Ironwood Pharmaceuticals (IRWD)

Rating	**NEUTRAL* [V]**
Price (29 Jun 10, US$)	12.62
Target price (US$)	14.00[1]
52-week price range	14.78 - 0
Market cap. (US$ m)	1,127.69
Enterprise value (US$ m)	866.13

**Stock ratings are relative to the relevant country benchmark.*
[1]Target price is for 12 months.
[V] = Stock considered volatile (see Disclosure Appendix).

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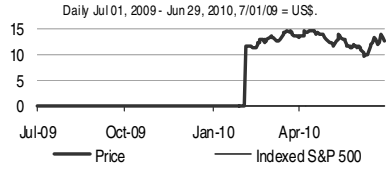
INITIATION

Initiating at Neutral; Linaclotide Best in Class Profile in Challenging Market

- **We are initiating coverage of Ironwood Pharmaceuticals with a Neutral rating and a $14 target price.** Our thesis is that linaclotide is a best in class prescription product with $1 billion U.S. potential in 2020, having further upside potential limited by challenging irritable bowel syndrome constipation predominant market (IBS-C), and chronic constipation (CC) dynamics, all of which are captured in the current stock price.
- **Credit Suisse's 100-physician survey supports our position that linaclotide has best in class profile.** At the 24 month (post approval) mark, physicians say they expect to apportion 50% more market share to linaclotide than competitor Amitiza in IBS-C and CC and that they will increase their share of prescription medications during this time.
- **The market potential for IBS-C and CC is big but not easy to secure.** Despite unmet medical needs for the more than 30 million patients with IBS-C or CC, barriers exist to product use. For instance, patients do not always seek treatment, cheaper front line options are used first and patient compliance is poor. The Credit Suisse survey revealed 80% of patients stop IBS-C and CC therapy for reasons other than symptom resolution. This may also drive the need for higher than expected commercial investment.
- **Our base case U.S. forecasts $1 billion in 2020, based on a 75% probability of success, with positive EPS in 2015 and beyond.**
- **The next key catalysts are likely to be positive but are largely discounted in the stock.** These include Phase III data for IBS-C (in the second half of 2010) and safety data (early 2011).
- **Valuation:** Our $14 target price is derived using a probability adjusted, sum of the parts; 79% of the valuation is derived from linaclotide (64% from the United States and 15% non-United States) and 21% from cash.

Share price performance



On 06/29/10 the S&P 500 index closed at 1041.24

Quarterly EPS	Q1	Q2	Q3	Q4
2009A	-2.56	-2.61	-1.53	-3.30
2010E	-0.18	-0.17	-0.19	-0.16
2011E	-0.14	-0.09	-0.16	-0.16

Financial and valuation metrics

Year	12/09A	12/10E	12/11E	12/12E
EPS (CS adj.) (US$)	-10.00	-0.69	-0.55	0.00
Prev. EPS (US$)	—	—	—	—
P/E (x)	NM	NM	NM	5,382.5
P/E rel. (%)	NM	NM	NM	57,976.8
Revenue (US$ m)	36.1	36.8	50.4	136.7
EBITDA (US$ m)	-67.5	-60.3	-54.2	-2.0
OCFPS (US$)	-0.56	-0.64	-0.11	-0.88
P/OCF (x)	—	-19.6	-116.7	-14.3
EV/EBITDA (current)	-14.9	-14.4	-16.2	-485.2
Net debt (US$ m)	-120	-262	-249	-157
ROIC (%)	—	—	—	—

Number of shares (m)	89.36	IC (12/09A, US$ m)	—
BV/share (current, US$)	-3.7	EV/IC (x)	—
Net debt (current, US$ m)	-295.7	Dividend (12/09A, US$)	—
Net debt/tot. cap. (%)(12/09A,	—	Dividend yield (%)	—

Source: Company data, Credit Suisse estimates.

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Investment Summary

We are initiating coverage of Ironwood Pharmaceuticals (IRWD) with a Neutral rating and a $14 target price.

Our investment thesis is based on the following tenets:

1. **Linaclotide is a best in class product in the poorly served chronic constipation (CC) and irritable bowel syndrome with constipation (IBS-C) markets.** We forecast $680 million by its fifth year in the U.S. Market (2016), $1billion in 2020 and peak sales of $1.2 billion by 2025. Our 100 physician survey supports our position of differentiation relative to prescription options.

2. **The Market Potential for IBS-C and CC is big but not easy to secure.** Despite unmet medical needs for the more than 30 million patients with IBS-C or CC, barriers exist to product use. For instance, patients do not always seek treatment, cheaper options are used front line, and patient compliance is poor. The Credit Suisse survey revealed that physicians believe that 80% of patients stop IBS-C and CC therapy for reasons other than symptom resolution. This may also drive the need for higher than expected commercial investment.

3. **Current valuation closely approximates our $14 target price**. Our $14 target price uses a sum of the parts NPV method and our base case forecast, which assumes a 75% probability of achievement; 79% of the $14 valuation is derived from linaclotide (64% from the United States and 15% non-United States), and 21% from cash. Expected value is also $14 if we assume 15% probability for a bull case scenario producing a net present value (NPV) of $24 and 10% odds of a bear case scenario (e.g., no approval) or $3 NPV.

Linaclotide—A Differentiated Treatment for CC/IBS-C

Efficacy and Safety Proven in CC; Phase III in IBS-C Likely to Succeed

Data from the two pivotal studies in CC demonstrated unequivocally clinical utility of linaclotide. These results coupled with results from a Phase IIb trial in IBS-C also bode well for the ongoing Phase III studies in IBS-C. The available data to date strongly supports the notion that linaclotide provides better efficacy with more convenient once daily dosing than Amitiza and Zelnorm.

We feel confident about the outcome of the Phase III studies in IBS-C, expected in the second half of 2010 for several reasons. First, the improvement in bowel movement from the Phase IIb trial in IBS-C is similar to what was seen in the Phase III trials in CC. Second, in the Phase IIb study, 300 mcg of linaclotide demonstrated statistically significant pain relief (47% improvement) from baseline, well above the threshold required in the Phase III trial (30% or more) using the same dose.

With regard to safety, linaclotide has a rather benign profile. The only side effect that caught our attention was diarrhea, which was observed in numerically higher incidences than the placebo across both Phase III CC trials as well as the Phase IIb IBS-C study. Also, the incidence of diarrhea from linaclotide appears to be higher than Zelnorm and Amitiza. Despite these rates, consultations with physicians who had experience with this agent in the clinic suggest diarrhea is not a severe side effect and will not hinder the market adoption of linaclotide. Further, we are comforted by the low rate of drug discontinuation due to diarrhea (3-5% in Phase III CC trials).

Phase III IBS-C Trial Design Should Please Regulators.

The Federal Drug Administration recently published a draft guidance for IBS trials, which emphasizes abdominal pain and defecation as co-primary endpoints. We have compared the linaclotide Phase III IBS trial design with the detailed guidelines governing study

design, enrollment criteria, endpoint, efficacy measurement, and definition of responders. Although IRWD trials were designed and initiated before this draft guidance was finalized in mid-March, IRWD's approach and measurement of clinical endpoints are largely in-line with the FDA's guidance. In our view, there is minimal risk that the design of the linaclotide Phase III IBS trials will be viewed as inconsistent with the FDA guidelines.

Linaclotide Overall Profile Was Seen as Differentiated in the Credit Suisse 100 Physician Survey

Overall, we believe linaclotide has arguably the best profile among the prescription therapies for CC and IBS-C (Exhibit 1). Looking across improvement in bowel movements, pain relief, dosing convenience, and safety, we believe linaclotide is well positioned to become a market leading treatment.

Exhibit 1: Branded Constipation Therapy - Comparison of Product Attributes

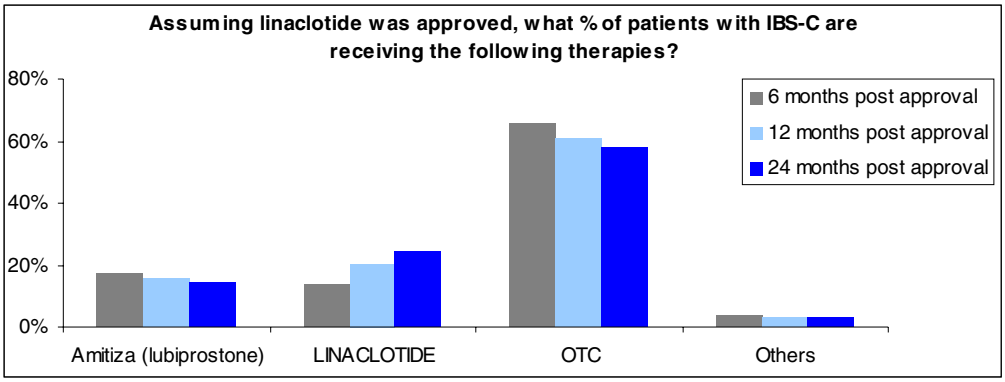
	Linaclotide	Amitiza	Zelnorm
Dosing schedule	✔		
Improvement in bowel movement (per CSBM)	✔		
Pain allevation	✔		
Cardiac risk	✔		
Nausea	✔		
Diarrhea		✔	✔

Source: Credit Suisse analysis.

This profile generated positive responses in the Credit Suisse survey in regards to expected future use.

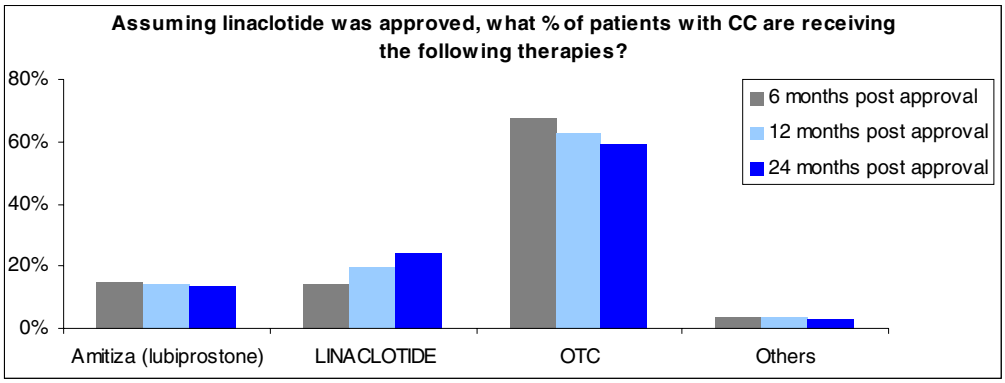
Overall, physicians are optimistic on the potential of linaclotide based on the Phase III data in CC and the Phase II data in IBS-C. If the Phase III data in IBS-C is positive and somewhat similar to what has been seen in Phase II, physicians see linaclotide obtaining significant market share within the first 24 months following approval, quickly surpassing Amitiza's share (Exhibit 2). At the 24 month mark post-approval, the market share that the respondents assigned to linaclotide is greater than 50% what they gave to Amitiza in both IBS-C (24.6% versus 14.5%) and CC (29.2% versus 16.2%), respectively. Only some of this share appears to be coming at the expense of Amitiza; however, as some share is coming from over the counter (OTC) medications and additional share will be obtained through using linaclotide in combination regimens. Similar enthusiasm appears to exist for linaclotide in CC (Exhibit 3).

Exhibit 2: Within two years of approval, respondents believe linaclotide will capture 25% of the U.S. IBS-C market…



Source: Credit Suisse proprietary survey.

Exhibit 3: … and the U.S. chronic constipation market



Source: Credit Suisse proprietary survey.

Despite the Market Size, Compliance and Market Expansion Pose Big Challenges

Since IRWD shares U.S. profits equally with partner Forest and is only eligible for royalty payments in Europe and Asia, the primary market opportunity is in the United States where pricing and reimbursement are also more favorable than in other territories. Approximately 64% of IRWD's NPV is from the U.S. partnership. CC and IBS-C are rather common gastrointestinal disorders with epidemiology reports suggesting that the prevalence rate stands around 10-20% or 30 million-plus patients in the United States.

The most common current treatment paradigm for constipation first encompasses life style modifications (diet and exercise), and/or bulking agents, stool softeners, laxatives, and then prescription medications. Often physicians utilize more than one therapy simultaneously to relieve the symptoms and existing treatments offer modest efficacy.

Before it was withdrawn from the market in 2007 on cardiovascular adverse events, Zelnorm was the prescription standard of care for CC and IBS-C in the United States. At its peak in 2006, Zelnorm posted worldwide sales of $561 million, with the majority ($488 million) coming from the United States. Amitiza is currently the only approved treatment for CC and IBS-C in the United States. Launched in 2006 by Sucampo/Takeda, Amitiza is not perceived to be as effective as Zelnorm and this may have contributed to the relatively slow market penetration. Furthermore, the drug is plagued by a high rate of nausea (32%

versus 3% in patients treated with a placebo). Despite these shortcomings of Amitiza, it managed to bring in U.S. sales of $209 million in 2009.

Although $1 billion in annual U.S. drug revenues are not common, our estimate for this amount in 2020 (eight and a half years on the market) and our $680 million in 2016 may be lower than management expectations and the predominance of sell-side coverage on the stock. In 2016, linaclotide would have been on the U.S. market for five years and our forecast assumes prescriptions are almost 15% greater than Zelnorm at five years post launch. Although we see substantial medical need and a better understanding of IBS-C than was the case during the Zelnorm launch, we also appreciate that the payor environment is more difficult and that may temper uptake of the product. Furthermore, the category will still be characterized as having low compliance rates. For IRWD and Forest to achieve higher targets, they may need to spend more than anticipated, despite the clinical profile of linaclotide having advantage over existing or previous prescription options.

Our U.S. linaclotide forecasts are based upon a prescription market model that we triangulate with compliance rates to reconcile patient penetration. Pre-launch prescription drugs make up less than 5.0% of demand, increasing to 13.5% by 2016. In 2016 linaclotide will make up 58% of branded prescriptions, which implies almost 1 million patients are on the drug.

U.S. Linaclotide Prospects Drives IRWD Valuation, but Market Potential Is Already Reflected in Stock Price

We believe the linaclotide upside potential is fully valued in the stock and hence our Neutral rating. Our $14 target price for IRWD is derived using NPV method by applying a 12% weighted average costs of capital (based on capital asset pricing model) to our forecasted cash flows through 2025. We assign no terminal value and no value to IRWD's pre-clinical and early-stage pipeline.

We model linaclotide's opportunity in CC and IBS-C together, along with further breakdown of Europe and Japan royalties based on sales forecasts from the Credit Suisse European and Japanese pharmaceutical analysts, and then probability adjust these revenues. This base case scenario is based on a 75% probability of success (POS) for linaclotide reaching the U.S. and European markets, and 50% POS in Japan to account for lesser visibility at this point. We assume non-U.S. royalty rates to increase gradually from 10% in launch year to 27% by 2025.

With Phase III CC data in hand and positive expectations towards Phase III IBS-C data due in the second half of 2010, we assume a 75% probability for linaclotide reaching the market in 2012 and $1.2 billion in peak market potential in the U.S. by 2025, bringing us to an NPV of $813 million or value of $9 per share. In Europe, we assume $403 million in peak sales for linaclotide resulting in a royalty income NPV of $146 million, and in Japan, we assume $197 million in peak sales for linaclotide, representing royalty income NPV of $49 million for IRWD. Adjusting for an estimated $262 million in net cash/marketable securities, we arrive at NPV and a target price of $14 per share (Exhibit 4).

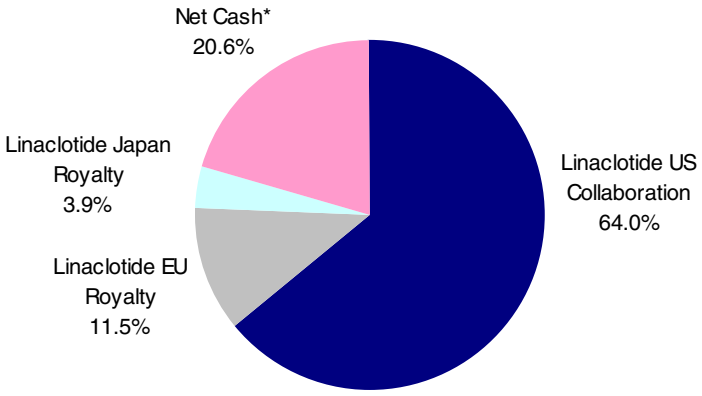
Overall, we estimate that linaclotide's U.S. collaboration contributes 64% to total NPV, followed by net cash and non-U.S. royalty income by 15% and 21%, respectively (Exhibit 5).

Exhibit 4: IRWD- Base Case Probability Adjusted NPV Summary

Drug	Peak Sales ($ millions)	Stage	(Estimated) Launch	Probability of Reaching Market	Economics	Probability Adjusted NPV	Per Share Value	% of Total Value
Pipeline								
Linaclotide Franchise								
Linaclotide US Collaboration	$1,202	Phase III	2012	75%	50/50 Profit Split w/ FRX	$813	$9.10	64.0%
Linaclotide EU Royalty	$403	Phase III	2012	75%	Tiered Royalty w/ Almirall	$146	$1.63	11.5%
Linaclotide Japan Royalty	$197	Phase III	2014	50%	Tiered Royalty w/ Astellas	$49	$0.55	3.9%
Total						**$1,008**	**$11.29**	**79.4%**
Other								
Net Cash (Cash/Equivalents - Debt)						$262	$2.93	20.6%
Other Costs NPV (not directly accounted for in programs above)						$0	$0.00	0.0%
Total Other						**$262**	**$2.93**	**20.6%**
Total						**$1,270**	**$14.21**	**100.0%**

Source: Company data, Credit Suisse estimates.

