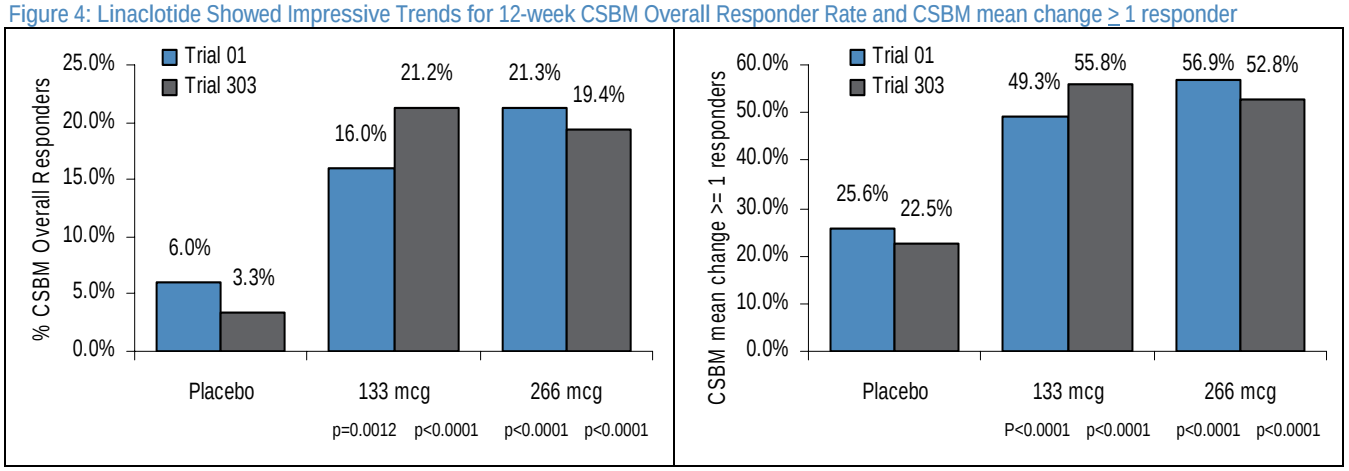
The primary efficacy endpoint was the percent of patients who were 12-week CSBM overall responders, defined as a patient who had three or more CSBMs per week and an increase of at least one CSBM per week over baseline for at least nine of the 12 weeks of the treatment period. During the baseline period, 72% of patients had no CSBMs. The key secondary endpoints included change from baseline in 12-week overall CSBM frequency rate, stool consistency, abdominal discomfort, bloating, constipation severity, and straining.

Robust, Consistent and Statistically Significant Efficacy

In both phase 3 trials, linaclotide met all 32 primary and secondary endpoints, showing robust and highly statistically significant improvements in abdominal

symptoms such as bloating and discomfort in addition to other constipation symptoms. In the two phase 3 studies, the 12-week CSBM overall responder rate (primary endpoint) was 16-21% in the 133 mcg linaclotide group and 19-21% in the 266 mcg linaclotide group. All of these were highly significant, representing a 3- to 6-fold increase when compared to the placebo group, which showed a 3-6% responder rate (see Figure 4). Additional endpoints of CSBM mean change ≥ 1 responder and CSBM rate ≥ 3 responder were also statistically significant at both the 133 mcg and 266 mcg dose levels.

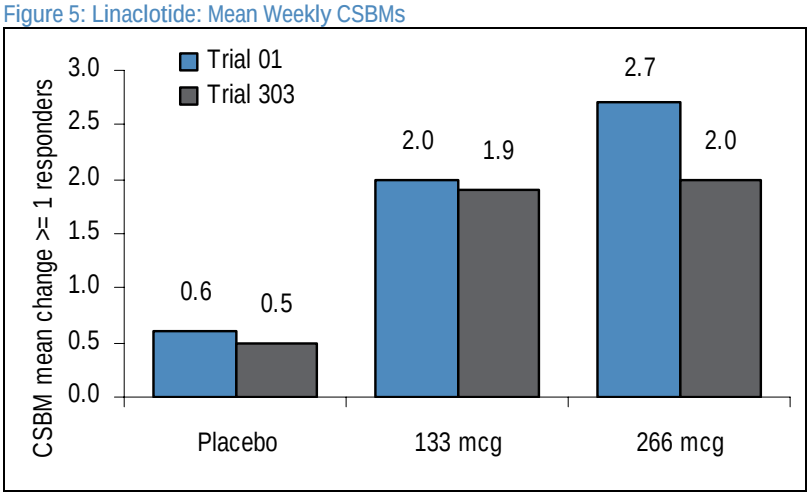
Figure 4: Linaclotide Showed Impressive Trends for 12-week CSBM Overall Responder Rate and CSBM mean change ≥ 1 responder



Source: Company reports.

Linaclotide-treated patients also demonstrated a significant increase in average weekly CSBMs (secondary endpoint) from baseline (0.5-0.6 for placebo; 1.9-2.0 for 133 mcg, p<0.0001; 2.0-2.7 for 266 mcg, p<0.0001) (see Figure 5).

Figure 5: Linaclotide: Mean Weekly CSBMs



Source: Company reports

As seen in Figure 6, increase in stool frequency occurred in the first week and was sustained over the 12 weeks of treatment. Importantly, during the 4 week randomized withdrawal period, the removal of linaclotide did not appear to make patients worse than baseline, and in fact there appeared to be a sustained benefit over baseline. Additionally, patients initially enrolled in the placebo group showed rapid