Exhibit 5: IRWD- NPV Contributors



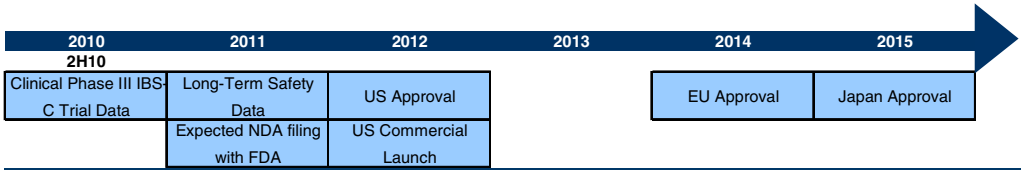
*Net Cash (Cash/Equivalents - Debt)

Source: Company data, Credit Suisse estimates.

Upcoming Catalysts

The major catalyst that will drive IRWD's price over the coming months will be the Phase III IBS-C data due in the second half of 2010 (Exhibit 6). After that, the 18 month long-term safety data will be the gating factor to IRWD's new drug application filing for linaclotide. Less certainty on timing relates to the competitive landscape for branded constipation therapies. Although Johnson & Johnson has not publically stated its intention to file Resolor (available in Europe via Movetis), this scenario cannot be ruled out.

Exhibit 6: Summary of Important Upcoming Catalysts for IRWD



Source: Company data, Credit Suisse estimates.

Key Risks to Our Investment Thesis

Clinical Risk with Phase III IBS-C Trial and Long Term Safety Study

With the Phase III IBS-C trials still ongoing, clinical risk exists ahead of the data that will be released in the second half of 2010. We expect the data to be both statistically and clinically significant in terms of abdominal pain improvement and weekly complete spontaneous bowel movements (CSBM) increases based on the Phase II data. However, as with any responder analysis, the risk of an unusual placebo response must always be considered. While we believe efficacy should be straightforward, the risks associated with safety will be more of a hurdle. The long-term safety study will dose patients on 266 mcg (the high dose in Phase III trials) for 18 months. This will be the longest duration that patients will be exposed to the drug, and to put the risk in context, concerns surrounding Zelnorm only emerged after a meta-analysis of data from 29 clinical studies; however, the mechanism of action for linaclotide should imply lower safety risk. Even if the safety profile appears benign at approval, we expect a post-marketing safety surveillance program will be mandated by regulators post-approval.

Risk of Delay or Setback in Approval Process

As with any Phase III compound, regulatory risk exists with the FDA approval process. With Phase III IBS-C data expected in the second half of 2010, IRWD plans to file a new drug application for linaclotide in the first half of 2011, with approval in the first half of 2012, and commercial launch in 2012. Any delay or setback in this timeline would affect the present value of our cash flow assumptions and our valuation.

Financing Risk

Having raised $203 million in net proceeds from the IPO, IRWD has $299 million in cash on hand as of the first quarter of 2010. IRWD intends to use most of the cash resources to launch linaclotide in the United States along with partner Forest. The costs of launch will be significant, we believe IRWD and Forest are expecting to spend around $100 million per year in marketing alone, including costs for physician education, patient education, promotional materials, and sampling. In addition, we expect the U.S. sales force to approximate 1,000 sales representatives including 200 employed by IRWD. As stated earlier, market dynamics could require the partnership to increase its commercial support of the brand. IRWD does have the benefit of roughly $200 million in pre-commercial milestones to sustain its cash balance ahead of profitability. Last, our model does assume $150 million new equity issuance in 2014.

Commercial Risk—Competition

With the lackluster penetration of Amitiza and with Zelnorm off the market, IRWD stands to benefit from the lack of current competition. However, the recent launch of Movetis' Resolor in Europe (in the first quarter of 2010) brings a novel 5 HT-4 agonist (in the same class as Zelnorm) to the constipation market without the cardiac safety risk. In addition, new agents are in development for constipation (e.g., Theravance's TD-5108) which, if approved, could put our commercial penetration rates of linaclotide at risk. In particular, SP-304, which, like linaclotide is a GC-C receptor agonist being developed by Synergy Pharmaceuticals to treat CC and IBS-C, has advanced into Phase IIa clinical development.

Assumed Market Size and Penetration Rates

As we discuss in more detail later, estimates for the prevalence, and hence patient population of chronic constipation are highly variable depending on the data source. Moreover, estimates of what proportion of chronic constipation patients visit their primary care physicians and are then referred to gastrointestinal specialists are even more rudimentary. We have used a broad range of literature sources and conducted a number of calls with physician consultants in order to attempt to attain more granularity with

respect to our modeling assumptions. We have erred on the side of caution, but nevertheless highlight that our modeling methodology remains somewhat subjective.

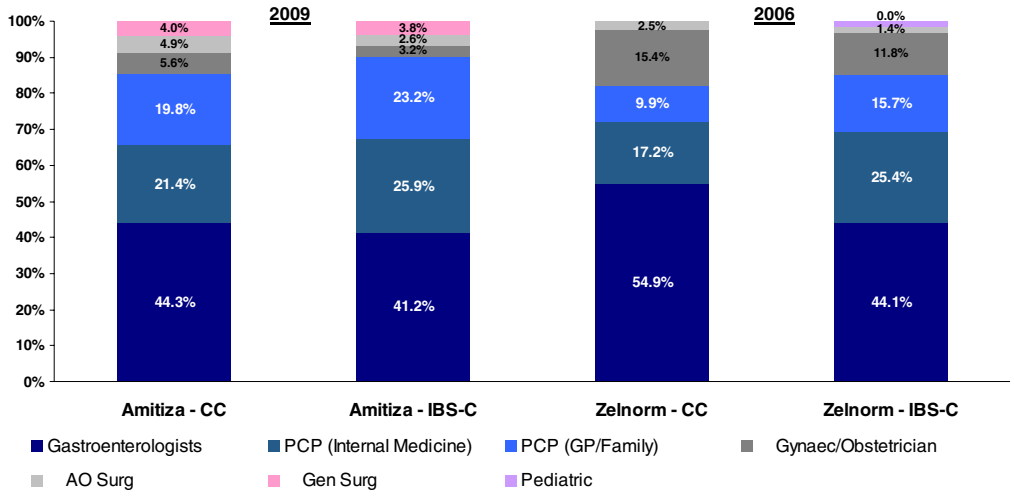
Slow Ramp Up in Sales

IRWD's global launch will be staggered owing to differing filing timelines. In developed markets, the increased influence that payers have on market acceptance of a drug will likely ensure that linaclotide's launch may be slower than what was seen previously with Zelnorm, even if linaclotide's clinical profile is arguably superior. Furthermore, constipation is a consumer driven market and adoption of linaclotide may turn out to be slower than our projections. Such a lack of visibility and/or extrapolation of initial launch revenues may be viewed negatively.

Credit Suisse Physician Survey Supports Our View of Linaclotide Novelty and Market Challenges.

To help elucidate the potential of linaclotide in the CC and IBS-C markets in the United States, we conducted a proprietary survey of 50 primary care physicians and 50 gastroenterologists to obtain their expert insights. These are the same types of physicians who wrote the bulk of Zelnorm prescriptions in 2006 and Amitiza prescriptions in 2009 (Exhibit 7). Of our respondents, 70% work in private practices while the remainder practices in an academic setting, seeing an average of about 40-45 patients with CC and 40-45 patients with IBS-C each month.

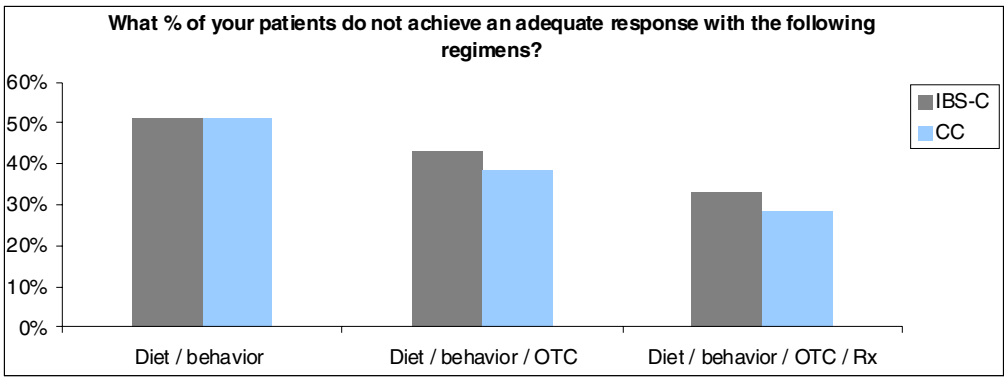
Exhibit 7: Physician Specialty Breakdown of Zelnorm and Amitiza Prescriptions



Source: PDDA Market Data.

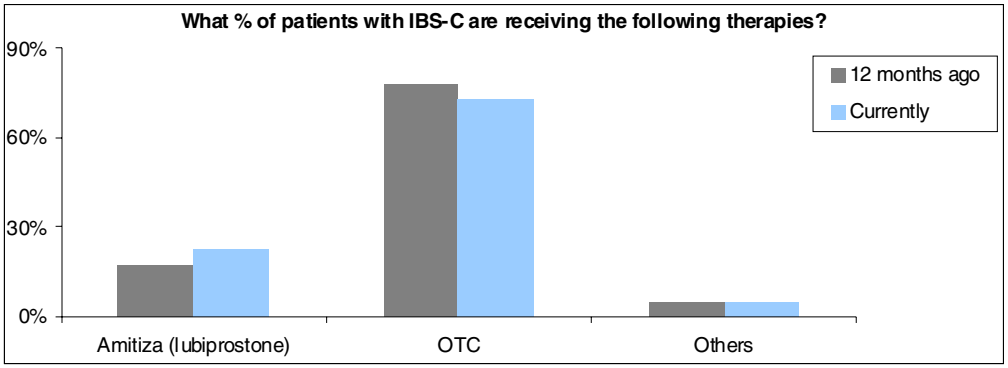
The respondents to our survey agree that the majority of their patients with either CC or IBC-C do not obtain an adequate response from diet and behavior modification alone (Exhibit 8). Fewer patients are left unsatisfied once OTC and prescription medications are added to the treatment regimen, but many patients still do not appear to be satisfied. Much of this dissatisfaction comes from the lack of effect OTC medications have on the other symptoms that go along with constipation (e.g., abdominal cramping, bloating, flatulence). Our survey respondents also confirmed that the IBS-C and CC markets are both dominated by OTC medications, while Amitiza is the only prescription drug of note (Exhibit 9 and Exhibit 10).

Exhibit 8: Significant percentage of patients do not have an adequate response with currently available treatment regimens



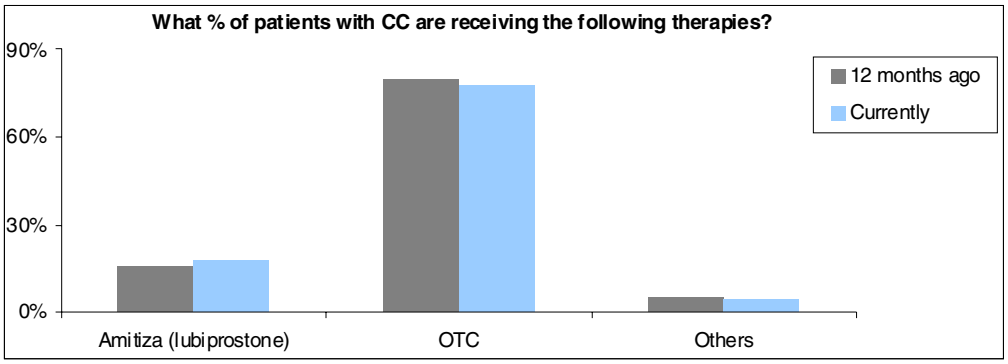
Source: Credit Suisse proprietary survey.

Exhibit 9: Survey results highlight dominance OTC medications have in the IBS-C market



Source: Credit Suisse proprietary survey.

Exhibit 10: OTC medications also dominate the CC market

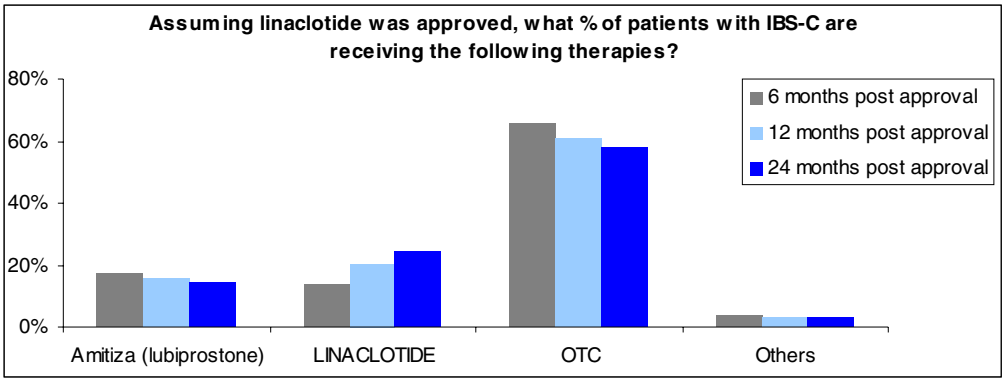


Source: Credit Suisse proprietary survey.

Physicians are optimistic on the upside potential of linaclotide based on the Phase III data in CC and the Phase II data in IBS-C. If the Phase III data in IBS-C is positive and somewhat similar to what has been seen in Phase II, physicians see linaclotide obtaining significant market share within the first 24 months following approval, quickly surpassing Amitiza's share (Exhibit 11). At the 24 month mark post-approval, the market share that the respondents assigned to linaclotide is greater than 50% what they gave to Amitiza in both IBS-C (24.6% versus 14.5%) and CC (29.2% versus 16.2%), respectively. Only some

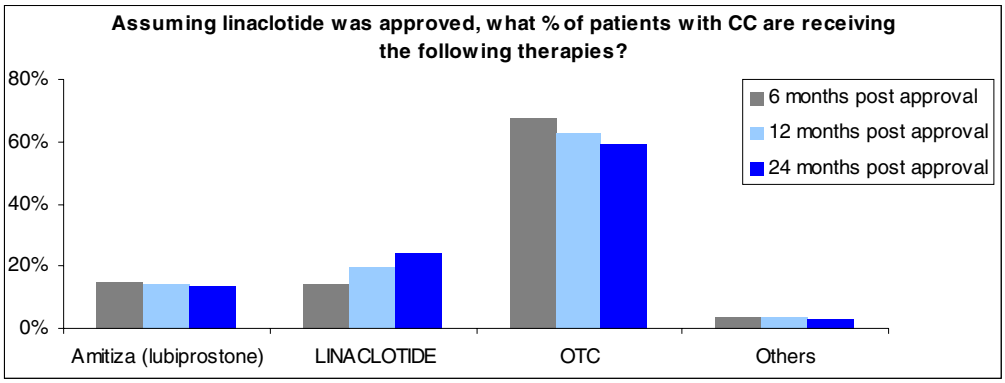
of this share appears to be coming at the expense of Amitiza; however, as some share is coming from OTC medications and additional share will be obtained using linaclotide in combination regimens. Similar enthusiasm appears to exist for linaclotide in CC. (Exhibit 12.)

Exhibit 11: Within two years of approval, respondents believe linaclotide will capture 25% of the U.S. IBS-C market…



Source: Credit Suisse proprietary survey.

Exhibit 12: … and the U.S. chronic constipation market



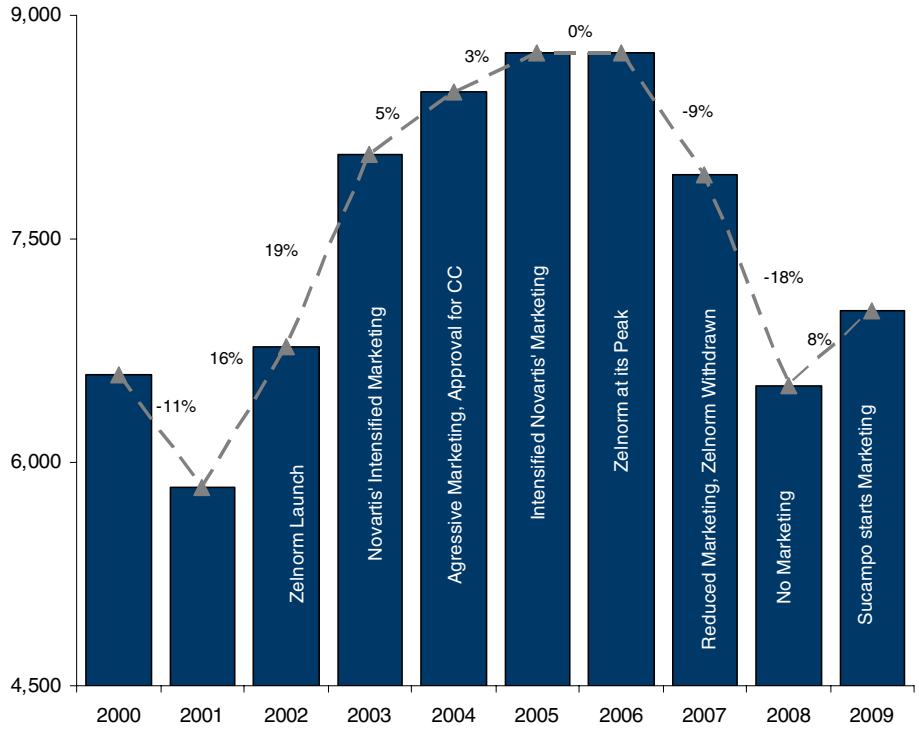
Source: Credit Suisse proprietary survey.

Zelnorm Experience Opens Door for Linaclotide

Novartis' Zelnorm had a brief stay on the CC and IBS-C markets, from its approval in 2002, until it was pulled from the market in March 2007 due to cardiovascular safety concerns. Physicians we spoke to viewed Zelnorm positively as an effective therapy but also stressed that an aggressive direct-to-consumer (DTC) campaign was instrumental in raising awareness for the condition. As a result of Novartis' aggressive marketing efforts, patient visits to gastroenterologists with complaints of constipation increased 50% from 2001 to 2006, highlighting how sensitive this disease category is to effective marketing. Upon withdrawal of Zelnorm, patient visits fell by 9% and 18% in 2007 and 2008, respectively, from its peak in 2006 (Exhibit 13). This decline has been leveling off and we believe linaclotide in conjunction with other product launches has the potential to restart growth in patient visits and build off of the disease awareness that now exists in the medical community for CC and IBS-C. With the introduction of Amitiza and Sucampo/Takeda's marketing efforts, patient visits increased 8% in 2009. While this rate of increase is more modest than what was seen with Zelnorm's introduction, that is

understandable given that Sucampo/Takeda have been running a less aggressive marketing campaign than Novartis did with Zelnorm.

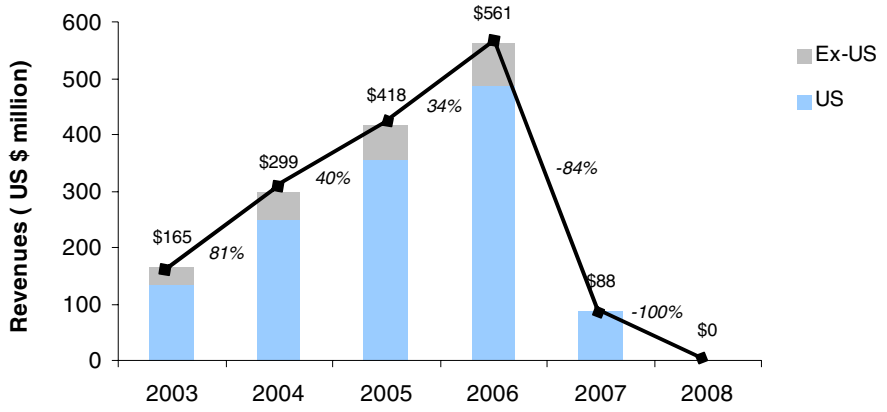
Exhibit 13: Number of Constipation Related Annual Patient Visits



Source: PDDA Market Data, Credit Suisse estimates.

Global sales for Zelnorm increased from $45 million to $561million from 2002 to 2006 (Exhibit 14), a CAGR of 88%, with $488 million in sales coming from the United States. Before being withdrawn in 2007, Zelnorm was approved for the treatment of IBS-C in women only, in more than 56 countries, including Australia, Switzerland, Canada, the United States, Mexico, China, and Brazil. Zelnorm was also approved for the treatment of CC in more than 20 countries, including the United States, Canada, and Mexico. Zelnorm accounted for 19.5% prescriptions of the approximately 15 million chronic laxative market in 2006.

Exhibit 14: Zelnorm Revenues U.S. versus Rest of World

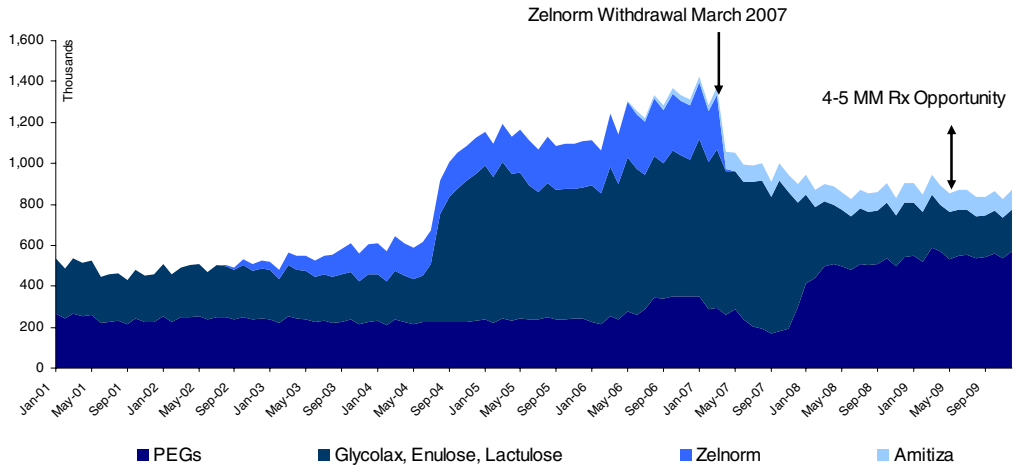


Source: Company data, Credit Suisse estimates.

By spreading disease awareness in the physician community with committed funding for DTC advertising and an experienced management team, IRWD and Forest are already working towards a comprehensive launch. In our opinion, if linaclotide is able to demonstrate significant superiority in Phase III IBS-C trials, it can become the therapy of choice in a much better appreciated CC and IBS-C market, and turn into a blockbuster opportunity.

Amitiza is currently the only FDA-approved prescription therapy for the treatment of CC in adults and IBS-C in adult women. Amitiza is associated with significant nausea; however, approximately 30% nausea rates in clinical trials, which severely limits its market opportunity. In 2009, prescription data indicates Amitiza has plateaued at a run rate of approximately 1.2 million prescriptions annually. The lack of safe and efficacious branded therapies leaves a window of opportunity for a new agent to grab 4-5 million prescriptions annually (with one prescription equals one month of therapy), if Zelnorm efficacy can be achieved (Exhibit 15). As a point of reference, Zelnorm peaked at 3.1 million prescriptions in 2006.

Exhibit 15: Chronic Laxative Market Prescriptions Pre and Post Zelnorm Withdrawal

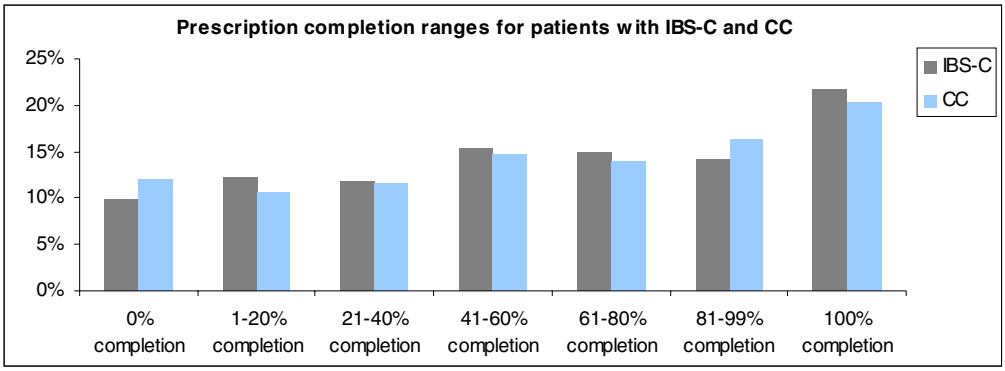


Source: Company data, Credit Suisse estimates.

Patient Compliance Will Be Instrumental in Determining Linaclotide's Success

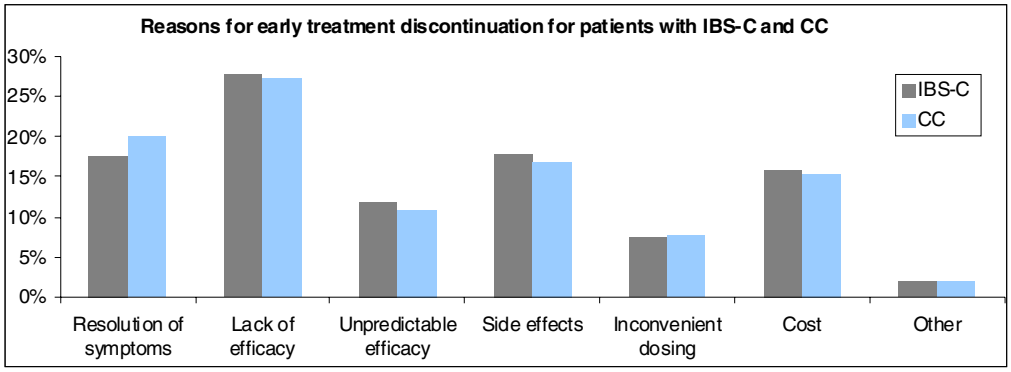
The longevity of patients remaining on therapy is a critical factor in linaclotide's overall potential. The doctors who responded to our survey highlighted the fact that only about half of the patients who receive a prescription medication to treat either their IBS-C or their CC end up completing more than 60% of the prescription (Exhibit 16). Some of these patients stop taking their medication due to a resolution of their gastrointestinal symptoms but the majority of patients stop for other reasons (Exhibit 17). If linaclotide is effective at treating patients' symptoms and has a reasonable tolerability profile, the rate of adherence to therapy will likely increase, but IBS-C and CC will likely remain conditions that are susceptible to patients only using prescription medications on an as needed basis.

Exhibit 16: Survey Respondents Believe that About Half of Their Patients with IBS-C and CC Complete Less than 60% of the Prescription That They Are Given for Their Illness



Source: Company data, Credit Suisse estimates.

Exhibit 17: 80% of Patients Stop Therapy for IBS-C and CC for Reasons other Than Resolution of Their Symptoms

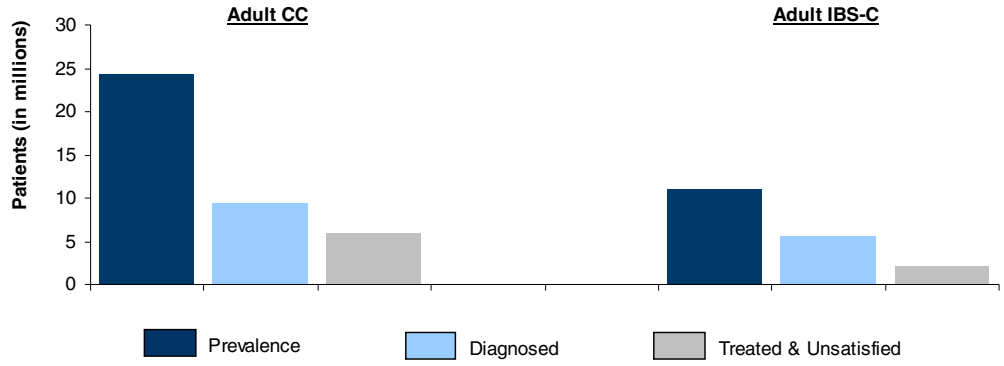


Source: Company data, Credit Suisse estimates.

Rx-Based Market Model Quantifies Linaclotide's Potential

We have developed a prescription-based market model to generate our U.S. sales estimates for linaclotide. Our model incorporates CC and IBS-C prescriptions written from 1999 to 2009, reflecting the past treatment paradigm for constipation, and our expectations on how treatment will change moving forward based on the results of our proprietary survey and due diligence into the CC and IBS-C markets. We view CC and IBS-C as a spectrum of diseases, both of which are included in the historical demand provided by IMS prescription audits, and thus do not differentiate them within our prescription-based model. Given the prevalence estimates, we assume that within the treated and unsatisfied population, CC patients represent two thirds of the market whereas IBS-C patients represent one third of the market (Exhibit 18).

Exhibit 18: Large Market Opportunity in Constipation

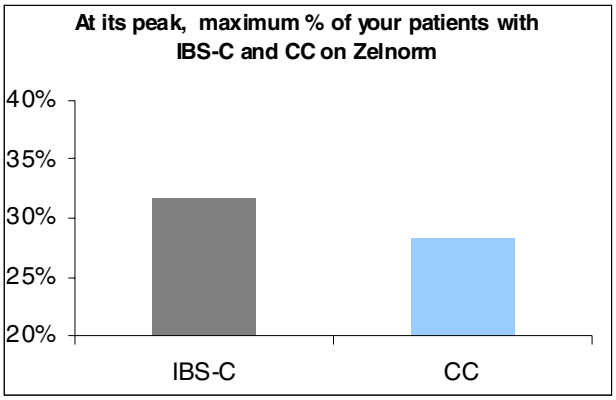


Source: Company data.

Our base case model assumes that the branded prescription market will grow to 15% of the overall prescription market for constipation by 2020. With the branded market obtaining 11% of the overall market in 2006 (Zelnorm's peak year), we believe that our 15% estimate is achievable given our view on linaclotide's favorable efficacy and safety profile versus Zelnorm and the fact that Zelnorm was pulled from the market just five years after its launch.

For linaclotide, we believe that it can obtain 58% of the prescription market share from Amitiza by 2016 (the fifth year linaclotide would be on the market) and 63% of the share by 2020. This implies that linaclotide would capture about 8% and 10% of the total IBS-C and CC market (including OTC and prescription medications) in 2016 and 2019. As a point of reference, our survey respondents said that they used Zelnorm in about 30% of their patients with either IBS-C or CC while the drug was on the market (Exhibit 19). However, this response should be considered along with physician input that patients often use their prescription medications for IBS-C and CC intermittently throughout the year, as opposed to on a chronic basis. Some physicians mentioned that patients tend to use their medications for only three to four months of the year.

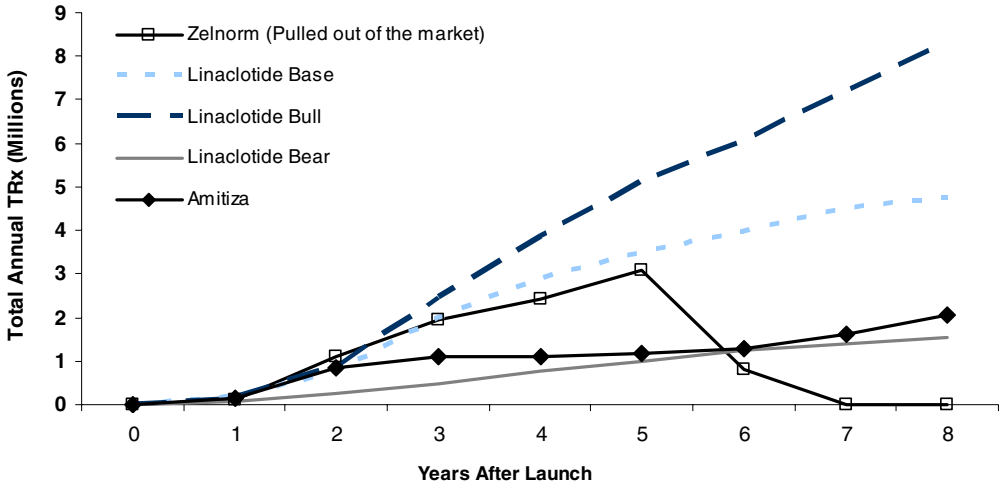
Exhibit 19: At Its Peak, Zelnorm Was Used by Roughly 30% of Our Respondents' Patients with IBS-C and CC



Source: Credit Suisse proprietary survey.

Overall, our model implies almost 3.5 million prescriptions of linaclotide being written in 2016, above Zelnorm's performance at a similar stage in its lifecycle. Compared to Zelnorm, we believe that linaclotide will have the advantage of a superior clinical profile in a better understood disease state. This will be offset by the fact that linaclotide is launching into a more difficult managed care environment than when Zelnorm launched in 2002 and it will also have to deal with competition from Amitiza. This leads to our base case for linaclotide roughly approximating Zelnorm's success in its first five years on the market (Exhibit 20).

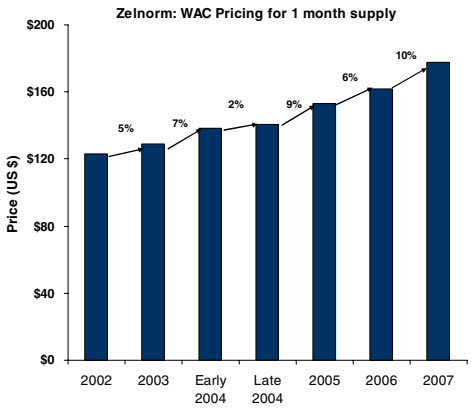
Exhibit 20: TRx Comparison: Linaclotide Estimates vs. Zelnorm Actual



Source: IMS Health, Credit Suisse estimates.

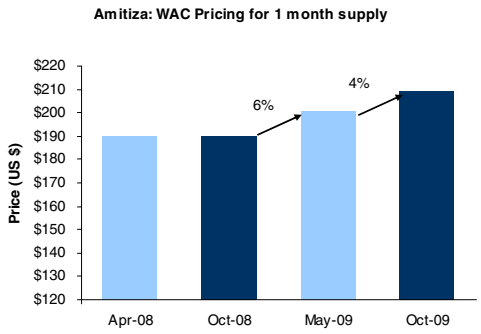
In our model, at launch we assume linaclotide to cost $180 per month, with cost of therapy per day at a 7.7% discount to the latest Amitiza pricing and in-line with management's guidance that linaclotide will be priced at $6 per day. Given linaclotide's superior efficacy and safety profile to Amitiza, we argue that these pricing assumptions are conservative. Going forward, our model contemplates a 2% price increase year over year, which is conservative considering that Zelnorm had an average price increase of 6% throughout its lifecycle (Exhibit 21) and since Amitiza's launch in 2008 Sucampo has raised prices twice, averaging 5% (Exhibit 22).

Exhibit 21: Zelnorm WAC Pricing



Source: Price Rx, Credit Suisse estimates.

Exhibit 22: Amitiza WAC Pricing



Source: Price Rx, Credit Suisse estimates.

In summary, our market model shows that U.S. sales for linaclotide should be about $680 million in 2016, $1 billion in 2020 and then peak at nearly $1.2 billion in 2025, the last year of linaclotide's patent protection on composition of matter. (Exhibit 23 and Exhibit 24).