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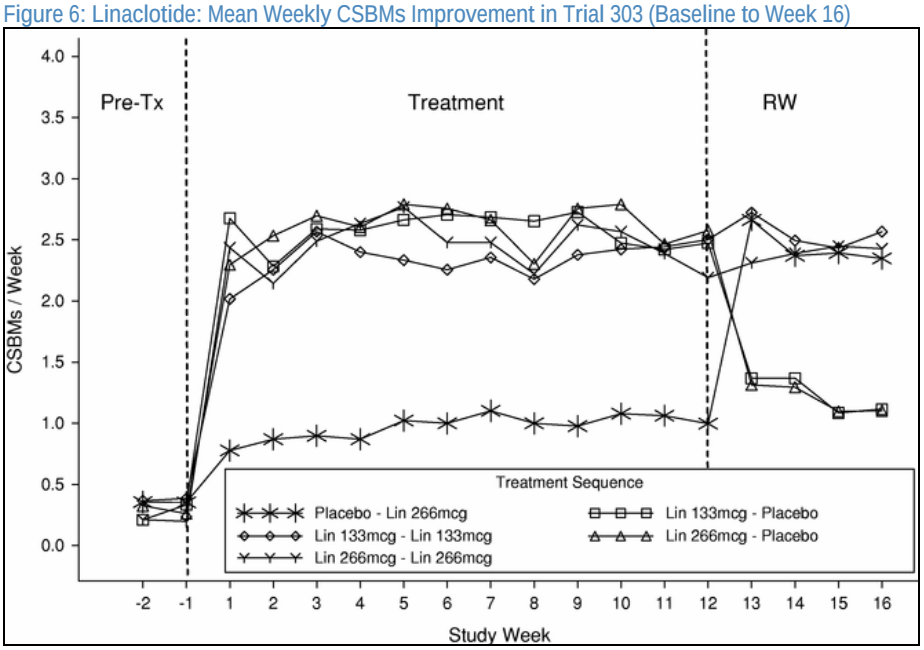
improvements when placed on linaclotide, with efficacy that was similar to the linaclotide treatment group.

Figure 6: Linaclotide: Mean Weekly CSBMs Improvement in Trial 303 (Baseline to Week 16)



Source: Company reports

Linaclotide also showed statistically significant improvements ($p<0.001$) over 12 weeks on all other key secondary endpoints, including stool consistency, abdominal discomfort, bloating, constipation severity, and straining (see Table 5). Baseline values for these endpoints ranged from 2.5 to 2.6 for abdominal discomfort, 2.7 to 2.8 for bloating, 3.2 to 3.3 for constipation severity, 2.3 to 2.5 for stool consistency, and 3.2 to 3.3 for straining severity.

Table 5: Improvement as % change from baseline at week 12 in ITT population

		Placebo	133 mcg	266 mcg
Abdominal discomfort	Trial 01	19.5%	31.1%	33.5%
	Trial 303	21.1%	32.9%	30.3%
Bloating	Trial 01	13.0%	24.3%	27.3%
	Trial 303	13.2%	26.9%	22.0%
Constipation severity	Trial 01	14.4%	40.2%	42.7%
	Trial 303	13.9%	40.5%	37.2%
Stool consistency	Trial 01	25%	75.0%	83.3%
	Trial 303	25%	79.2%	75.0%
Straining severity	Trial 01	18.5%	33.8%	36.9%
	Trial 303	15.4%	33.8%	36.9%

Source: Company reports

CC: Safety Profile Appears Clean

Overall, the safety findings in the randomized phase 3 trials of linaclotide are encouraging, in our view. Across both trials, diarrhea was the most common AE in the treatment period, and the AEs seen did not appear to be dose related (see Table

7). The numbers of serious adverse events (SAEs) were low at 2% in both studies, and there was no apparent difference between the linaclotide and placebo groups. Overall, we think the safety profile looks quite clean, which could be a key differentiating factor when compared with other CC therapies.

Table 7: Treatment Emergent Adverse Events

		Linaclotide		
	Placebo (n=209)	133 mcg (n=217)	266 mcg (n=217)	All (n=434)
Trial 01				
SAE	5 (2%)	4 (2%)	4 (2%)	8 (2%)
Any TEAE	116 (54%)	138 (65%)	116 (57%)	254 (61%)
Diarrhea	6 (3%)	42 (20%)	30 (15%)	72 (17%)
Flatulence	13 (6%)	16 (8%)	13 (6%)	29 (7%)
Upper respiratory tract infection	14 (7%)	16 (8%)	9 (4%)	25 (6%)
Abdominal pain	5 (2%)	11 (5%)	11 (5%)	22 (5%)
Nausea	7 (3%)	8 (4%)	9 (4%)	17 (4%)
Abdominal distension	7 (3%)	7 (3%)	8 (4%)	15 (4%)
Urinary tract infection	8 (4%)	8 (4%)	6 (3%)	14 (3%)
Sinusitis	5 (2%)	8 (4%)	4 (2%)	12 (3%)
Nasopharyngitis	7 (3%)	3 (1%)	8 (4%)	11 (3%)
Trial 303				
SAE	4 (2%)	3 (1%)	7 (3%)	10 (2%)
Any TEAE	105 (50%)	122 (56%)	119 (55%)	241 (56%)
Diarrhea	14 (7%)	27 (12%)	30 (14%)	57 (13%)
Headache	8 (4%)	7 (3%)	10 (5%)	17 (4%)
Flatulence	9 (4%)	8 (4%)	8 (4%)	16 (4%)
Nausea	8 (4%)	7 (3%)	9 (4%)	16 (4%)
Abdominal distension	3 (1%)	8 (4%)	7 (3%)	15 (3%)
Abdominal pain	8 (4%)	6 (3%)	9 (4%)	15 (3%)
Nasopharyngitis	6 (3%)	6 (3%)	9 (4%)	15 (3%)
Sinusitis	3 (1%)	5 (2%)	7 (3%)	12 (3%)
Abdominal pain upper	3 (1%)	7 (3%)	3 (1%)	10 (2%)

Source: Company reports

Safety concerns heightened following Zelnorm withdrawal

Only two drugs have been approved by the FDA for IBS-C and CC: Zelnorm (Novartis) and Amitiza (Takeda). Zelnorm was withdrawn at the FDA's request on March 30, 2007,[13] due to cardiovascular concerns after roughly 4.5 yrs on the market. The FDA indicated concern over a higher incidence of cardiovascular side effects in patients receiving Zelnorm versus comparator arms (0.1% vs. 0.01%). Zelnorm was reintroduced 4 months later, but under severe marketing and prescribing restrictions (an emergency treatment protocol) that prohibits use in most patients. This recent FDA stance has prompted scrutiny over the cardiac serious adverse events in linaclotide phase 2 trials. However, we believe this concern is unfounded as there is no indication of cardiac toxicity in the phase 3 studies. The incidence of atrial fibrillation (the only observed CV SAE) was low and looked numerically better in the linaclotide group (placebo: 0.96%, linaclotide: 0.46%).