Exhibit 23: US Market Model for Linaclotide in IBS-C and CC- Base Case

U.S. Rx Model	2011E	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Total Rx	28,231,568	29,643,147	32,607,461	36,520,357	40,537,596	44,591,355	48,158,664	50,566,597	52,083,595	53,125,267	54,187,772	55,271,528	56,376,958	57,504,497	58,654,587
Absolute Growth	553,560	1,411,578	2,964,315	3,912,895	4,017,239	4,053,760	3,567,308	2,407,933	1,516,998	1,041,672	1,062,505	1,083,755	1,105,431	1,127,539	1,150,090
YoY growth %	*2%*	*5%*	*10%*	*12%*	*11%*	*10%*	*8%*	*5%*	*3%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*
Laxatives/Fecal Softeners	26,961,148	27,864,558	29,672,790	32,137,914	35,267,708	38,571,522	41,657,244	43,487,273	44,791,892	45,422,103	46,330,545	46,980,799	47,638,530	48,303,778	49,269,853
% of Market	*96%*	*94%*	*91%*	*88%*	*87%*	*87%*	*87%*	*86%*	*86%*	*86%*	*86%*	*85%*	*85%*	*84%*	*84%*
Branded Rx	1,270,421	1,778,589	2,934,672	4,382,443	5,269,887	6,019,833	6,501,420	7,079,324	7,291,703	7,703,164	7,857,227	8,290,729	8,738,429	9,200,720	9,384,734
YoY growth %	*8.0%*	*40.0%*	*65.0%*	*49.3%*	*20.3%*	*14.2%*	*8.0%*	*8.9%*	*3.0%*	*5.6%*	*2.0%*	*5.5%*	*5.4%*	*5.3%*	*2.0%*
% of Market	*5%*	*6%*	*9%*	*12%*	*13%*	*13.5%*	*13.5%*	*14.0%*	*14.0%*	*14.5%*	*14.5%*	*15.0%*	*15.5%*	*16.0%*	*16.0%*
Amitiza (+ generic lubiprostone)	1,270,421	1,600,730	2,054,270	2,410,344	2,371,449	2,407,933	2,275,497	2,194,590	2,041,677	2,002,823	1,964,307	2,072,682	2,184,607	2,300,180	2,346,183
% of Prescription Rx Market	*100%*	*90%*	*70%*	*55%*	*45%*	*40%*	*35%*	*31%*	*28%*	*26%*	*25%*	*25%*	*25%*	*25%*	*25%*
Linaclotide		177,859	733,668	1,972,099	2,898,438	3,491,503	3,965,866	4,530,767	4,739,607	4,852,993	4,792,908	4,891,530	4,980,904	5,152,403	5,161,604
% of Prescription Rx Market		*10%*	*25%*	*45%*	*55%*	*58%*	*61%*	*64%*	*65%*	*63%*	*61%*	*59%*	*57%*	*56%*	*55%*
Other (TD-5108, etc…)			146,734	0	0	120,397	260,057	353,966	510,419	847,348	1,100,012	1,326,517	1,572,917	1,748,137	1,876,947
% of Prescription Rx Market		*0%*	*5%*	*0%*	*0%*	*2%*	*4%*	*5%*	*7%*	*11%*	*14%*	*16%*	*18%*	*19%*	*20%*
Cost per Rx															
Linaclotide		$180.00	$183.60	$187.27	$191.02	$194.84	$198.73	$202.71	$206.76	$210.90	$215.12	$219.42	$223.81	$228.28	$232.85
Revenues															
Linaclotide		32.0	134.7	369.3	553.7	680.3	788.2	918.4	980.0	1,023.5	1,031.0	1,073.3	1,114.8	1,176.2	1,201.9

Source: IMS Health, Credit Suisse estimates.

Exhibit 24: Linaclotide Commercial Opportunity Assumptions

Scenario	Probability	Assumptions
Base Case	75%	(1) Branded Rx captures 16% of total market by 2025 (2) Linaclotide peak branded Rx market share of 55% by 2025 (3) Linaclotide annual price increases of 2%
Bull Case	15%	(1) Branded Rx captures 25% of total market by 2025 (2) Linaclotide peak branded Rx market share of 70% by 2025 (3) Linaclotide annual price increases of 5%
Bear Case	10%	Non approval scenario due to negative long-term safety data. NPV is comprised of net cash and phase 3 and filing-related linaclotide milestones.

Source: IMS Health, Credit Suisse estimates.

CC and IBS-C Have High Prevalence and Unmet Need

CC and IBS-C are rather common gastrointestinal disorders with epidemiology reports suggesting that CC and IBS-C have a 10-20% prevalence rate, or 30 million-plus patients in the United States alone. While the exact cause of disease is unknown, the slowing of colonic transit may be due to a motor disorder of an associated disease or a side effect of another drug (Exhibit 25). Prevalence studies show that constipation is more frequently reported in older women and may correlate with low levels of physical activity, low income, and poor education. Constipation is a heterogeneous disease and, contrary to popular belief, can involve multiple other symptoms besides the inability to defecate including incontinence, painful or hard bowel movements, or large stools, all occurring at least once per week for two months or longer.

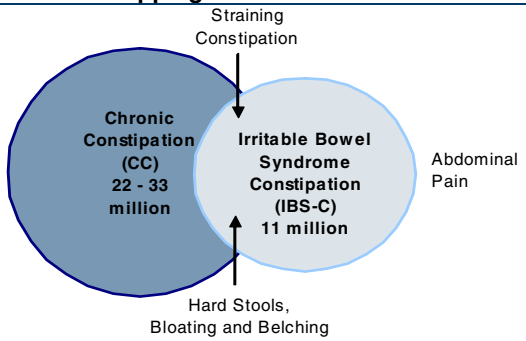
Exhibit 25: Classification of Chronic Constipation

Classification		Description
Primary Constipation	Functional Constipation	No underlying pathology is found. Subtypesinclude colonic inertia, delayed transit. Patients with IBS also have pain and bloating as part of their symptoms.
	Constipation-predominant IBS (IBS-C)	
	Outlet disorders	Scar tissue, tumors and strictures can lead to outlet obstruction, pelvic floor dysfunction
Secondary to medication		Main drugs includeopioid pain medication, anti-depressants and diuretics
Secondary to neurological disorders		The main diseases include Parkinson's disease, diabetes, multiple sclerosis or spinal cord injury

Source: Credit Suisse research.

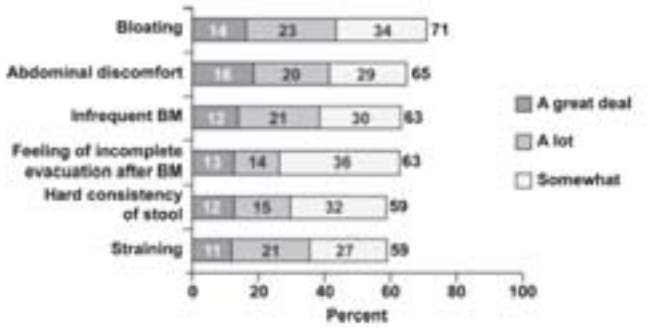
While the criteria define IBS-C as a separate gastrointestinal disorder from CC, the disease is largely similar to CC with the addition of abdominal pain. Therefore, we view CC and IBS-C as overlapping diseases, with IBS-C on the more severe end of the spectrum and including abdominal pain (Exhibit 26). The chronic nature of both diseases can be quite debilitating, with the majority of patients reporting that constipation affects their quality of life and citing bloating and abdominal discomfort as the most detrimental (Exhibit 27). In a survey of more than 37,000 people (Johanson JF, 2007), straining was found to be the most common symptom of chronic constipation with gas and hard consistency of stool following in close succession (Exhibit 28). Furthermore, from a patient's own perspective, bloating and straining were noted to be the two most bothersome symptoms of chronic constipation, with infrequent bowel movements relegated to fifth place (Exhibit 29).

Exhibit 26: Overlapping Prevalence of CC/IBS-C



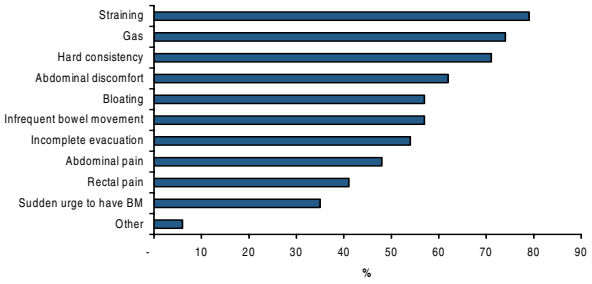
Source: Company data.

Exhibit 27: Most Detrimental Symptoms of CC/IBS-C



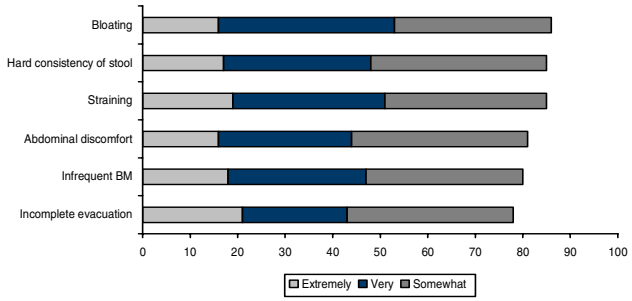
Source: Stewart et. al., Journal of Gastroenterology 1999.

Exhibit 28: Symptoms of Chronic Constipation



Source: Adapted from Johanson 2007.

Exhibit 29: Severity of Constipation Symptoms



Source: Adapted from Johanson 2007.

While no single set of criteria qualify constipation, the independent non-profit Rome Foundation has developed a system to classify functional CC and IBS-C (Exhibit 30), with the two diseases appearing as a continuum of a single disease process (Exhibit 31).

Exhibit 30: ROME III Criteria for CC vs. IBS

C3. Functional Constipation

*Diagnostic criteria**

1. Must include *two or more* of the following:
   a. Straining during at least 25% of defecations
   b. Lumpy or hard stools in at least 25% of defecations
   c. Sensation of incomplete evacuation for at least 25% of defecations
   d. Sensation of anorectal obstruction/blockage for at least 25% of defecations
   e. Manual maneuvers to facilitate at least 25% of defecations (e.g., digital evacuation, support of the pelvic floor)
   f. Fewer than three defecations per week
2. Loose stools are rarely present without the use of laxatives
3. Insufficient criteria for irritable bowel syndrome

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

C1. Irritable Bowel Syndrome

*Diagnostic criterion**

Recurrent abdominal pain or discomfort** at least 3 days/month in the last 3 months associated with *two 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

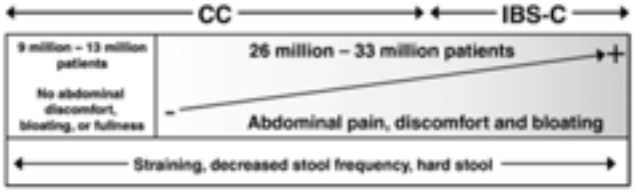
* Criterion fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

** "Discomfort" means an uncomfortable sensation not described as pain.

In pathophysiology research and clinical trials, a pain/discomfort frequency of at least 2 days a week during screening evaluation is recommended for subject eligibility.

Source: Longstreth, et al, Gastroenterology 2006.

Exhibit 31: A Continuum of Disease



Source: Ironwood S1.

For many patients constipation is short-lived, for a significant group of people it is a long-term condition with persistence beyond six months deemed to be chronic. The full extent of the public health burden of chronic constipation is unknown, but with prevalence rates estimated to be as high as 27% of the population in the developed world (Pare et al, 2001), the burden is undoubtedly significant.

While the ROME III criteria are (by definition) a robust academic way of defining constipation, in the real world clinical setting physicians rarely use it. Rather, most people view constipation as infrequent bowel movements. Physicians, tend to focus in on this, with less than three bowel movements per week being the arbitrary cut-off. However, we highlight that this approach is problematic for a number of reasons, not least because it neglects the actual symptoms of which patients complain. First, it is worth noting that while less than three bowel movements per week is perceived to be a relatively objective measure, there is no clinical consensus as to what qualifies as a bowel movement. Profoundly constipated individuals may pass small hard fecal pellets many times a day. This underscores the importance of focusing on complete bowel movements, rather than partial evacuations. Second, while less than three bowel movements per week is unusual, it need not be pathological nor even associated with any symptoms.

Prevalence estimates for CC approximate the high teens whereas the prevalence IBS is roughly 12% of adults in the United States, and this is further divided into three subgroups: IBS-C (constipation), IBS-D (diarrhea), or IBS-A (both symptoms in alternating fashion), each representing one third of the total IBS population. With the umbrella of IBS at 12% prevalence, and assuming seven monthly prescriptions per year, the IBS market could size up to the current gastroesophageal reflux disorder (GERD) ($15 billion) and depression ($14 billion) markets (Ashburn, Nature Reviews, February 2006). Thus, the IBS-C prevalence of 4% of the adult population is roughly a third of the size of CC at 8-12 million patients versus 25 million patients, though both represent areas of unmet medical need and attractive commercial opportunity. The diagnostic tipping point for IBS-C as compared to CC is the presence of abdominal pain, discomfort, and bloating.

Linaclotide—Solid Data in IBS-C and CC

CSBM: The Gold Standard Endpoint in Treating Constipation

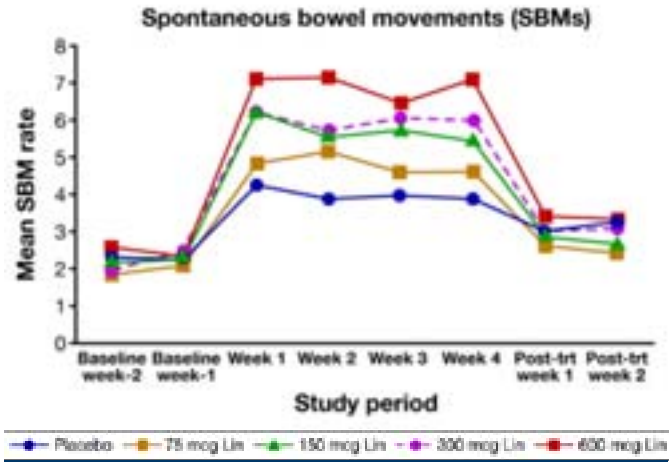
The most common endpoint that clinical trials in constipation use is measuring the increase in complete spontaneous bowel movements (CSBM) on a weekly basis. CSBMs are bowel movements accompanied by the patient self reporting a feeling of complete evacuation that occur without the use of laxatives, enema, or other aid, within 24 hours. In previous studies for Zelnorm and Amitiza, these were the primary endpoints. The linaclotide Phase III trials also use this metric to defile the primary endpoint of a 12-week CSBM responder.

12-week primary CSBM responder - a patient with three-plus CSBMs per week and an increase of one-plus CSBM per week over baseline for at least nine of the 12-week treatment period.

Phase II CC Data Were Transformative In Accelerating Transit

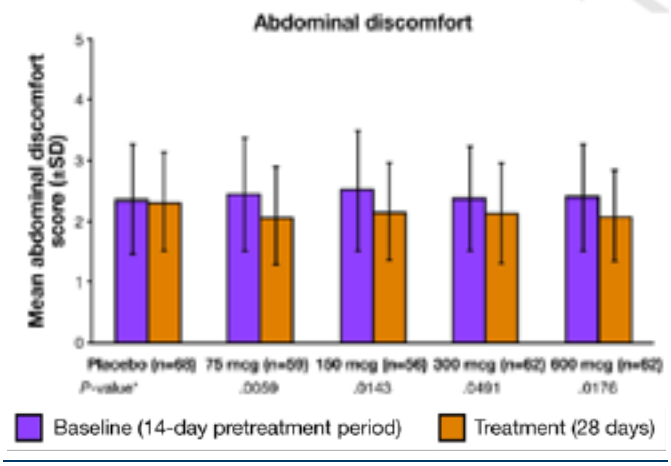
In a Phase II trial in 310 CC patients, linaclotide demonstrated a statistically significant improvement in the weekly spontaneous bowel movement (SBM) frequency versus placebo at all doses ranging from 75 mcg to 600 mcg (see Exhibit 32). These improvements were clinically meaningful and sustained over the four-week treatment period. Additional efficacy endpoints were met with statistical significance including mean CSBMs per week, stool consistency, straining, abdominal discomfort, bloating, and quality of life endpoints. What is more, linaclotide demonstrated an improvement in abdominal discomfort from baseline (see Exhibit 33), a claim that current therapies including laxatives and Amitiza cannot make.

Exhibit 32: Change in Weekly SBM Frequency Linaclotide vs. Placebo



Source: Lembo, et al. Gastroenterology, 2010.

Exhibit 33: Change in Abdominal Discomfort from Baseline- Linaclotide vs. Placebo



Source: Lembo, et al. Gastroenterology, 2010.

Phase III: Unparalleled Efficacy and Manageable Safety

The Phase III CC data, including two large trials enrolling a total of over 1,200 patients, form the basis of our enthusiasm in linaclotide. While rather promotional, IRWD has effectively marketed its data in a table that shows how every single primary and secondary endpoint in this trial was met with statistical significance (see Exhibit 34:). On the primary

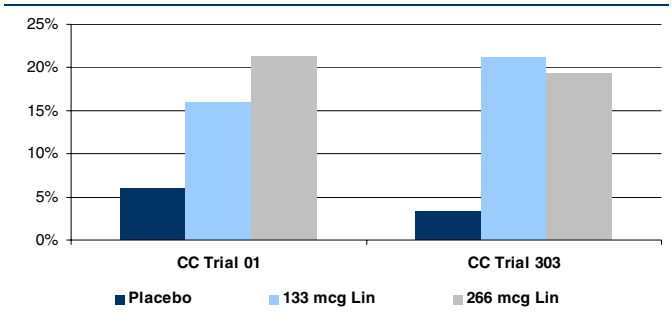
endpoint of CSBM responder, linaclotide showed a 10-18% placebo-adjusted responder rate in the Phase III CC trials. (See Exhibit 35.)

Exhibit 34: Statistically Significant Results Achieved Across a Variety of Endpoints

Endpoint	Trial 305 (n=642) 133 mcg	Trial 305 (n=642) 266 mcg	Trial 01 (n=630) 133 mcg	Trial 01 (n=630) 266 mcg
Primary endpoint				
12-week CSBM overall responder	p<0.0001	p<0.0001	p=0.0012	p<0.0001
Secondary endpoints				
CSBM frequency	p<0.0001	p<0.0001	p<0.0001	p<0.0001
SBM frequency	p<0.0001	p<0.0001	p<0.0001	p<0.0001
Stool consistency	p<0.0001	p<0.0001	p<0.0001	p<0.0001
Severity of straining	p<0.0001	p<0.0001	p<0.0001	p<0.0001
Constipation severity	p<0.0001	p<0.0001	p<0.0001	p<0.0001
Abdominal discomfort	p=0.0003	p=0.0063	p=0.0006	p<0.0001
Bloating	p<0.0001	p=0.0049	p=0.0005	p<0.0001

Source: Company data, Credit Suisse estimates.

Exhibit 35: 12-Week CSBM Responder Rate in Ph III CC

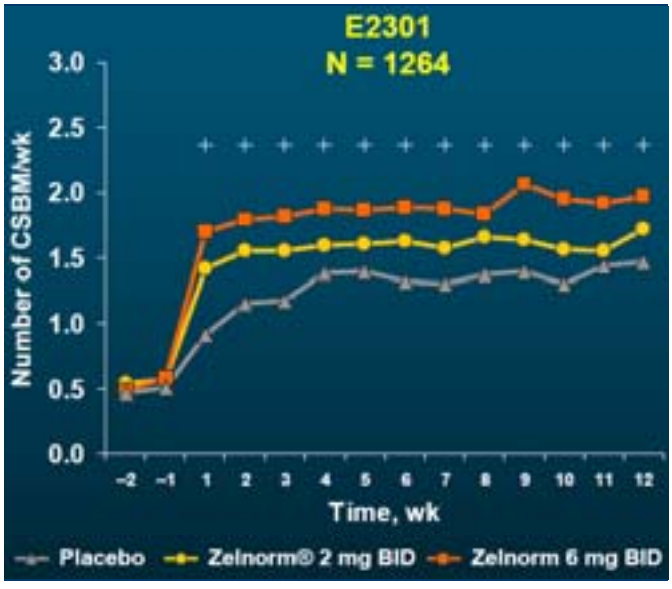


Source: Company data, Credit Suisse estimates.

Apples-to-Apples Comparison Shows Linaclotide Efficacy Benefit Over Zelnorm

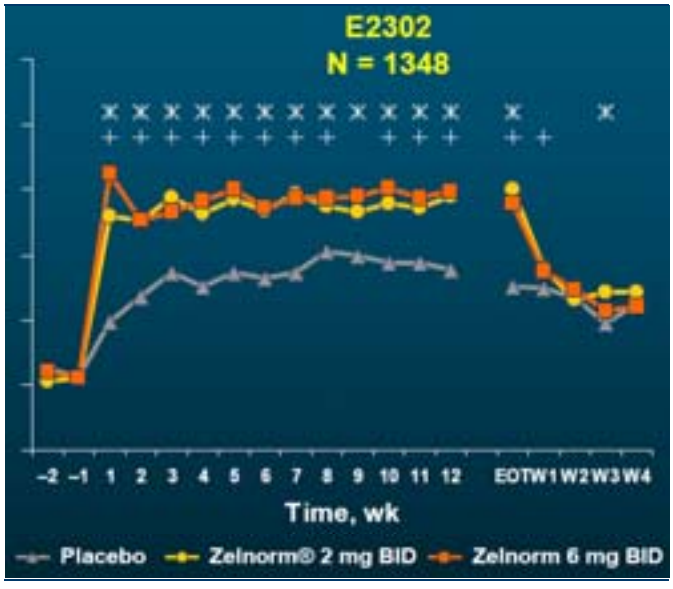
While responders were defined differently in the Zelnorm Phase III trials, the plethora of endpoints and data allows us to compare both drugs on the endpoint of number of CSBM per week over the course of the 12-week trial. In the pivotal Phase III trials, Zelnorm increased CSBM per week to 1.5–2.0 in low and high dose arms (see Exhibit 36 and Exhibit 37). This compares to linaclotide, which demonstrated efficacy of roughly 2.5 CSBM per week on drug arm. linaclotide provides better efficacy at a much lower effective dose, in micrograms, rather than milligrams. In addition, while the CSBM responder rate seems low at approximately 20% for linaclotide, the endpoint requires three-plus CSBMs per week for nine of the 12 weeks, linaclotide successfully increased CSBMs to a rate of two-plus per week and makes the responder results somewhat deceiving. In other words, if the responder endpoint was defined as two-plus CSBMs per week, linaclotide would have shown a much better effect versus placebo.

Exhibit 36: Zelnorm Phase III CSBM/week in Trial 1



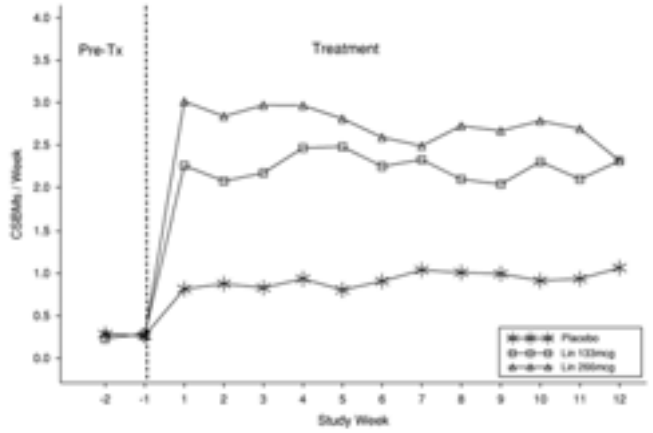
Source: Company data, Credit Suisse estimates.

Exhibit 37: Zelnorm Phase III CSBM/week in Trial 2



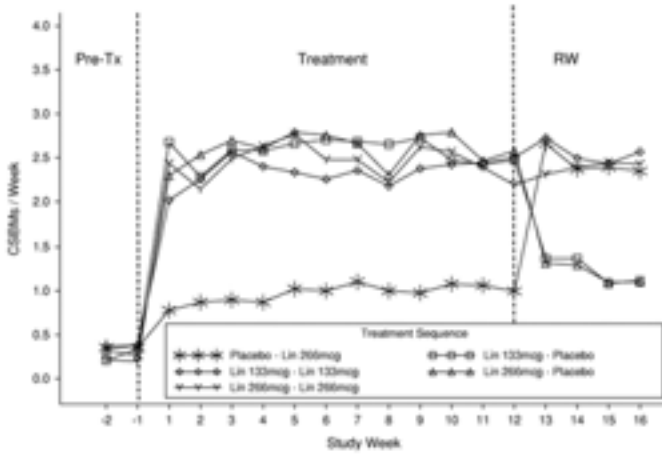
Source: Company data, Credit Suisse estimates.

Exhibit 38: Linaclotide Phase III CSBM/week in Trial 1



Source: Company data, Credit Suisse estimates.

Exhibit 39: Linaclotide Phase III CSBM/week in Trial 2



Source: Company data, Credit Suisse estimates.

As such, we feel quite confident that linaclotide can rival Zelnorm's penetration based on improved efficacy and better safety as a result of no systemic exposure.

Exhibit 40: Comparison of IBS-C Data for Branded Therapies

	Linaclotide Phase IIb		Zelnorm Phase III		Zelnorm Phase II			Amitiza Phase III	
Inclusion Criteria	<3 CSBM/wk, pain/ discomfort>=2 on 1-5 scale		at least two of following: <3 BM/wk, hard/lumpy stools, or straining		at least two of following: <3 BM/wk, hard/lumpy stools, or straining			at least two of following: <3 BM/wk, hard/lumpy stools, or straining	
Dose	300 mcg	placebo	6 mg BID	placebo	6 mg BID	2 mg BID	placebo	8 mcg BID	placebo
n =	84	85	767	752	294	299	288	769	385
Abdominal Pain	-0.90	-0.49	-1.01	-0.80	-14.4	-13.3	-10.9	-0.45	-0.36
Improvement in Abdominal Pain	46.8%	25.6%	26.6%	21.6%	24%	22%	18%	22%	17%
CSBM/wk	3.61	1.01	6.4*	5.7*	6.9*	6.8*	6.1*	Not statistically significant	
Diarrhea	16.5%	1.2%	6.4%	2.9%	9.6%	7.1%	2.5%	6.0%	4.0%

** Bowel movements*

Source: Company data, Credit Suisse estimates.

Linaclotide Has Solid Overall Profile

We have applied a segment framework to compare the branded therapies across common drug characteristics. Our segment framework seeks to measure the branded therapies approved for constipation across six product attributes including: dosing, CSBM, pain alleviation, cardiac risk, nausea, and diarrhea.

Overall, we believe linaclotide has the best profile among the prescription therapies for CC and IBS-C (Exhibit 41). Looking across improvement in bowel movements, pain relief, dosing convenience, and safety, we believe linaclotide is well positioned to become a market leading treatment.

Exhibit 41: Branded Constipation Therapy—Comparison of Product Attributes

	Linaclotide	Amitiza	Zelnorm
Dosing schedule	✔		
Improvement in bowel movement (per CSBM)	✔		
Pain allevation	✔		
Cardiac risk	✔		
Nausea	✔		
Diarrhea		✔	✔

Source: Credit Suisse analysis.

- **Dosing.** In a patient population with traditionally low compliance, we like the once-a-day dosing of linaclotide as opposed to twice-a-day Amitiza.
- **Improvement in bowel movement.** CSBMs are a gold standard measuring the effectiveness, degree of evacuation, ease, and satisfaction of a bowel movement. In Phase III chronic constipation trials for linaclotide, 2.1 placebo-adjusted increases in CSBMs were reported. While both Zelnorm and Amitiza are both effective and result in increase of bowel movements, the use of CSBM as a study endpoint is a harder measurement for efficacy than bowel movements. Furthermore, our conversations with treating physicians have led us to take a view that linaclotide is more effective than the other two in improving bowel movement frequency.
- **Pain relief.** One of the main characteristics that makes IBS-C a relatively more serious disease than chronic constipation is the abdominal pain associated with IBS-C. After analysis of available clinical data, we believe that greater pain-relief was provided by linaclotide in Phase IIb studies with patients reporting 21.2% placebo-adjusted improvement in pain as compared with 5.0%, 6.0%, and 4.4% in two Zelnorm Phase III and one Amitiza Phase III studies, respectively.
- **Cardiac Risk.** Linaclotide is a locally acting molecule with no systemic exposure and data to date does not suggest the presence of cardiac toxicity. Recall that Zelnorm, a 5-HT$_4$ agonist, was withdrawn from the market in 2007 owing to the cardiovascular adverse events observed in 0.11% patients from a meta-analysis of 29 clinical trials. Given that IBS-C is not a life-threatening disease; the FDA deemed the risk-benefit profile of Zelnorm to be unfavorable. Despite being in the same category as Zelnorm, Amitiza's label does not carry a warning on cardiac risk. We await longer term linaclotide safety data expected in 2011 but we feel comfortable about its safety profile on existing data.
- **Nausea.** While 30% of patients complain about severe nausea upon consuming Amitiza, no subject was hospitalized during the clinical trials. Linaclotide and Zelnorm cause less nausea than Amitiza. However, a certain level of nausea is reported in almost all laxative treatments.
- **Diarrhea.** In comparing the drugs for diarrhea incidence, linaclotide stood out with 16.5% patients suffering from diarrhea compared with 6-9% in the Zelnorm and Amitiza studies. This is the only attribute out of six for which linaclotide does not compare favorably to the other agents.

Positive Phase III IBS-C Data Expected in Second Half of 2010

Two Phase III IBS-C trials, '302 and'31 are expected to read out later this year and look very similar to the Phase III CC trials in design. The major difference is in primary endpoints, while the CC trials only incorporated the 12-week CSBM responder primary endpoint, the IBS-C trials include three responder endpoints:

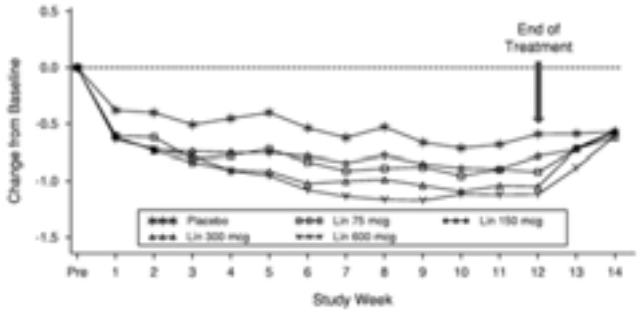
12-Week APC (abdominal pain & constipation) Responder: A patient who has both a 30%-plus improvement in abdominal pain and three-plus CSBMs per week that increased by one-plus from pretreatment, for at least nine of the 12–week treatment period

12-Week CSBM Responder: a patient with three-plus CSBMs per week and an increase of one-plus CSBM per week over baseline for at least nine of the 12-week treatment period.

12-Week Abdominal Pain Responder: a patient who has a 30%-plus improvement in abdominal pain for at least nine of the 12-week treatment period.

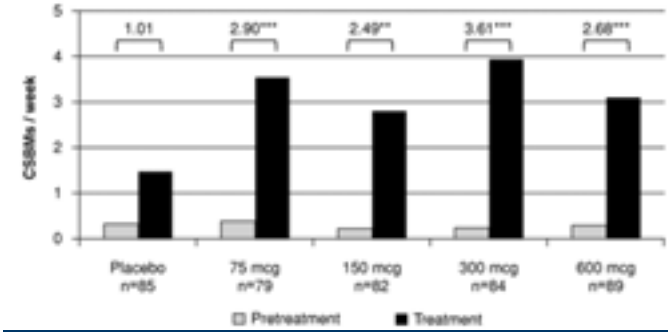
Using a step-down procedure, patients who respond to the APC endpoint will not be counted towards the other two endpoints, making the trial largely a test of hitting the composite endpoint. Secondary efficacy endpoints will be the same as the CC trial with addition of abdominal pain and percent of abdominal pain-free days. As such, the IBS-C trial is an evaluation of linaclotide's ability in reducing abdominal pain. Based on Phase II data, we are confident that linaclotide will demonstrate the improvement necessary to show a pain benefit. In a Phase IIb trial in IBS-C patients, linaclotide demonstrated a significant improvement in abdominal pain from baseline (see Exhibit 42), with the 300 mcg dose reaching a 46.8% improvement, well above the threshold required in the Phase III trial (of 30% or more) using the same dose. In terms of CSBM increases, the 300 mcg arm showed a significant change from pre-treatment of 3.61 CSBMs per week (see Exhibit 43), which provides us with comfort in passing the 3.0 CSBM threshold to meet the Phase III endpoint.

Exhibit 42: Ph IIb IBS-C Abdominal Pain Improvements



Source: Company data, Credit Suisse estimates.

Exhibit 43: Ph IIb IBS-C CSBM/week Improvements



Source: Company data, Credit Suisse estimates.

Ironwood IBS-C Trials Reflect Newly Issued FDA Draft Guidance

The FDA recently published guidelines for conducting a well designed trial in IBS patients. The draft guidance, which is open for comments until mid-May, is not a mandate but rather incorporates the FDA's most current thinking in determining appropriate trial design. In the past, IBS trials have incorporated a single primary endpoint assessing adequate or satisfactory patient relief, such the single item subject global assessment of relief (SGA) of IBS symptoms. However, the latest FDA guidance highlights that a single item assessment does not capture a range of symptoms or provide information on the patient's current symptom state. Without the current availability of an instrument to capture this array of information, the FDA has issued guidance for sponsors to keep in mind when conducting IBS-C trials. Although IRWD trials were designed and initiated before this draft guidance was finalized in mid-March, IRWD's approach and measurement of clinical improvement are largely in-line with the FDA's thinking. (See Exhibit 44.)

Exhibit 44: FDA Draft Guidance vs. Ironwood Design on IBS-C Trials

Trial Guideline	Ironwood Phase III IBS-C	Criteria Met?
Design: Randomized, placebo-controlled trial design should include a 1- to 2-week screening period, 8- to 12-week treatment period, and 2-week post-treatment period.	**Trial '31:** Pre-treatment period followed by 12 week treatment period and a 4 week randomized withdrawl period **Trial '302:** 26-week treatment period	**LIKELY**
Enrollment Criteria: Pain Intensity: weekly average of worst abdominal pain in past 24 hours score of > 3.0 on a 0 to 10 point (11-point) scale Stool Frequency: < 3 CSBMs per week	Patients enrolled in the IBS-C trials are to have fewer than three CSBMs and no more than five SBMs per week during the pretreatment period, with an average abdominal pain score of at least 3.0 on an 11-point scale (0=none, 10=very severe).	**YES**
Primary Endpoint(s): Evaluation of a co-primary endpoint that includes the two major IBS symptoms: abdominal pain and defecation (constipation measured as stool frequency for IBS-C	**3 Primary Endpoints:** 1) 12-week APC (abdominal pain & constipation) Responder 2) 12-week CSBM responder 3) 12-week Abdominal Pain Responder * tested in a step-down procedure, so first endpoint is a co-primary endpoint	**YES**
Abdominal Pain vs. Discomfort: Abdominal pain and discomfort may be different symptoms that should, therefore, be assessed by different questions. Abdominal pain intensity recommended as the primary pain assessment in IBS trials, while abdominal discomfort can be evaluated as a secondary endpoint.	Abdominal Pain Responder is a primary endpoint. Abdominal Pain and Abdominal Discomfort are secondary endpoints.	**YES**
Abdominal Pain Measurement: Evaluate abdominal pain intensity by using an 11-point (i.e., 0 to 10) numeric rating scale that asks patients daily to rate their worst abdominal pain over the past 24-hours	Abdominal pain intensity is measured on a numeric scale, but the scale consists of a 5-point ordinal severity scale (1=none, 2=mild, 3=moderate, 4=severe, and 5=very severe).	**SOMEWHAT**
Efficacy Measures: Format for daily symptom assessment (e.g., interactive voice response, personal digital assistant, or paper diaries) so that patients can evaluate their IBS symptoms on a daily basis throughout the trial. The weekly average of 7 daily assessments can be used to calculate a weekly response to treatment.	Phase IIb IBS-C trials measure daily abdominal symptoms (pain, discomfort, and bloating).	**LIKELY**
Definition of Responder: A patient is categorized as a weekly responder if the patient is a weekly responder in both pain intensity and stool frequency. • A Pain Intensity Responder for IBS-C is defined as a patient who experiences a decrease in weekly average of worst abdominal pain in past 24 hours score of equal to or greater than 30 percent compared with baseline. • A Stool Frequency Responder is defined as a patient who experiences an increase of at least one CSBM per week from baseline.	• A 12-Week Abdominal Pain Responder is a patient who, for at least 9 out of the 12 weeks in the Treatment Period, has a ≥ 30% improvement in abdominal pain. • A 12-Week CSBM Responder is a patient who, for at least 9 out of the 12 weeks in the Treatment Period, has a weekly CSBM Rate ≥ 3 that is increased ≥ 1 from Pretreatment.	**YES**

Source: Company data, Credit Suisse estimates.