IBS-C: Phase 2 Data Set the Stage for Solid Phase 3 Data

Ironwood announced positive phase 2 data in IBS-C in October 2008. The placebo-controlled, double-blind, dose-range-finding phase 2b trial enrolled 420 IBS-C patients and evaluated four doses of linaclotide (75, 150, 300 and 600mcg/d). Upon enrollment, patients had a two-week pre-treatment baseline period, a 12-week

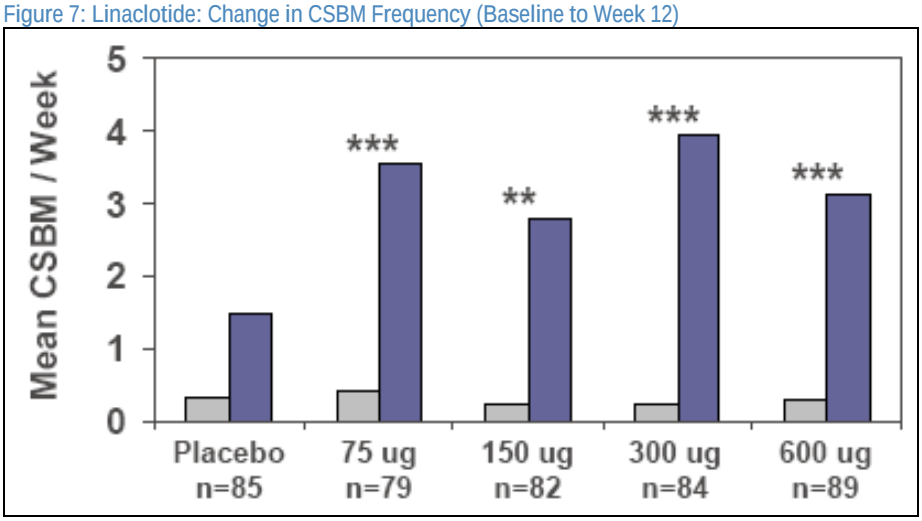
[13] http://www.fda.gov/Drugs/DrugSafety/PublicHealthAdvisories/ucm051284.html

treatment, and a two-week post treatment period. The primary endpoint was change in weekly CSBM frequency from baseline to week 12. The key secondary endpoints included change from baseline in other bowel symptoms, daily abdominal symptoms, and weekly global severity assessments.

Efficacy

Linaclotide showed impressive improvements in CSBM frequency compared with placebo, with the 75, 150, 300, and 600 mcg groups showing improvements over baseline of 2.90, 2.49, 3.61, and 2.68 CSBMs/week compared with placebo at 1.01 (see Figure 7).

Figure 7: Linaclotide: Change in CSBM Frequency (Baseline to Week 12)



Source: Company reports: Note: * = p<0.05, ** = p<0.01, *** = p<0.001

While CSBM frequency is important, the even more compelling efficacy data from this study relate to pain. For an IBS-C patient, pain tends to be the most difficult component of the disease to manage, and according to physicians this is by far the biggest unmet need. Pain was measured using a scale from 1 to 5, with 5 being the most severe pain. As can be seen in Figure 8, abdominal pain was significantly reduced compared with placebo at all doses (-0.7 to -0.9 change from baseline vs. placebo at -0.5; p = 0.024 to <0.0001), with the biggest improvement coming from the 300 mcg group. Additionally, in the 26% of patients with severe/very severe baseline abdominal pain, improvement was even more pronounced (-0.8 to -1.3 vs. placebo at-0.3). Moreover, the treatment effect of linaclotide was rapid (within the first week of treatment) and was maintained throughout the entire 12 week treatment period without a worsening of clinical effects following the cessation of treatment.

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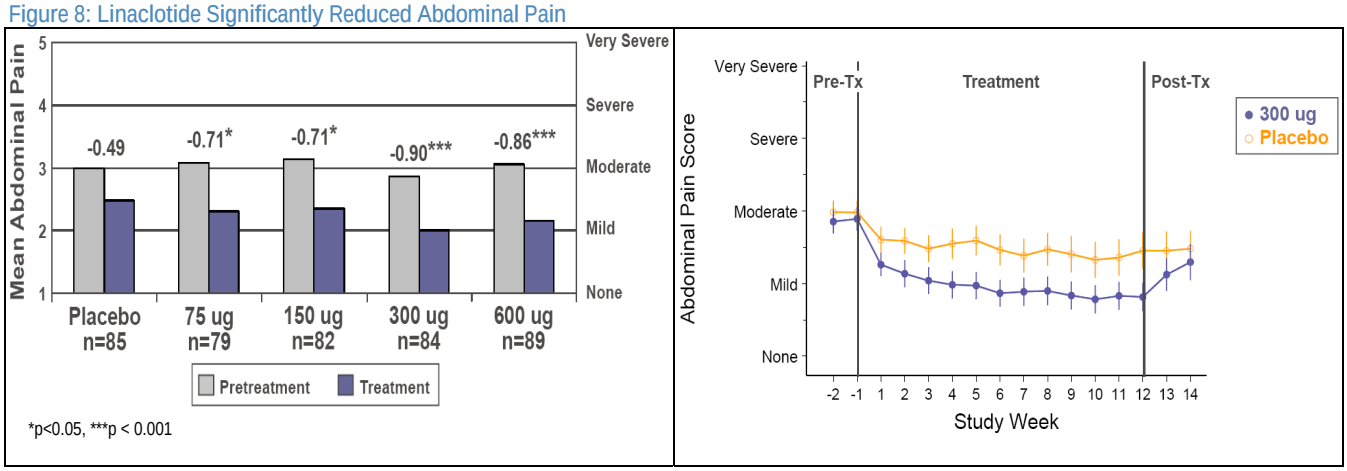
Figure 8: Linaclotide Significantly Reduced Abdominal Pain



Source: Company reports.

Linaclotide also demonstrated significant improvements in other bowel related endpoints, including CSBM frequency, stool consistency, straining, abdominal discomfort, bloating, and IBS symptom severity (see Table 8). In particular, the 300 mcg dose (266 mcg active linaclotide) being assessed in phase 3 showed the most dramatic improvements, hitting statistical significance across all endpoints.

Table 8: Improvement as % change from baseline at week 12 in ITT population

	Placebo (n=85)	75 mcg (n=79)	150 mcg (n=82)	300 mcg (n=84)	600 mcg (n=89)
Abdominal pain	25.6%	37.1%	36.9%	46.8%	44.4%
Abdominal discomfort	22.1%	31.3%	32.5%	42.7%	38.6%
Bloating	16.1%	27.3%	25.5%	37.3%	31.6%
IBS severity	22.2%	35.0%	34.1%	42.1%	41.0%
Constipation severity	23.3%	42.3%	41.1%	53.8%	48.8%

Source: Company reports

Safety/Tolerability

Linaclotide was well tolerated at all doses with no treatment related serious adverse events. The most common adverse event was diarrhea (11-18% of patients); however, there were no associated dehydration or electrolyte abnormalities (see Table 9). Diarrhea resulted in the discontinuation of 1% to 7% of linaclotide treated patients and none of the placebo treated patients. Other TEAEs appeared to be similar across the arms of the study.