Existing Safety Data Support Approval—18-Month Safety Study Expected in 2011

IRWD is currently running two open label long-term safety studies to evaluate over 2,500 patients over 18 months. Patients who completed any linaclotide Phase II or III studies are eligible to enroll, and the trial will evaluate safety and tolerability of linaclotide at the 266 mcg dose. More than 1,500 patients have been enrolled and we expect these data in 2011. While there is no certainty that a long term safety study could reveal a hair, the safety data that we have to date suggest linaclotide's local exposure and extremely small dosing will lead to a clean profile that supports approval.

In the IBS-C Phase IIb trials, diarrhea, the most common serious adverse reaction, was observed in 15% of total patients, with the rate being 16% in the 300 mcg arm and 18% in the 600 mcg arm. Abdominal pain, occurring in 5% of total patients, was the second most prevalent adverse event, from 4-8% in the 150 mcg arm and the 600 mcg arm, respectively. Urinary tract infection and nausea were observed in 4% of all patients. Overall, 57% patients reported a treatment-emergent adverse event.

Diarrhea incidence in Zelnorm Phase III trials was lower at 9%, but nausea, flatulence, and abdominal pain were higher than with linaclotide at 8%, 6%, and 12%, respectively. Another common side effect with Zelnorm was headache observed in 15% patients.

While nausea incidence was higher with Amitiza (8%), diarrhea (7%), and abdominal pain (5%) were lower or equal to reported occurrence in linaclotide trials.

Exhibit 45: Pooled Safety Data from Phase IIb Linaclotide Trials for IBS-C

P2b IBS-C	Placebo	75 mcg	150 mcg	300 mcg	600 mcg	All
n=	85	79	82	85	89	33
Diarrhea	1%	11%	12%	16%	18%	15%
Abdominal Pain	4%	5%	4%	5%	8%	5%
Urinary tract infection	2%	9%	1%	6%	1%	4%
Nausea	6%	1%	10%	1%	3%	4%
Nasopharyngitis	6%	4%	7%	1%	1%	3%
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%
Any TEAE	41%	52%	49%	59%	69%	57%

Source: Company data, Credit Suisse estimates.

In the Phase III trials of linaclotide for chronic constipation, 15% of patients developed diarrhea, the most common adverse reaction. The next most prevalent adverse reaction was flatulence, which was observed in 5% patients abd 4% patients reported abdominal pain, nausea, and abdominal distention individually. Overall, 58% of all patients reported at least one treatment-emergent adverse event. Diarrhea incidence was significantly lower than linaclotide with both Zelnorm (7%) and Amitiza (12%). On the other hand, Amitiza reported significantly higher nausea incidents at 29% while nausea with Zelnorm was almost in-line with linaclotide's (5%). Headache was observed in 11% of patients taking Amitiza which is 9% more than that observed with patients taking linaclotide.

Exhibit 46: Pooled Safety Data from 2 Phase III Linaclotide Trials for CC

PIII CC	Placebo	133 mcg	266 mcg	All
n=	320	430	422	852
Diarrhea	6%	16%	14%	15%
Abdominal Pain	4%	4%	5%	4%
Urinary tract infection	3%	2%	1%	2%
Nausea	5%	3%	4%	4%
Nasopharyngitis	4%	2%	4%	3%
Upper respiratory tract infection	4%	4%	2%	3%
Sinusitis	3%	3%	3%	3%
Headache	3%	2%	2%	2%
Flatulence	7%	6%	5%	5%
Abdominal Distention	3%	3%	4%	4%
Abdominal pain upper	1%	2%	1%	1%
Any TEAE	69%	60%	56%	58%
Dropped due to TEAE	6%	7%	7%	7%
Dropped due to Diarrhea	1%	4%	4%	4%
SAE	3%	2%	3%	2%

Source: Company data, Credit Suisse estimates.

An average of 7% discontinuation owing to a treatment-emergent adverse event was observed in the CC Phase III trials, of which 56% cases were attributable to diarrhea. Serious adverse events were reported at an average of 2%, in-line with those reported with patients that were on placebo.

Linaclotide Is Protected by Patent Until 2025

IRWD's intellectual property consists of two issued U.S. patents, a granted European patent, as well as several other patents in other territories. In the United States, linaclotide's composition of matter patent expires in 2025, while the patent covering room

temperature stable formulation expires in August 2029. The European patent, which expires in 2024, also covers claims to composition. Additional patents covering formulation and process for making the molecule are pending and would expire between 2024 and 2030. The pending Japanese composition of matter patent would expire in 2024.

Exhibit 47: Patent Protection for Linaclotide and Amitiza

Country	Patent Type	Expiration
	LINACLOTIDE	
US	Composition of Matter	2025
US	Room Temperature Stable Formulation	2029
EU	Composition of Matter	2024
Japan	Composition of Matter	Pending, would expire in 2024
	AMITIZA	
US	Composition of Matter	2014

Source: Company data, Credit Suisse estimates.

Amitiza's composition patent expires in 2014 and corresponding generic entry could possibly cannibalize IRWD's sales. In the base case scenario, we model Lubiprostone scripts growing from roughly 1.3 million total prescriptions (TRx) per year at patent expiration in 2014 to 2.2 million TRx per year in 2025.

Exhibit 48: Linaclotide Key US Patent

US Patent Number	Description
20100048489	Stable Solid Formulation of A GC-C Receptor Agonist Polypeptide Suitable for Oral Administration

Source: Company data, Credit Suisse estimates.

Current Treatment Paradigm

The current treatment paradigm for constipation is highly fragmented, by mode of action and specific agent within each class of drug. As discussed above, there is a high degree of dissatisfaction with the currently available agents, even when used in combination. Furthermore, the majority of laxatives are available over the counter, reflecting their relatively simple mechanism of action. While simplicity is clearly a beneficial quality, the principle of parsimony should not come at the expense of efficacy. Exhibit 49 summarizes the main types of laxative and their relative advantages and disadvantages.

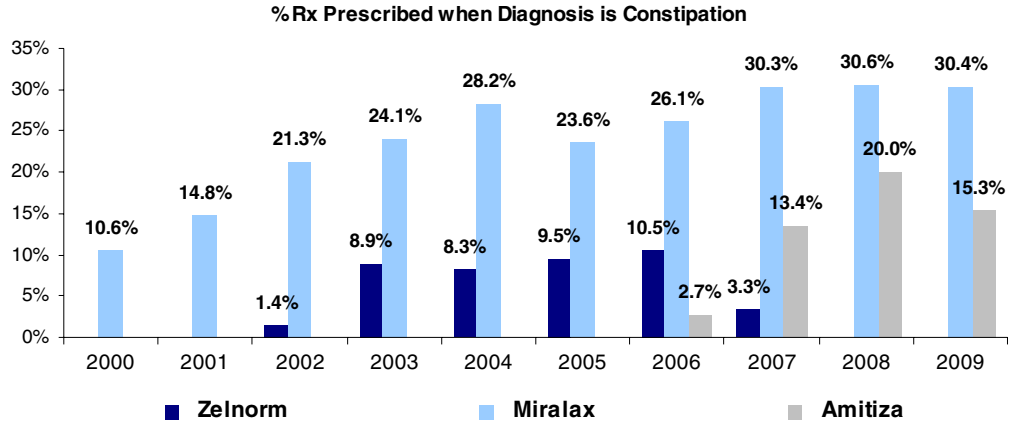
Exhibit 49: Drugs used in the treatment of chronic constipation

Laxative type	Estimated market share in US	Examples	Mode of Action	Limitations
Bulking Agents	25-35%	Celevac, Fybogel, Isogel	They contain fibre and work by absorbing water into the stool. They are usually available as powder or granules	Flatulance and bloating. Delayed onset of action
Fecal Softners	10-15%	Dioctyl, Doculsol, Norgalax	They result in luminal water binding and are particlaerly useful for haemorrhoids	Stomach cramping
Osmotic Laxatives	40-50%	Lactulose, Miralax, Movicol	They retain water in the bowel and soften the stool	Require large amount of water to be ingested. Often have bad taste. May cause electrolyte disturbances
Stimulant laxatives	10-25%	Bisacodyl, Dulcolax, Senna	They stimulate intestinal movement through irritating the myenteric plexus of nerves in the gut	Abdominal discomfort and cramps. Tolerance may develop and as such use is limited to short durations.

Source: Adapted from Longstretch et al, 2006.

When a patient visits a doctor with a complaint of constipation, roughly 30% of the time the doctor prescribes Miralax (polyethylene glycol 3350), an OTC osmotic laxative that is often considered the standard of care (Exhibit 50). In addition, the patient is asked to modify his/her diet, increase water intake, and exercise.

Exhibit 50: Line of Treatment when Diagnosis is Constipation

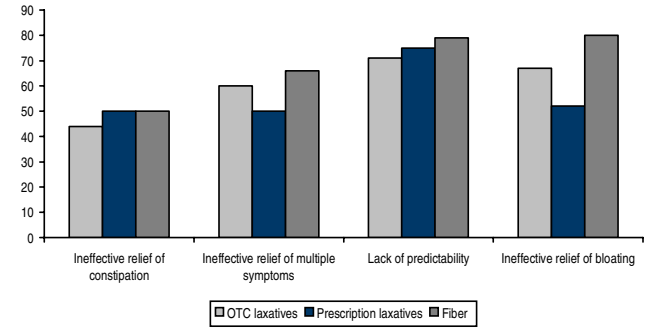


Source: PDDA Market Data, Credit Suisse estimates.

In a 2002 meta-analysis of laxatives for the treatment of constipation by Jones et al, the authors concluded that "there is insufficient comparable quantitative evidence to conclude that laxatives overall are superior to placebo in chronic constipation." More interestingly (and surprisingly) he notes that while both laxatives and placebo were associated with increased stool frequency, there was a greater increase with placebo than with laxatives.

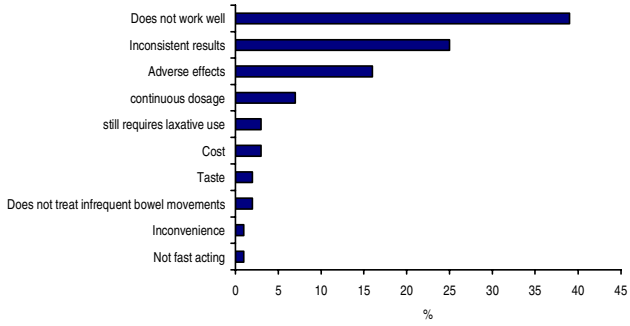
Some experts have commented that existing laxatives are at best only modestly efficacious. However, in the absence of rigorous clinical trials, we believe definitive scientific conclusions are not possible. The lack of patient satisfaction is probably the most telling benchmark. As seen in our physician survey, as well as in a study by Johanson (2007), many patients are not completely satisfied with their current constipation treatment (Figure 51). The majority of patients reported their reason for dissatisfaction to be efficacy related (Figure 52). However, there are numerous other reasons for patient dissatisfaction; such as, osmotic laxatives tend to have a bad taste and bulk-forming laxatives often need to be ingested with large quantities of water.

Figure 51: Ratings for current constipation treatments



Source: Adapted from Johanson 2007.

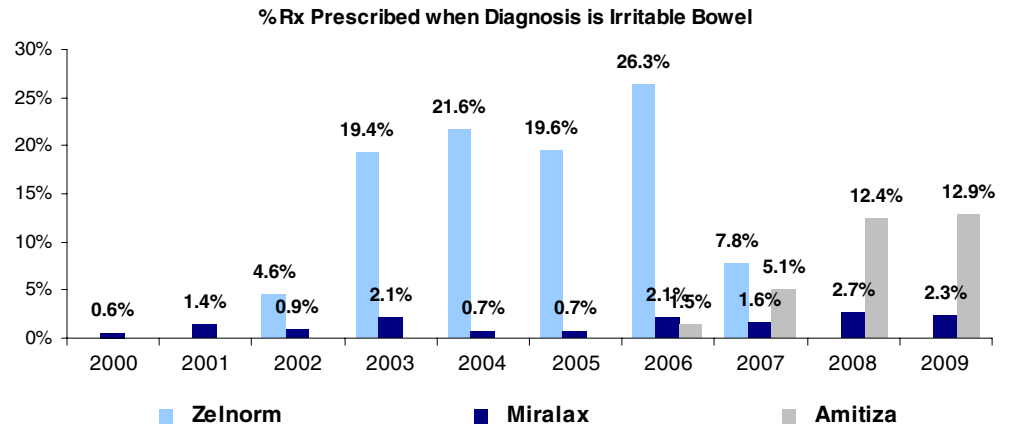
Figure 52: Reasons for dissatisfaction



Source: Adapted from Johanson 2007.

If patients have additional complaints like pain or discomfort, the doctor typically prescribes available branded therapies for IBS-C. At its peak, a medical practitioner used Zelnorm 26% of the time for treating IBS-C and Amitiza comprised about 13% of all medicines used to treat IBS-C in 2009.

Exhibit 53: Line of treatment when diagnosis is Irritable Bowel

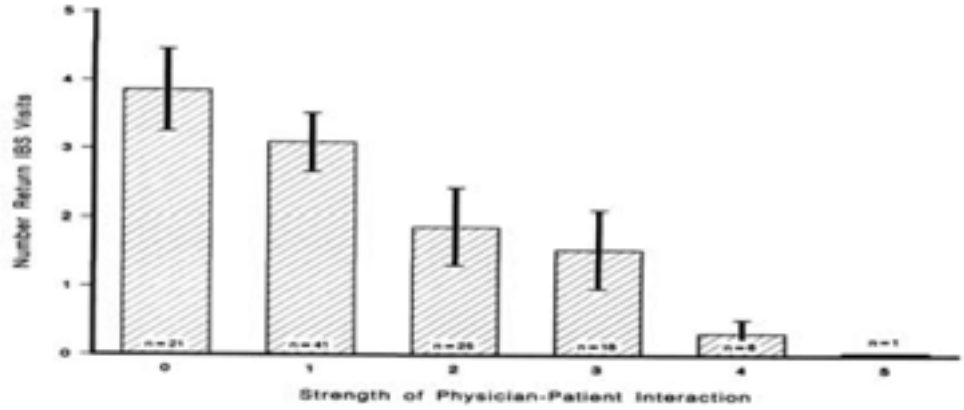


Source: PDDA Market Data, Credit Suisse estimates.

A strong patient-physician relationship ironically acts as a placebo and can direct patient behavior towards low compliance. Owens (1995) reported in his paper that there is an inverse relationship between number of return visits made for IBS-C related symptoms

and strength of the physician-patient interaction (Exhibit 54), which is hypothesized to be because effective communication can allay patient fears of having a more sinister gastrointestinal condition (such as cancer). Once comforted, patients do not feel the need to take any medications that they are prescribed and often do not return for follow-up visits for the same complaint.

Exhibit 54: Relationship between Quality of Physician-Patient Interaction & Return Visits

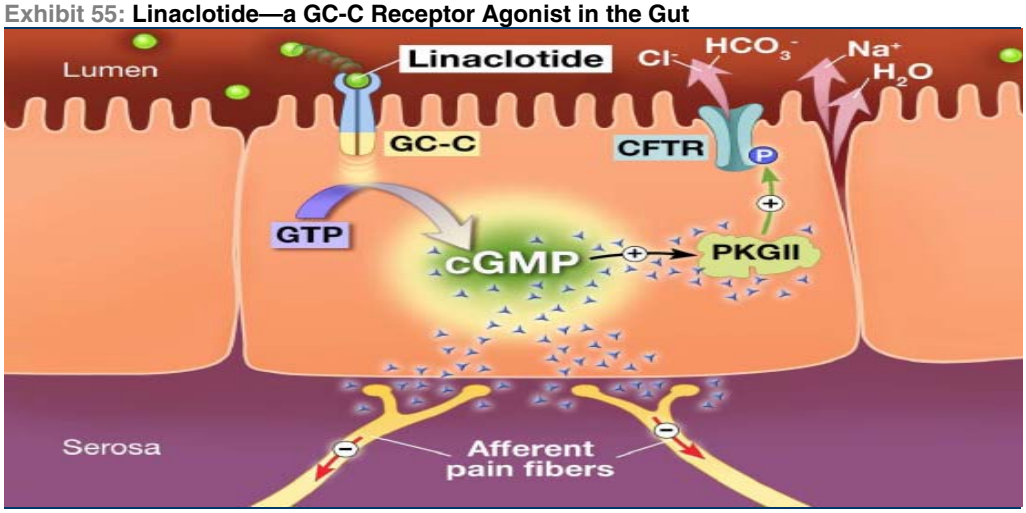


Source: Adapted from Owens 1995.

Linaclotide Mechanism is Novel Relative to Marketed Therapies

Linaclotide is a novel amino acid peptide that works locally in the gut to increase fluid secretion and accelerate transit time in the intestines, thereby improving symptoms of patients with constipation. Moreover, it is a 14 amino acid peptide that acts as an agonist of guanlyate cyclase-C (GC-C), a receptor located on the lining of the intestine. By activating GC-C receptors, linaclotide increases cyclic guanosine monophosphate (cGMP) which in turn causes a release of chloride (Cl^-), sodium (Na^+, bicarbonate (HCO_3), and water (H_2O) into the intestine (Exhibit 55). Potentially more differentiating for linaclotide, is that the increase of cGMP inhibits some of the nerves in the gastrointestinal (G) tract, leading to decreased pain sensitivity. Perhaps most important to the mechanism of linaclotide is that the drug works locally within the GI tract site and, at therapeutic doses, there is no detectable systemic exposure. This differentiates linaclotide from previous and current GI therapies that are less specific and have an effect on the serotonin system, including Zelnorm, Propulsid, Lotronex, all of which were withdrawn from the market due to safety concerns.