Table 9: Treatment Emergent Adverse Events

		Linaclotide				
	Placebo (n=85)	75 mcg (n=79)	150 mcg (n=83)	300 mcg (n=85)	600 mcg (n=89)	All (n=335)
Any TEAE	41%	52%	49%	59%	69%	57%
Diarrhea	1%	11%	12%	16%	18%	15%
Abdominal pain	4%	5%	4%	5%	8%	5%
Upper tract infection	2%	9%	1%	6%	1%	4%
Nausea	6%	1%	10%	1%	3%	4%
Upper respiratory tract infection	4%	0%	2%	5%	6%	3%
Sinusitis	2%	4%	2%	4%	2%	3%
Bronchitis	0%	3%	1%	1%	3%	2%
Back pain	1%	0%	5%	1%	1%	2%
Fecal incontinence	0%	0%	1%	0%	3%	1%

Source: Company reports

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Phase 3 IBS-C: Trial Design

Ironwood and Forest are conducting two phase 3 trials of linaclotide in IBS-C (Trial 302 and Trial 31), with data likely to read out in 4Q10. In our view, these data will be the most important clinical catalyst for IRWD shares in 2010.

In both randomized, double-blind, placebo-controlled trials, patients will be randomized 1:1 to receive placebo or 266 mcg QD linaclotide. Trial 31 includes a 12-week treatment period followed by a four-week randomized withdrawal period, and enrollment of the expected 800 IBS-C patients is complete. Enrollment of the 800 patients in trial 302 is also complete, and the important characteristic of this study is that it includes a 26-week treatment period, which should help characterize the efficacy of linaclotide over time and also give physicians comfort using the agent for extended durations.

Both studies have three primary efficacy endpoints: 1) CSBM responder at 12 weeks ($\geq$3 CSBMs/week and an increase of $\geq$1 CSBM over baseline for $\geq$9 of 12 weeks); 2) abdominal pain responder at 12 weeks ($\geq$30% relative reduction in abdominal pain over baseline for $\geq$9 of 12 weeks); and 3) patients who are both pain and CSBM responders. Of note, the pain scale in phase 3 was increased from 1 to 5 to 0 to 10, which should allow for increased sensitivity of changes in pain. Secondary endpoints include CSBM frequency, stool consistency, straining, abdominal discomfort, and bloating.

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Linaclotide: Commercial Considerations

We are assuming an NDA filing in the US in 1H 2011 for both CC and IBS-C, with approval and launch by Ironwood and Forest expected around mid 2012. In Europe, our model assumes an MAA filing for IBS-C in 2H 2011 and approval and launch by partner Almirall in 1H 2013. Ironwood receives a royalty on EU sales beginning in the low 20% and reaching 35% (and potentially higher) at peak. Our model excludes any economics from the Asian linaclotide opportunity (CC or IBS-C), which is being led by Astellas. This is due to uncertain launch timelines and a regulatory path that potentially may require additional studies in Asian populations. Overall, our peak sales forecast in the US is in 2025 (final year of IP protection) with close to $3B in the model, and our peak opportunity in the EU is assumed in 2024 (final year of IP protection) with sales of $1.8B.

Aside from upside to our current linaclotide forecasts based on greater uptake, additional sources of upside to our Ironwood model include:

- linaclotide sales in any pediatric indication in any geography
- linaclotide sales in opioid-induced or post-surgical induced constipation in any geography
- linaclotide sales in other GI disorders such as dyspepsia or GERD in any geography
- linaclotide sales in any emerging market geography such as South America, India, or Asian territories not covered by the Astellas agreement and
- as noted above, linaclotide sales in any indication in Asia by partner Astellas.

Partnerships

Ironwood has partnered linaclotide across the largest global pharmaceutical markets: Forest Labs in the US, Almirall in Europe, and Astellas in Asia. While these companies may not be at the top of the list when one thinks about major pharma partnerships, we think linaclotide matters economically to these partners, compared to partnerships with Big Pharma where the drug may not be a commercial focal point. From a P&L perspective, the US market with Forest has the highest impact for Ironwood, but the OUS partners also provide significant longer term value should linaclotide prove commercially successful in these markets.

Forest Labs
Ironwood entered into a partnership with Forest Labs in September 2007 to co-develop and co-market linaclotide in the US. Under the terms of the agreement, Ironwood and Forest share the cost of linaclotide clinical development and commercialization as well as the profits from linaclotide sales in the US market. Additionally, Forest has exclusive rights in Canada and Mexico and will pay Ironwood a royalty on sales (we estimate in the mid-20% range) in these countries. Forest has paid $125M in license fees and milestone payments to Ironwood thus far, and total payments could reach $330 million over the term of the collaboration, if linaclotide is successfully developed and commercialized in the US. Importantly, Forest still owes Ironwood $105M in pre-commercialization milestones, which we

estimate could come in 2011 and 2012. Overall, we view Forest as an attractive partner given their primary care infrastructure and sales force of 2,000+ reps.

Almirall

In April 2009, Ironwood signed a license agreement with Almirall, S.A. to develop and commercialize linaclotide throughout Europe for the treatment of IBS-C and other gastrointestinal conditions. Almirall has paid Ironwood $53M in near-term milestones with pre-commercial milestone payments totaling up to $40M. In addition, Ironwood will receive escalating royalties on linaclotide sales in Europe with overall economics that could approach that of the Forest partnership. Almirall is responsible for activities and expenses relating to regulatory approval and commercialization in the European market. To most investors, Almirall isn't a household name, but the company does have a formidable commercial presence in all of the large markets in Europe with 2009 sales of €925M (+2.5% y/y). It is worth pointing out that the MAA filing to the EMEA could occur by mid 2011, shortly after the NDA filing in the US, which could lead to a 2012 launch. Our model, however, formally assumes a 2013 launch.

Astellas

Ironwood signed a license agreement with Astellas Pharma in late 2009 to develop and commercialize linaclotide for the treatment of IBS-C and other gastrointestinal conditions in Japan, South Korea, Taiwan, Thailand, the Philippines, and Indonesia. Under the agreement, Astellas paid Ironwood an upfront payment of $30M, and Ironwood is eligible to receive another $43M in pre-commercial milestones and escalating royalties on linaclotide sales. Astellas is responsible for all activities and expenses relating to clinical development, regulatory approval, and commercialization in Asian territories highlighted above. In terms of the commercial impact on Ironwood, we have excluded sales in Asia or any of the Astellas territories from our model, but see it as a long-term upside driver. Quite often, a comparability study is needed in Asian populations for formal approval, which introduces clinical risk and delays approval timelines. Therefore, we've elected to exclude economics from this partnership in our Ironwood model.

Our Linaclotide Revenue Model

Our revenue model for Linaclotide includes the chronic constipation (CC) and irritable bowel syndrome with constipation (IBS-C) sales (see Table 8). Given the unmet need, we believe there is significant opportunity, and we forecast a $3B peak sales opportunity in the US in 2025.

Our US Assumptions

We conservatively assume 36M chronic constipation patients in the US by 2012, of whom around 25% seek medical care. Over 40% of patients are dissatisfied with traditional treatment options and look for alternate drug therapies. For IBS-C, we estimate 12.6M sufferers by 2012, of which 64% seek medical attention for their symptoms. Again, we conservatively assume nearly half are not satisfied and seek alternatives. We are assuming linaclotide CC product sales of $20M, $82M, $212M, and $373M in the first four years of launch (2012-2015), which reflects penetration rates of 3%, 6%, 10%, and 14%, respectively. Our IBS-C sales estimate for 2012-2015 are $9M, $46M, $150M, and $324M.

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Table 8: US Linaclotide Revenue Model

CC	2012E	2013E	2014E	2015E	2016E	2017E	2018E
Patients in thousands							
CC prevalence	36,061	36,421	36,785	37,153	37,525	37,900	38,279
Seeking Care	25%	25%	25%	25%	25%	25%	25%
Patients in care	9,015	9,105	9,196	9,288	9,381	9,475	9,570
Seeking alternatives	41%	41%	41%	41%	41%	41%	41%
Addressable population	3,696	3,733	3,770	3,808	3,846	3,885	3,924
Penetration	3%	6%	10%	14%	18%	21%	22%
Treated patients	111	224	377	533	692	816	863
Duration of therapy (days)	30	60	90	110	130	135	145
Price ($, daily)	6.00	6.12	6.24	6.37	6.49	6.62	6.76
Price ($, annual)	180	367	562	700	844	894	980
CC sales ($M)	20	82	212	373	585	730	846
		312%	158%	76%	57%	25%	16%

IBS-C	2012E	2013E	2014E	2015E	2016E	2017E	2018E
Patients in thousands							
IBS-C prevalence	12,570	12,695	12,822	12,951	13,080	13,211	13,343
Seeking Care	64%	64%	64%	64%	64%	64%	64%
Patients in care	8,045	8,125	8,206	8,288	8,371	8,455	8,539
Seeking alternatives	47%	47%	47%	47%	47%	47%	47%
Addressable population	3,741	3,778	3,816	3,854	3,893	3,932	3,971
Penetration	2%	4%	7%	12%	16%	20%	23%
Treated patients	75	151	267	462	623	786	913
	0	0	0	0	0	0	0
Duration of therapy (days)	20	50	90	110	130	135	145
Price ($, daily)	6.00	6.12	6.24	6.37	6.49	6.62	6.76
Price ($, annual)	120	306	562	700	844	894	980
IBS-C sales ($M)	9	46	150	324	526	703	895
		0%	225%	116%	62%	34%	27%
Total Linaclotide sales		128	362	697	1,110	1,433	1,741

Source: J.P. Morgan estimates.

Our OUS Assumptions

We have fairly conservative assumptions for Europe as we expect linaclotide use to be largely limited to the IBS-C population, with minimal uptake in CC patients. Indeed, we assume European sales will be $279M by 2015, which represents 40% of our US sales assumption. We currently forecast no Asian sales in our model as it is unclear at this time what studies will be required ahead of approval and how long these studies could take. Hence, we view Asia as a potential upside driver.

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J.P.Morgan

Our US Linaclotide P&L

To help understand the costs related to linaclotide, we created a linaclotide-specific P&L. We assume the gross margins for linaclotide will start at 90% and increase over time to 93% by 2018. As for R&D, we assume once linaclotide is launched in CC and IBS-C the ongoing R&D cost will decline from $15M in 2012 to $10M by 2018. Our R&D estimates exclude costs for label expansion studies, which we feel is reasonable as this is excluded from our revenue assumptions as well. SG&A will clearly be the biggest component of the linaclotide spend. We model a sales force of 1,000 reps, and given that the Forest reps will likely be promoting multiple products, we assume 2/3 of each rep will be attributed to linaclotide, implying $107M in selling costs in 2012 increasing to $159M by 2018. We then assume non-selling (i.e., marketing campaigns, etc) costs of $70M increasing to $94M by 2018, implying total SG&A costs of $177M in 2012 increasing to $253M by 2018. Our estimates imply the Linaclotide operating margin will increase from 27% in 2014 to 78% by 2018.

Table 9: Linaclotide P&L

($ in mil except per share data)	2012E	2013E	2014E	2015E	2016E	2017E	2018E
Linaclotide US sales		128	362	697	1,110	1,433	1,741
COGS	3	12	33	59	89	107	122
Gross Margin	90%	91%	91%	92%	92%	93%	93%
Gross Profit	26	116	329	638	1,022	1,325	1,619
R&D	15	15	13	13	11	11	10
R&D % of Sales	52%	12%	4%	2%	1%	1%	1%
Sales Reps	800	1,000	1,000	1,000	1,000	1,000	1,000
FTE on Average	67%	67%	67%	67%	67%	67%	67%
FTE Cost (thousands)	200	206	212	219	225	232	239
FTE Cost Increase	0%	3%	3%	3%	3%	3%	3%
Selling	107	137	141	146	150	155	159
Non-selling SG&A	70	74	77	81	85	89	94
Non-selling Increase	0%	5%	5%	5%	5%	5%	5%
SG&A	177	211	219	227	235	244	253
SG&A % of Sales	611%	164%	60%	33%	21%	17%	15%
Total Operating Expenses	195	238	264	299	335	362	385
0	0	0	0	0	0	0	0
Operating Profit	-166	-110	98	398	775	1,070	1,356
Operating Margin	0	0	27%	57%	70%	75%	78%

Ironwood US Linaclotide P&L							
($ in mil except per share data)	2012E	2013E	2014E	2015E	2016E	2017E	2018E
US Revenue	14	64	181	349	555	716	870
COGS	1	6	16	30	44	54	61
R&D	8	8	7	7	6	6	5
SG&A	88	105	109	113	118	122	127
Total Operating Expenses	97	119	132	150	167	181	192
Ironwood US Linaclotide Profit	-83	-55	49	199	388	535	678

Source: J.P. Morgan estimates.