Exhibit 55: **Linaclotide—a GC-C Receptor Agonist in the Gut**



Source: Company presentation

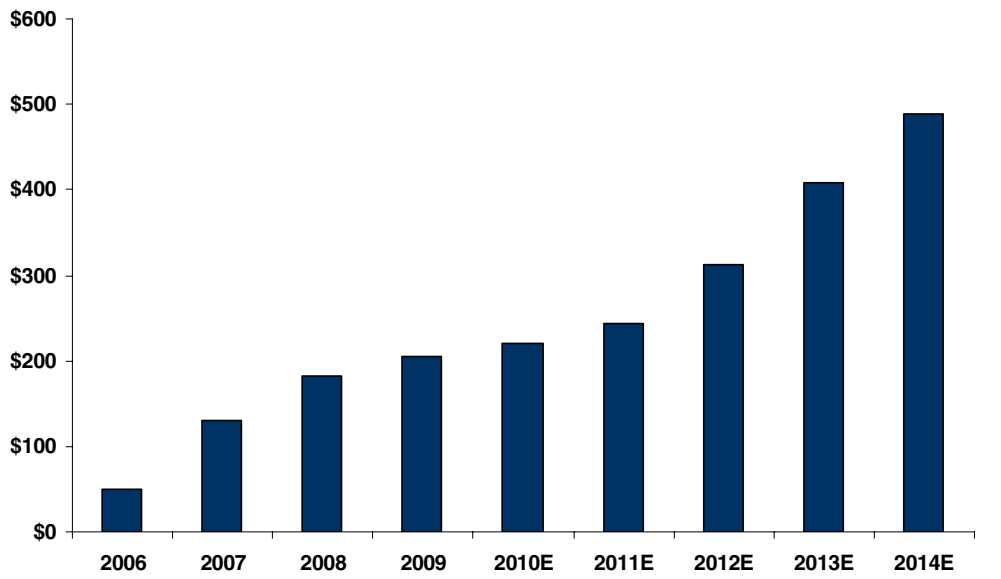
Branded Therapies Leave a Window of Opportunity

Amitiza (Takeda-U.S./Sucampo-ROW)

Amitiza (lubiprostone) was launched in April 2006 in the United States. It is currently approved for CC in adults and IBS-C in adult women. It works by activating chloride channels in the gut wall, resulting in more fluid in the bowel and as such facilitates the passage of stool.

The drug demonstrated clear efficacy in several trials including a four-week trial where patients achieved 5. CSBMs per week compared with 2.9 CSBMs per week for placebo. However, a key shortcoming with Amitiza is the high level of side-effects (adverse events were seen in 51% of patients treated with Amitiza as compared to 21% of patients treated with placebo) and in particular the problem of nausea (32% versus 3% for placebo).

Exhibit 56: Credit Suisse U.S. Amitiza Sales Estimates
in millions, unless otherwise stated



Source: IMS Health, Company data, Credit Suisse estimates.

In Europe, the marketing authorization application was withdrawn by Sucampo in September 2009. While the company has not provided the reason for this, we believe several key factors are at play; (1) a high level of nausea, (2) the short duration of the Phase III trial, and (3) use of the SBM endpoint rather than CSBM. For these reasons, we believe Sucampo has been unable to partner the drug in Europe.

Zelnorm – 5HT4 Receptor Agonist With Risky Safety Profile

Previous standard of care, Novartis' Zelnorm (tegaserod maleate) launched in 2001 but was pulled from the market in 2007 due to cardiovascular safety concerns. The drug did reach $488 million in U.S. sales and $561 million globally in four years.

The previous standard of care for the treatment of IBS-C and CC was Novartis' Zelnorm (tegaserod maleate), which is a partial 5HT4 (serotonin) receptor agonist. Zelnorm's mechanism enhanced gastric motility, decreased colonic transit time, and increased chloride and water secretion to relieve constipation. Zelnorm was FDA approved in July 2002 for short-term treatment of female patients with IBS-C. In August 2004, Zelnorm's label was expanded for treatment of chronic constipation in adults less than 65 years old. After approval, the label was amended various times the first being in April 2004 to include warnings with respect to serious adverse events related to diarrhea, including hypovolemia, hypotension, and syncope and even potential hospitalization for rehydration. Post-marketing surveillance suggested that, between 2004-07, 44 patients suffered serious digestive problems after using Zelnorm. The Zelnorm side effects associated with these cases included:

- intestinal ischemia
- ischemic colitis and severe diarrhea
- hospitalization and
- abdominal surgery

Exhibit 57: **Zelnorm - Drug History**

Zelnorm Timeline	
June-01	FDA rejection for IBS-C treatment
July-02	FDA approval for short-term treatment of IBS-C in women
April-04	FDA warnings about diarrhea and ischemic colitis
August-04	Expansion of Label - To treat CC in adults < 65 years
January-06	EMEA rejection for IBS-C
March-06	CHMP recommendation against approval for treatment of IBS-C
Late 2006	Clinical trials undertaken to evaluate safety as per Swiss officials' request
March-07	Drug withdrawal from market over cardiovascular concern

Source: Company data, Credit Suisse estimates.

Zelnorm was suspended in March 2007, after a meta-analysis of 29 clinical trials demonstrated that, of the 11,614 patients who used Zelnorm 13 (0.11%) experienced cardiovascular events including angina (6), myocardial infarction (4), or stroke. Compared to the placebo rate of 0.01%, the FDA concluded that the cardiovascular adverse events were drug related. John Jenkins, MD, head of FDA's office of new drugs, stated in a conference call following the FDA decision to withdraw the drug that, "based on our review of the data we believed that the risk versus benefit profile for Zelnorm was no longer favorable." Zelnorm's efficacy data was unparalleled at the time. In two phase III studies, Zelnorm 2 mg and 6 mg bid showed significant benefit versus placebo over 12 weeks in eliciting efficacy response. It is noteworthy that the drug never gained European Medicines Agency (EMEA) marketing approval in the first place because of the safety concerns.

Key Attributes for New Therapeutics—Physician and Patient Perspectives

The fragmented nature of the laxative market is testament to the fact that no one product works for all. While this likely reflects the heterogeneity of chronic constipation, in terms of which of the underlying causes predominate, we also note that existing treatments are relatively limited in their potency. Therefore, there is a substantial need for an effective, well-tolerated, treatment for chronic constipation that targets more than just one constipation symptom in isolation.

Our research suggests that GI specialists and patients have different priorities in terms of qualities of a new therapeutic for chronic constipation. The physician consultants we talked to highlighted the following as key priorities:

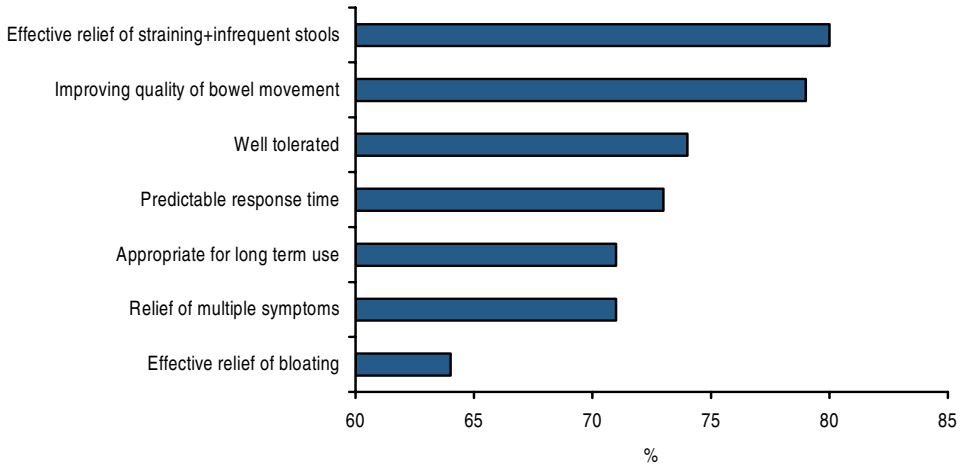
1. **High potency:** GI experts expressed notable frustration that they had few options to offer patients who had been referred from primary care. Although drug optimization by an expert gastroenterologist had some benefits, they noted that dissatisfaction levels still remained high.
2. **Novel mechanism:** The GI experts that we sampled expressed the view that current treatments are relatively basic and that there has been relatively little innovation in this field for the past 20 years. While stimulant laxatives are functionally more sophisticated (they encourage the gut's own propulsive contractions), from a mechanistic perspective they also remain relatively crude (they act by irritating the nerves in the gut—myenteric plexus). Stimulating the 5HT4 receptor was viewed to be an innovative approach. However, in light of Zelnorm and Propulsid, GI experts noted the importance of the potential toxicities with this approach.

3. **Side effects:** Potency and mechanistic sophistication should not be to the detriment of the safety profile. GI experts expressed concerns with the safety profile of 5HT-4 agonists, highlighting in particular the CV side effects of Zelnorm and Propulsid. They note that for a new 5HT-4, extensive CV safety data, together with post-marketing surveillance, would be needed to reassure physicians.
4. **Prescription only:** GI experts expressed a preference for a new treatment to be prescription only rather than available OTC. When asked why, they associated prescription only with increased potency.
5. **Pricing:** The GI experts we talked to conceptually agreed that a novel agent for chronic constipation with a beneficial therapeutic effect could warrant a premium pricing over established agents. However, they also highlighted that in the real world setting they did not think the reimbursement authorities would pay a notable premium.
6. **Dosing:** Compliance rates for chronic diseases tend to be low. The GI experts noted that on account of dosing (e.g., bad taste, requirement to drink lots of water), compliance in chronic constipation was particularly problematic. This has been partly alleviated by the introduction of new flavors for drugs such as the laxative Movicol. Nonetheless, they noted that a once-daily tablet would mark a significant improvement on current dosing regimens.

These views are likely to differ substantially from those of primary care physicians. In marketing a new therapeutic for chronic constipation, an astute awareness of the intended audience is required. However, regardless of whether a drug is targeted at GI specialists, primary care physicians or directly to the patient, patients' views remain important.

Whereas GI specialists focused on mechanistic considerations and potency, patients spoke more of the alleviation of specific symptoms and the predictability of response. Figure 58 illustrates the patient perspective regarding qualities of any new therapeutic for chronic constipation.

Figure 58: Patient Perspective—Qualities of Any New Therapeutic for Chronic Constipation



Source: Adapted from Johanson 2007.

Competitive Drugs in Development

The competitive landscape of treatment for CC and IBS-C is summarized in Exhibit 59. The bottom-line conclusion from our analysis of the competitive environment for linaclotide is that the drug faces a relatively benign competitive threat, with most products at least two years behind in development, giving the advantage of design trials as per the new FDA guidelines.

Exhibit 59: Selected Competitive Drugs on the Market or in Development

Compound	Company	Mechanism of Action	Development Stage	Comment
Chloride channel activators				
Amitiza (lubiprostone)	Sucampo/ Takeda (US)	Calcium channel activator (prostone)	Marketed	FDA approved for the treatment of chronic constipation and for IBS-C. Phase III data generated in OIC. Sucampo had submitted a CTD through the decentralised procedure in Europe but the Marketing Authorisation Application was withdrawn by Sucampo in September 2009. Two phase III studies were initiated with Amitiza in OIC—one was clearly negative.
Resolor (prucalopride)	Movetis/Johnson and Johnson	Once-daily agonist of guanylate cyclase type-C	Marketed (EU)	EMEA approved for the treatment of chronic constipation in October 2009. JNJ retains the US and ROW rights. Unclear if they will look to file the product in the US.
Guanylate cyclase agonists				
SP-304	Synergy Pharmaceuticals/ Callisto	Guanylate cyclase agonist	Phase II	Phase II studies started in early 2010. Results expected in late 2010.
5HT4 agonists				
TD-5108	Theravance	Selective oral 5-HT4 receptor agonist	Phase II	Phase III to be started. No recent developments reported but likely waiting partnership.
ATI-7075	Aryx	Non-selective oral 5-HT4 receptor agonist	Phase II	Rights were returned to Aryx by Procter&Gamble after latest trial results became available. Unclear if further development is ongoing.
Sodium-bile acid co-tranporter inhibitors				
A3309	Albireo/ AstraZeneca	Apical sodium dependent bile acid transporter (ASBT) inhibitor	Phase II	Once-daily, oral compound. In a multiple ascending-dose Phase II study for chronic constipation. May also prove beneficial in IBS-C but development there is further behind.
Opioid antagonists				
Relistor (methylnaltrexone)	Progenics	Subcutaneous mu-opioid receptor antagonist	Approved (OIC)	Approved in US and EU (IV formulation) for opioid-induced constipation only (not competitive in the chronic constipation market). Phase IIb data for oral formulation available in non-cancer OIC. Rights returned to Progenics by Pfizer/Wyeth in October 2009.
Entereg (alvimopan)	Adolor/GSK	Subcutaneous mu-opioid receptor antagonist	Approved (POI)	Potential competitive threat for opioid-induced constipation and post operative Ileus (POI) only. Approved in US for POI and on clinical hold for OIC. Oral formulation in Phase II.
NKTR-118	Astra Zeneca/ Nectar	Peripheral opioid antagonist	Phase II/III	Potential competitive threat for OIC. Phase IIb completed with positive results, but significant degree of abdominal pain. Designing Phase III, planned filing 2013.
TD-1211	Theravance	Opioid receptor antagonist	Phase II	Once-daily treatment for constipation in patients treated with opioids. A multiple ascending-dose Phase II study is ongoing.
ALKS 37	Alkermes	Opioid receptor antagonist	Phase II	In Phase II development for opioid induced constipation. Results expected in 1Q 2011.
ADL5945	Adolor/GSK	Opioid receptor antagonist	Phase I	Potential competitive threat for OIC only. Both a Phase I single and multiple, escalating dose placebo-controlled safety study have been conducted with ADL5945. Adolor intends to initiate Phase I exploratory efficacy clinical studies in early 2010.

Source: Company data, Credit Suisse estimates.

Key Partnerships Offer Global Exposure

IRWD has developed commercial alliances with Forest in the United States, Almirall in Europe, and Astellas in Asia, to achieve global exposure and maximize the value of linaclotide. We credit IRWD's deal-making abilities in establishing these partnerships with attractive upfront and milestones, while still leaving favorable back-end economics to capture IRWD's commercial potential. (See Exhibit 60 for partnership details.)

Exhibit 60: Linaclotide Partnership Agreements

Region	Partner	Launch / Expiration	Agreement Signed	Terms of Agreement
US, Canada and Mexico	Forest	4Q 2011 / Mar-2025	Sept-2007	1.) IRWD and FRX signed a 50/50 partnership to co-develop and co-market in the US. 2.) Canada & Mexico: FRX has exclusive rights and will pay IRWD royalties on net sales. 3.) US: IRWD and FRX will share profits equally. 4.) FRX initially paid IRWD $70m in licensing fees, which was split into $50m in 2007 and $20m in 2008. These payments are amortized over a 5 year development period, which was defined by both parties at the agreement signing. 5.) FRX paid IRWD $10m as a development milestone payment in 2008 and $20m in 2009. These payments are also amortized over the remaining development period. 6.) IRWD received $9m in 2007 as revenue from the contingent equity investment, which is also amortized over the initial 5 year development period. 7.) IRWD has the potential to collect a total of $330m in upfront/ milestone/ commericialization payments from FRX. 8.) All pre-commercialization payments are amortized over the defined development period. Payments made during commercialization are reported as a one-time revenue stream in the receiving year.
Europe	Almirall	4Q 2012 / Mar-2025	Apr-2009	1.) Almirall acquired the commercialization rights to the European market, bearing the expenses related to regulatory approval and commercialization. IRWD will provide API and receive a reimbursement. 2.) Almirall will pay IRWD escalating royalty payments based on sales. 3.) Almirall paid $40m in upfront payments in 2009, which was paid out as a net of withheld foreign taxes and totaled $38m. 4.) IRWD received $6m in 2009 as revenue from the contingent equity investment. 5.) IRWD has the potential to receive an additional $55m in upfront/ milestone/ commercialization payments. 6.) Pre- and post-commercialization milestones are reported as described in the FRX agreement (above).
Japan, South Korea, Taiwan, Thailand, the Philippines, and Indonesia	Astellas	4Q 2013 / Mar-2025	Nov-2009	1.) Astellas acquired the commercialization rights to the Asian market, bearing the expenses for clinical development, regulatory approval, and commercialization. 2.) Astellas will pay IRWD escalating royalty payments based on sales. 3.) Astellas paid $30m in upfront payments in 2009, which were deferred to 2010 and will be amortized. 4.) IRWD has the potential to receive an additional $45m in pre-commercialization payments. 5.) Pre- and post-commercialization milestones are reported as described in the FRX agreement (above).

Source: Company data, Credit Suisse estimates.