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Financial Projections

P&L Highlights

Our forecasted revenues for 2010-15 are $35M, $110M, $95M, $150M, $249M, and $456M, respectively. We expect limited royalty revenue from EU sales of linaclotide, with the launch anticipated in 2013 and associated 2013-15 revenues of $10M, $33M, and $73M, respectively. We are not including any royalties from Asia, as of now. We forecast profitability in 2014, the second full year of linaclotide sales from both IBS-C and CC. Our projected 2010-15 EPS estimates are ($0.83), ($0.28), ($0.74), ($0.47), $0.17 and $1.45. We expect net operating loss carry-forwards will negate taxes throughout this timeframe (see Table 10).

Table 10: Ironwood Pharmaceuticals: Our Operating Model

($ in mill except per sh data)	2009E	2010E	2011E	2012E	2013E	2014E	2015E
US linaclotide sales	-	-	-	28.9	128.5	361.9	697.3
EU linaclotide sales	-	-	-	-	51.4	144.8	278.9
Asia linaclotide sales	-	-	-	-	-	-	-
WW linaclotide sales	-	-	-	28.9	179.9	506.7	976.3
Revenues							
Collab and service revenue	36.7	35.0	110.0	80.0	75.0	35.0	35.0
linaclotide JV (US)	-	-	-	14.5	64.2	181.0	348.7
linaclotide royalties (EU)	-	-	-	-	10.3	33.3	72.5
linaclotide royalties (Asia)	-	-	-	-	-	-	-
Total Revenues	36.7	35.0	110.0	94.5	149.5	249.2	456.2
Operating Expenses							
Cost of sales	-	-	-	1.4	6.1	16.3	29.6
R&D	78.4	85.0	65.0	63.0	65.0	70.0	75.0
SG&A	23.1	35.0	75.0	110.0	130.0	140.0	155.0
Total Operating expenses	101.5	120.0	140.0	174.4	201.1	226.3	259.6
Operating Income	(64.8)	(85.0)	(30.0)	(80.0)	(51.6)	23.0	196.6
Total Other Income	(0.3)	2.5	1.5	1.5	1.5	0.5	1.5
Pretax Income	(65.1)	(82.5)	(28.5)	(78.5)	(50.1)	23.5	198.1
Income tax (benefit)	-	-	-	-	-	-	-
Net Income (loss)	(65.1)	(82.5)	(28.5)	(78.5)	(50.1)	23.5	198.1
Non-GAAP EPS	(0.83)	(0.83)	(0.28)	(0.74)	(0.47)	0.17	1.45
Fully diluted shares outstanding	78.2	99.9	103.4	99.9	107.4	134.4	136.4

Source: Company reports and J.P. Morgan estimates.

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Balance Sheet and Cash Flow

As of September 30, 2009, Ironwood had $114M in cash, cash equivalents, and marketable securities, and following its IPO the company had $320M (see Table 11).

Table 11: Ironwood Pharmaceuticals: Projected Balance Sheet

($ in millions except per share data)	FY09E	FY10E	FY11E	FY12E
Assets				
Cash and cash equivalents	96.3			
Marketable Securities	17.6			
Total Cash and Marketable Securities	113.9	229.4	211.4	150.0
Accounts receivable	0.2	0.2	0.2	0.2
Related party accounts receivable	9.8	9.8	9.8	9.8
Prepaid expenses and other current assets	3.1	3.1	3.1	3.1
Forward purchase contracts	0.0	0.0	0.0	0.0
Total Current Assets	127.0	242.5	224.5	163.0
Property, plant & equipment, net	23.4	28.4	33.4	38.4
Restricted cash	8.4	8.4	8.4	8.4
Forward purchase contracts	0.0	0.0	0.0	0.0
Other assets	0.0	0.0	0.0	0.0
Total Long Term Assets	31.8	36.8	41.8	46.8
Total Assets	158.8	279.3	266.3	209.8
Liabilities and Equity				
Accounts payable	6.4	6.4	6.4	6.4
Accrued expenses	4.1	4.1	4.1	4.1
Accrued R&D	6.1	6.1	6.1	6.1
Current portion of LT debt	1.4	0.0	0.0	0.0
Current portion of deferred rent	0.2	0.0	0.0	0.0
Current portion of capital lease obligations	0.1	0.0	0.0	0.0
Deferred revenues	32.8	32.8	32.8	32.8
Total Current Liabilities	51.1	49.4	49.4	49.4
Long term debt, net of current portion	2.0	2.0	2.0	2.0
Deferred revenue, net of current	71.7	71.7	71.7	71.7
Capital lease obligations, net of current	0.1	0.0	0.0	0.0
Deferred rent, net of current	10.7	10.7	10.7	10.7
Convertible preferred stock	-	-	-	-
Total Long Term Liabilities	84.5	84.4	84.4	84.4
Total Liabilities	135.6	133.8	133.8	133.8
Total Shareholders' Equity	23.2	145.5	132.5	76.1
Total Liabilities and Equity	158.8	279.3	266.3	209.8

Source: Company reports and J.P. Morgan estimates.

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Cash Flows

Ironwood's cash flow has been dominated by incoming flows from the Forest, Almirall, and Astellas partnership deals, as well as the 2010 equity raise (see Table 12). We do not model further capital raises based on the strong current cash position, where, in our view Ironwood has sufficient cash to fund operations through FY2013, when cash flow from operations turns positive.

Table 12: Ironwood Pharmaceuticals: Projected Cash Flows

($ in millions except per share data)	FY09E	FY10E	FY11E	FY12E
Cash Flows from Operating Activities:				
Net Income	(65.1)	(82.5)	(28.5)	(78.5)
Depreciation and Amortization	3.9	5.0	7.5	10.0
Loss (gain) on PPE disposal	0.1	-	-	-
Remeasurement of forward purchase contracts	0.1	-	-	-
share-based comp expense	3.2	5.0	8.0	12.0
accretion of discount/premium on investment securities	0.2	-	-	-
Net change in Working Capital	27.0	-	-	-
Net Cash From Operations	(30.7)	(72.5)	(13.0)	(56.5)
Cash Flows from Investing Activities:				
PPE (net)	(5.0)	(15.0)	(5.0)	(5.0)
Proceeds from Sale/Maturities Mkt Sec.	30.9	-	-	-
Purchases of marketable securities available for sale	(26.7)	-	-	-
Other Investing	0.0	0.0	0.0	0.0
Net Cash from Investing	(0.8)	(15.0)	(5.0)	(5.0)
Cash Flows from Financing Activities:				
proceeds from issuance of preferred stock, net of costs	25.2	-	-	-
proceeds from issuance of common stock	0.0	203.0	-	-
proceeds from exercise of stock options and res stock	0.1	-	-	-
proceeds from sale of non controlling int in sub	0.0	-	-	-
proceeds from borrowings	(1.1)	-	-	-
Net Cash from Financing	24.2	203.0	0.0	0.0
Net Increase (Decrease) in Cash	(7.3)	115.5	(18.0)	(61.5)
Cash and cash equivalents at beginning of period	65.6	58.3	173.8	155.8
Cash and cash equivalents at end of period	58.3	173.8	155.8	94.4

Source: Company reports and J.P. Morgan estimates.

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Valuation

Our $18 December 2010 price target for IRWD shares is supported by our sum-of-the-parts analysis, which is based on the NPV of linaclotide profits in the US and future royalties from Almirall in Europe. We assign no value to the pipeline or royalties from Astellas on future linaclotide sales in Asia, where we see these as a long-term upside driver. Since we do not expect Ironwood to be profitable until 2014, we think a sum-of-the-parts analysis is a more reasonable valuation tool as opposed to comparable multiples.

We conducted our NPV analysis using a discount rate of 12% and probability adjusted our analysis by the risk we feel is associated with the linaclotide program. In our analysis, we assume a 75% probability of success for linaclotide, which we feel is appropriate given that the two phase 3 studies in CC are already complete, and the phase 3 studies in IBS-C are supported by strong phase 2b data. We assume the IP for linaclotide runs out in 2025 in the US and 2024 in the EU, and we assume no terminal value in our analysis. In addition, our comparables analysis supports our Overweight rating as IRWD shares are trading at a discount to the group on an EV/revenue and P/E multiple basis when we discount from 2015 to 2012.

Sum-of-the-Parts

Our sum of the parts suggests that linaclotide US is worth $11 per share, while linaclotide OUS is worth $4 per share. We assume net cash of $317M, or $3 per share. Taken together, our sum-of-the parts analysis supports our December 2010 price target of $18 (see Table 13).

Table 13: Sum-of-the-Parts Valuation

Sum of the Parts	Total	Per Share
Linaclotide – US	$1,303	$11
Linaclotide – OUS	$500	$4
Total Linaclotide	$1,804	$15
Net Cash	$317	$3
Total	$2,120	$18

Source: J.P. Morgan estimates.

Ironwood Derives Significant Value in the Outer Years

It is important to understand that we believe the Ironwood story is not one whose fate will be determined in the first few years of the launch, which is why we feel an NPV analysis is the best way to accurately capture the full area under the curve for linaclotide. Indeed, as is illustrated in Figure 9, the bulk of the contribution for our NPV analysis for Ironwood begins in 2015 and remains robust out to 2025. This is a function of the upfront costs related to the marketing effort for linaclotide, which should lay the foundation for strong growth in the outer years. Hence, we see the Ironwood story as one with significant longevity, which should serve to keep investors engaged over the long term.

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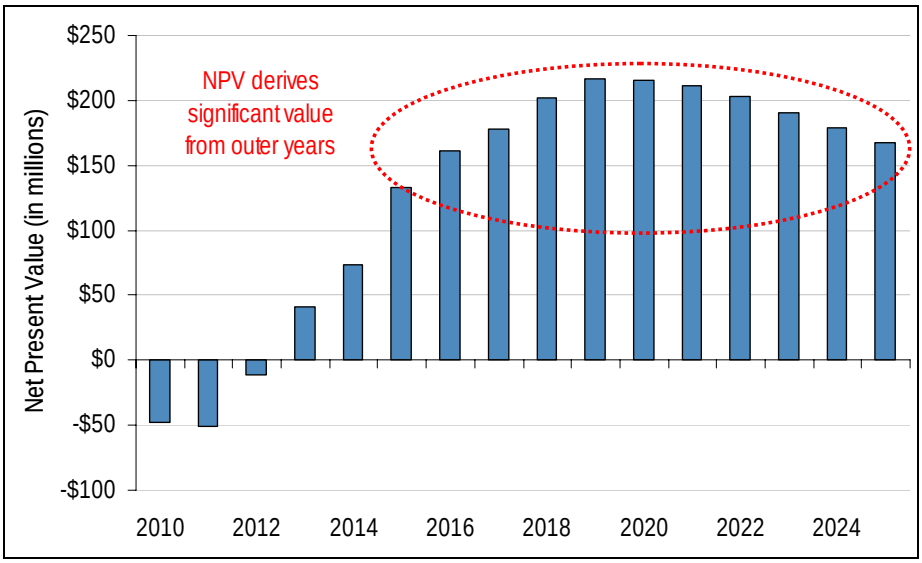
Figure 9: Ironwood NPV analysis over time



Source: J.P. Morgan estimates.

Comparable Company Analysis

We think IRWD shares are undervalued on the basis of EV/2012E revenues relative to comparable biotech companies and also on the basis of 2012E P/E. Indeed, when we discount our 2015 revenue and EPS estimates of $456M and $1.45 back to 2012 by 20%/year, this implies IRWD shares are trading at 3.6x on a EV/revenue basis compared with peers at 3.9x, and 16x on a P/E basis compared with peers at 23x. Hence, on both metrics IRWD shares are trading at a discount to peers, which further supports our Overweight rating (see Table 14).

Table 14: Comparative Valuation Analysis

Company	Ticker	JPM Rating	Price Mar 12, 2010	52-wk hi	52wk lo	Mkt Cap	EV	2012E Revs	2012E EPS	EV/2012E Revs	2012E P/E
Alexion	ALXN		52.84	54.08	32.26	4,832	4,666	813.9	2.94	5.7	18.0
Allos	ALTH	OW	7.90	8.79	5.34	806	648	247.2	0.40	2.6	19.8
Acorda	ACOR	OW	35.87	36.48	15.52	1,357	1,092	393.0	3.02	2.8	11.9
AMAG	AMAG	OW	35.98	58.23	29.67	619	539	184.0	0.85	2.9	42.6
Amylin	AMLN	N*	20.26	21.58	8.56	2,872	2,848	1230.2	0.97	2.3	20.8
BioMarin	BMRN	OW*	23.02	23.87	11.37	2,358	2,555	522.5	0.76	4.9	30.3
Human Genome	HGSI	OW*	32.64	33.13	0.68	5,572	5,451	1082.9	0.95	5.0	34.2
Onyx	ONXX	OW*	30.86	36.75	21.85	1,919	1,513	397.5	1.15	3.8	26.8
OSI	OSIP	N	57.68	57.84	27.01	3,705	3,437	581.7	2.25	5.9	25.6
Vertex	VRTX	OW	43.46	44.24	25.94	8,061	6,777	2144.5	3.95	3.2	11.0
United Therapeutics	UTHR	N	58.76	61.97	27.35	3,169	2,970	817.8	3.70	3.6	15.9
Mean						1,282	2,954			3.9	23.3
Ironwood**	IRWD	OW	12.91	13.58	11.2	1,257	941	264.0	0.80	3.6	16.1

Source: Company reports, Bloomberg, and J.P. Morgan estimates.
*Covered by Cory Kasimov. Prices as of Mar 12, 2010. Estimates for companies not covered are consensus estimates from Bloomberg.
**Ironwood 2012 Revenue and EPS based on 2015 estimates of $456M and $1.45 discounted to 2012 at 20%/year

Management

Peter M. Hecht, Ph.D.
CEO
Dr. Hecht has been CEO of Ironwood since the company was founded in 1998. Prior to founding Ironwood, Dr. Hecht was a research fellow at Whitehead Institute for Biomedical Research. Dr. Hecht serves on the boards of directors of Whitehead Institute and Microbia, Inc., a majority-owned subsidiary of Ironwood. He also serves on the Leadership Council for The David H. Koch Institute for Integrative Cancer Research at the Massachusetts Institute of Technology and the advisory board of Infante Sano.

Mark G. Currie, Ph.D.
Senior Vice President, R&D and Chief Scientific Officer
Dr. Currie has been with Ironwood since 2002 and leading Ironwood's R&D programs since then. Prior to Ironwood, Dr. Currie served as vice president of discovery research at Sepracor. Previously, Dr. Currie played a senior leadership role and also served as director of arthritis and inflammation at Monsanto Company.

Michael J. Higgins
Chief Operating Officer and Chief Financial Officer
Mr. Higgins has served as COO and CFO since 2003. Prior to Ironwood, Mr. Higgins served in several senior level positions at Genzyme Corporation, including vice president of corporate finance. He also serves on the board of directors of Microbia, a majority-owned subsidiary of Ironwood.

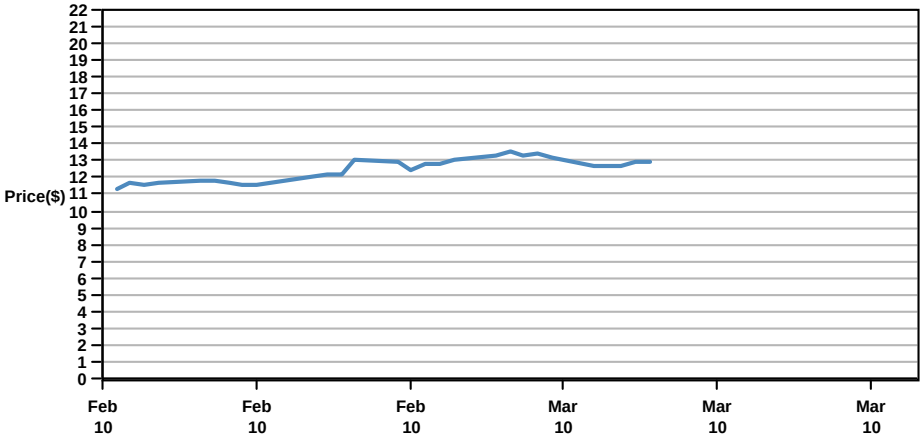
Thomas A. McCourt
Senior Vice President, Marketing and Sales and Chief Commercial Officer
Mr. McCourt has been with Ironwood since September 2009 and is the company's SVP of marketing and sales and CCO. Prior to Ironwood, Mr. McCourt worked at Amgen from April 2008 to August 2009, where he led the U.S. brand team for denosumab. Previously, Mr. McCourt also worked at Novartis AG, where he specifically worked in a senior commercial role on the launch of Zelnorm for IBS-C and chronic constipation.

Analyst Certification:
The research analyst(s) denoted by an "AC" on the cover of this report certifies (or, where multiple research analysts are primarily responsible for this report, the research analyst denoted by an "AC" on the cover or within the document individually certifies, with respect to each security or issuer that the research analyst covers in this research) that: (1) all of the views expressed in this report accurately reflect his or her personal views about any and all of the subject securities or issuers; and (2) no part of any of the research analyst's compensation was, is, or will be directly or indirectly related to the specific recommendations or views expressed by the research analyst(s) in this report.

Important Disclosures

- **Market Maker:** JPMSI makes a market in the stock of Ironwood Pharmaceuticals.
- **Lead or Co-manager:** JPMSI or its affiliates acted as lead or co-manager in a public offering of equity and/or debt securities for Ironwood Pharmaceuticals within the past 12 months.
- **Client of the Firm:** Ironwood Pharmaceuticals is or was in the past 12 months a client of JPMSI; during the past 12 months, JPMSI provided to the company investment banking services.
- **Investment Banking (past 12 months):** JPMSI or its affiliates received in the past 12 months compensation for investment banking services from Ironwood Pharmaceuticals.
- **Investment Banking (next 3 months):** JPMSI or its affiliates expect to receive, or intend to seek, compensation for investment banking services in the next three months from Ironwood Pharmaceuticals.

Ironwood Pharmaceuticals (IRWD) Price Chart



Source: Bloomberg and J.P. Morgan; price data adjusted for stock splits and dividends.
This chart shows J.P. Morgan's continuing coverage of this stock; the current analyst may or may not have covered it over the entire period.
J.P. Morgan ratings: OW = Overweight, N = Neutral, UW = Underweight.

Explanation of Equity Research Ratings and Analyst(s) Coverage Universe:
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