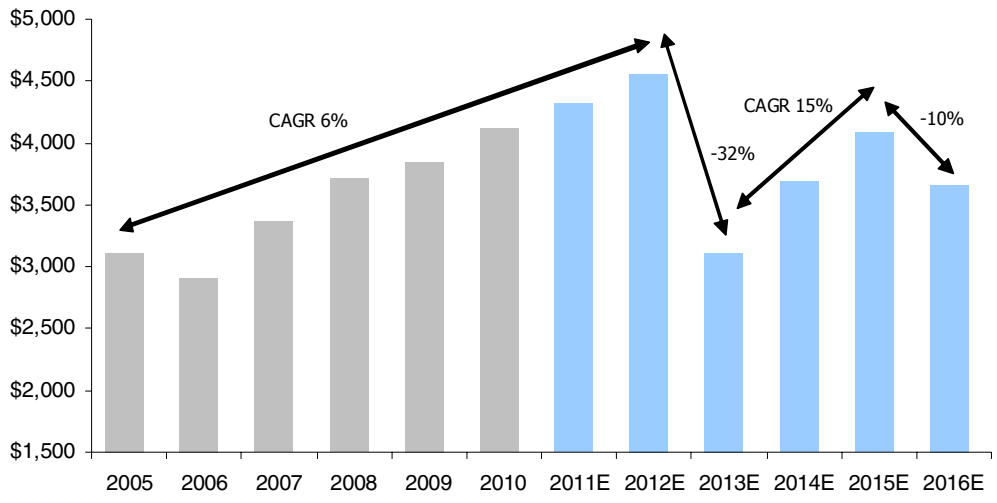
Forest Committed to Linaclotide's Success in the Face of Patent Cliff

In September 2007, IRWD (then Microbia) announced its partnership with Forest to co-develop and co-market linaclotide within the United States. We believe that the partnership offers each party a critical component to linaclotide's commercial success.

The terms of the deal agree on a 50/50 development cost, commercialization, and profit share of linaclotide. The Canadian and Mexican commercialization rights were also retained by Forest, for which Ironwood will receive royalties based on sales. Forest paid an initial upfront payment of $70 million and has agreed to a total of up to $330 million in development and sales milestones. Currently $105 million of pre-commercialization milestones remain.

Forest is very experienced with the primary care markets, having successfully commercialized blockbuster products such as Lexapro and Namenda. This will allow IRWD to leverage Forest's core competency in primary care sales and marketing, which we believe will lead to a more widespread adoption of linaclotide in the IBS-C and CC markets. In addition, Forest's upcoming patent cliff of its key products, Lexapro and Namenda (Exhibit 61), will motivate them towards a concerted sales effort for the linaclotide.

Exhibit 61: Credit Suisse Forest (FRX) Revenue Estimates



Source: Company data, Credit Suisse estimates.

Almirall and Astellas Partnerships Provide Access to Europe and Japan

IRWD's partnership with Almirall, announced in May 2009, included an upfront payment of $40 million, which was paid out net of withheld foreign tax, totaling $38 million. Almirall received the exclusive European rights to linaclotide, entitling IRWD to escalating royalties based on a percentage of European revenues. Almirall has a strong presence in the European market, which will allow IRWD to access the top European markets (primarily the E.U. five including U.K., Italy, France, Germany, and Spain) as well as other smaller European countries. In addition, Almirall bears the cost of regulatory approval and commercialization, whereas IRWD is responsible for providing the active pharmaceutical ingredient (API). Ironwood is reimbursed at cost for API, representing no net spending.

Almirall is a mid-sized pharmaceutical company based in Spain with 2009 sales of €925.5 million. The company has grown through acquisitions and in-licensing transactions although more than half of its sales come from within Spain. The current product spectrum spans many therapeutic areas, while development activity focuses on treatments for asthma, COPD, rheumatoid arthritis, multiple sclerosis, and dermatology indications. Bringing focus to Forest's existing relationship with Almirall on aclidinium, we view the linaclotide partnership with Almirall as a natural extension of Forest/IRWD alliance.

Based on discussion with the EMEA, Almirall believes the U.S. studies conducted by Forest/IRWD will also be sufficient for European approval. Owing to the pricing differences for the IBS-C and CC indications, Almirall plans to submit a marketing application for IBS-C first in an effort to establish premium pricing for linaclotide. We expect that the selling price of linaclotide in Europe will be significantly lower, likely half of the U.S. price (e.g., roughly $3 per day in Europe versus $6 per day in the United States). The initial commercial launch will be geared towards GI specialists using a relatively small sales force. Although Almirall does not have the marketing reputation of a major pharmaceutical company, like GlaxoSmithKline or Sanofi, it is motivated to be successful to aide the company's expansion plans.

In November 2009, IRWD announced its licensing agreement with Astellas to develop and commercialize linaclotide in Japan, South Korea, Taiwan, Thailand, the Philippines, and Indonesia. IRWD received $30 million in an upfront payment and is eligible to receive an additional $45 million in pre-commercial milestones. IRWD is eligible for escalating royalties as a percentage of Japanese revenues. Astellas is responsible for all activities and expenses relating to clinical development, regulatory approval, and commercialization in the above mentioned territory. As one of Japan's largest pharmaceutical companies, Astellas has established commercial capabilities in both primary care and specialty categories throughout Asia.

Our sales forecast for Europe and Japan are derived from Credit Suisse's European and Japanese pharmaceutical analysts. Our base case NPV scenario is based on 75% POS for linaclotide reaching the U.S. and E.U. markets, and 50% POS in Japan to account for lesser visibility at this point. We assume royalty rates in Europe and Japan to increase gradually from 10% in launch year to 27% by 2025. (Exhibit 62)

In the EU, we assume $403 million in peak sales for linaclotide resulting in a royalty income NPV of $146 million, and in Japan, we assume $197 million in peak sales for linaclotide, representing royalty income NPV of $49 million for IRWD. Overall, linaclotide non-U.S. collaboration contributes approximately 15% to our $14 NPV estimate for IRWD (Exhibit 65).

Exhibit 62: Probability Adjusted Europe and Japan Linaclotide Revenue and Royalty Income NPV Forecasts

PROBABILITY- ADJUSTED	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Probability			*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*
EU Revenue			20	60	100	140	168	202	232	267	293	323	355	373	391	403
YoY Revenue Growth			*na*	*200.0%*	*66.7%*	*40.0%*	*20.0%*	*20.0%*	*15.0%*	*15.0%*	*10.0%*	*10.0%*	*10.0%*	*5.0%*	*5.0%*	*3.0%*
Prob. Adjusted Revenue			15	45	75	105	126	151	174	200	220	242	266	279	293	302
EU Royalty			2	5	8	11	15	23	31	40	48	56	64	70	76	82
EU Royalty Rate (post-tax)			*10%*	*10%*	*10%*	*10%*	*12%*	*15%*	*18%*	*20%*	*22%*	*23%*	*24%*	*25%*	*26%*	*27%*
NPV of Cash Flows	**0**	**0**	**1**	**3**	**5**	**6**	**7**	**10**	**12**	**14**	**15**	**15**	**15**	**15**	**15**	**14**
Probability-Adjusted NPV ($MM)	**$146**															

JAPAN PROBABILITY- ADJUSTED	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Probability			*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
Japan Sales			0	0	20	70	98	118	135	149	164	172	180	186	191	197
YoY Sales Growth					*na*	*250.0%*	*40.0%*	*20.0%*	*15.0%*	*10.0%*	*10.0%*	*5.0%*	*5.0%*	*3.0%*	*3.0%*	*3.0%*
Prob. Adjusted Revenue			0	0	10	35	49	59	68	74	82	86	90	93	96	99
Japan Royalty			0	0	1	4	6	9	12	15	18	20	22	23	25	27
Japan Royalty Rate (post-tax)			*10%*	*10%*	*10%*	*10%*	*12%*	*15%*	*18%*	*20%*	*22%*	*23%*	*24%*	*25%*	*26%*	*27%*
NPV of Cash Flows	**0**	**0**	**0**	**0**	**1**	**2**	**3**	**4**	**5**	**5**	**5**	**5**	**5**	**5**	**5**	**5**
Probability-Adjusted NPV ($MM)	**$49**															

Source: Company data, Credit Suisse estimates.

M&A Can't Be Ruled Out, But Anti-Takeover Provisions Makes It Challenging

In the scenario where the product is either more or less successful than planned, we believe an acquisition by an existing partner cannot be ruled out. With the mechanisms in place precluding a hostile bid, the takeover would have to be a white knight arrangement.

Highlights of IRWD's anti-takeover mechanisms:

1. **Existing standstill agreements between partners in linaclotide**. Existing standstill agreements between IRWD and each of its three partners, Forest, Almirall, and Astellas, preclude the potential for a hostile acquisition by one of the partners, but do not rule out a friendly merger.
2. **Change of control mechanisms.** Each of the partnership agreements incorporates change of control provisions, which would make an acquisition less likely as the rights to linaclotide could be purchased away from the acquiror.
3. **Dual class common stock structure that provides class B common stockholders concentrated control to approve M&A.** The Class B common stock, which was not sold in the offering but is held by pre-IPO investors, founders, directors, executives, and employees, has ten votes per share in change of control transactions (as opposed to one vote per share from Class A stock issued from the IPO). As a result of the dual class structure, Class A stock holders have only 2.4% of total votes versus Class B stockholders with 97.6% of total votes in transaction matters. Therefore, there is a risk that management and class B stockholders may take actions at the expense of class A stockholders.
4. **Ability of board of directors to issue preferred stock with voting/other rights without stockholder approval.** This may impede the success of potential acquiror's attempt.
5. **Board of directors is divided into three classes serving staggered three-year terms.**

Financial Outlook

We estimate Ironwood will achieve its first positive earnings per share (EPS) in 2015, with rapid EPS compound annual growth rate of 38% through 2020.

The consensus estimates for the company may not be too reliable at this point due to limited analyst coverage and lack of visibility for future operational results at this time.

Exhibit 63: IRWD Credit Suisse versus Consensus Revenue and EPS Estimates

	Cons	CS	Cons	CS	Sales Growth
2009A	(10.00)	(10.00)	36	36.1	
2010E	(0.87)	(0.69)	37	36.8	*2%*
2011E	(0.22)	(0.55)	81	50.4	*37%*
2012E	(0.74)	0.00	114	134.0	*166%*
2013E	(0.47)	(1.13)	150	23.6	*(82%)*
2014E	0.18	(0.24)	N/A	103.2	*338%*
2015E	1.46	0.32	N/A	155.6	*51%*

Source: FactSet, Credit Suisse estimates.

Balance Sheet Analysis

As of the end of the first quarter of 2010, IRWD had a combined $299 million in cash and cash equivalents ($76 million), and available for sale securities ($222 millioin). IRWD has very small amount of debt ($2.9 million), which consists of long-term debt ($2.7 million) and capital lease obligations ($200,000). IRWD's long-term debt relates to its master loan agreement for the financing of purchases of laboratory, computer, and other equipment. In our model, we have assumed modest equity offering of $150 million in 2014 to help finance ramp up in cash spend on post linaclotide launch. We believe the company will be able to achieve sustainable free cash flow beginning in 2015.

Valuation

Net Present Value (NPV) Analysis

We believe the linaclotide potential is fully valued in the stock and hence our Neutral rating. Our $14 target price for IRWD is derived using NPV method, by applying a 12% WACC (based on capital asset pricing model) to our forecasted cash flows through 2025. We assign no terminal value and no value to Ironwood's pre-clinical and early-stage pipeline.

We model linaclotide's opportunity in CC and IBS-C together, along with further breakdown of Europe and Japan royalties based on sales forecasts from the Credit Suisse European and Japanese pharmaceutical analysts, and then probability adjust these revenues. This base case scenario is based on 75% probability of success (POS) for linaclotide reaching the U.S. and E.U. markets, and 50% POS in Japan to account for lesser visibility at this point. We assume non-U.S. royalty rates to increase gradually from 10% in launch year to 27% by 2025.

With Phase III CC data in hand and positive expectations towards Phase III IBS-C data due in the second half of 2010, we assume a 75% probability for linaclotide reaching the market in 2012 and $1.2 billion in peak market potential in the United States by 2025, bringing us to an NPV of $813 million or value of $9.1 per share. In the E.U., we assume $403 million in peak sales for linaclotide resulting in a royalty income NPV of $146 million, and in Japan, we assume $197 million in peak sales for linaclotide, representing royalty income NPV of $49 for IRWD. Adjusting for an estimated $262 in net cash/marketable securities, we arrive at NPV and target price target of $14 per share (Exhibit 64).

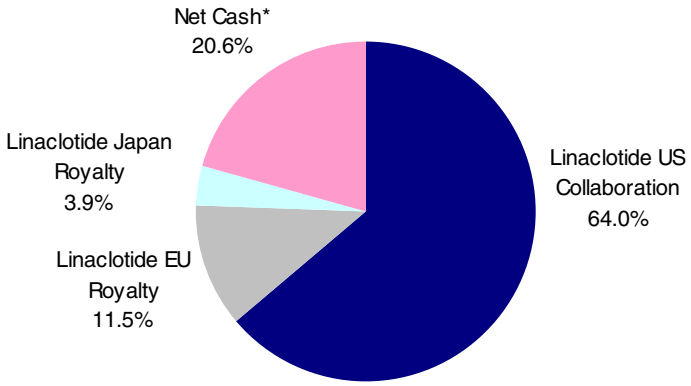
Overall, we estimate that linaclotide U.S. collaboration contributes 64% to total NPV, followed by net cash and non-U.S. royalty income by 21% and 15%, respectively (Exhibit 65).

Exhibit 64: IRWD- Base Case Probability Adjusted NPV Summary

Drug	Peak Sales ($ millions)	Stage	(Estimated) Launch	Probability of Reaching Market	Economics	Probability Adjusted NPV	Per Share Value	% of Total Value
Pipeline								
Linaclotide Franchise								
Linaclotide US Collaboration	$1,202	Phase III	2012	75%	50/50 Profit Split w/ FRX	$813	$9.10	64.0%
Linaclotide EU Royalty	$403	Phase III	2012	75%	Tiered Royalty w/ Almirall	$146	$1.63	11.5%
Linaclotide Japan Royalty	$197	Phase III	2014	50%	Tiered Royalty w/ Astellas	$49	$0.55	3.9%
Total						**$1,008**	**$11.29**	**79.4%**
Other								
Net Cash (Cash/Equivalents - Debt)						$262	$2.93	20.6%
Other Costs NPV (not directly accounted for in programs above)						$0	$0.00	0.0%
Total Other						**$262**	**$2.93**	**20.6%**
Total						**$1,270**	**$14.21**	**100.0%**

Source: Company data, Credit Suisse estimates.

Exhibit 65: IRWD- NPV Contributors



*Net Cash (Cash/Equivalents - Debt)

Source: Company data, Credit Suisse estimates.

Moreover, a quantification of upside potential and downside risk relative to our investment case appears in Exhibit 66. Our bear case is suggestive of material downside risk to the current stock price, but the probability of this scenario is approximately 10%. We believe our base and bull case are 75% and 15% probable. We choose 75% as it corresponds to our base POS estimate of 75% for U.S. and EU linaclotide. Therefore, the expected valuation considering a blend of probability and DCF valuation would suggest value of $14.5, higher than our NPV-based target price of $14.

Our bear-case and bull-case analysis yield NPV-based target prices of $3 (see Exhibit 67) and $24 (Exhibit 68). The key assumptions for our various scenario analyses are outlined in Exhibit 69.

Exhibit 66: Summary of Credit Suisse Target Price Under Bear-, Base-, and Bull Case Scenarios

	CS Assumed Probability	CS Price Target		Expected Valuation Price
		Price Target*	Upside/ (Downside)	
Bear Case	10%	$3	(75%)	$0.3
Base Case	**75%**	**$14**	**2%**	**$10.7**
Bull Case	15%	$24	69%	$3.5
TOTAL				**$14.5**

* Target Price is based on NPV valuation

*Source: Credit Suisse estimates. *Target price is based on NPV valuation.*

Exhibit 67: IRWD- Bear Case Probability Adjusted NPV Summary

Drug	Peak Sales ($ millions)	Stage	(Estimated) Launch	Probability of Reaching Market	Economics	Probability Adjusted NPV	Per Share Value	% of Total Value
Pipeline								
Linaclotide Franchise								
Linaclotide US Collaboration	$0	Phase III	2012	0%	50/50 Profit Split w/ FRX	$28	$0.32	9.8%
Linaclotide EU Royalty	$0	Phase III	2012	0%	Tiered Royalty w/ Almirall	$0	$0.00	0.0%
Linaclotide Japan Royalty	$0	Phase III	2014	0%	Tiered Royalty w/ Astellas	$0	$0.00	0.0%
Total						**$28**	**$0.32**	**9.8%**
Other								
Net Cash (Cash/Equivalents - Debt)						$262	$2.93	90.2%
Other Costs NPV (not directly accounted for in programs above)						$0	$0.00	0.0%
Total Other						**$262**	**$2.93**	**90.2%**
Total						**$290**	**$3.25**	**100.0%**

Source: Credit Suisse estimates.

Exhibit 68: IRWD- Bull Case Probability Adjusted NPV Summary

Drug	Peak Sales ($ millions)	Stage	(Estimated) Launch	Probability of Reaching Market	Economics	Probability Adjusted NPV	Per Share Value	% of Total Value
Pipeline								
Linaclotide Franchise								
Linaclotide US Collaboration	$2,924	Phase III	2012	75%	50/50 Profit Split w/ FRX	$1,674	$18.74	78.6%
Linaclotide EU Royalty	$403	Phase III	2012	75%	Tiered Royalty w/ Almirall	$146	$1.63	6.9%
Linaclotide Japan Royalty	$197	Phase III	2014	50%	Tiered Royalty w/ Astellas	$49	$0.55	2.3%
Total						**$1,870**	**$20.92**	**87.7%**
Other								
Net Cash (Cash/Equivalents - Debt)						$262	$2.93	12.3%
Other Costs NPV (not directly accounted for in programs above)						$0	$0.00	0.0%
Total Other						**$262**	**$2.93**	**12.3%**
Total						**$2,131**	**$23.85**	**100.0%**

Source: Credit Suisse estimates.

Exhibit 69: Assumptions Used in Generating Base/Bull/Bear Cases for IRWD

Scenario	Probability	Assumptions
Base Case	75%	(1) Branded Rx captures 16% of total market by 2025 (2) Linaclotide peak branded Rx market share of 55% by 2025 (3) Linaclotide annual price increases of 2%
Bull Case	15%	(1) Branded Rx captures 25% of total market by 2025 (2) Linaclotide peak branded Rx market share of 70% by 2025 (3) Linaclotide annual price increases of 5%
Bear Case	10%	Non approval scenario due to negative long-term safety data. NPV is comprised of net cash and phase 3 and filing-related linaclotide milestones.

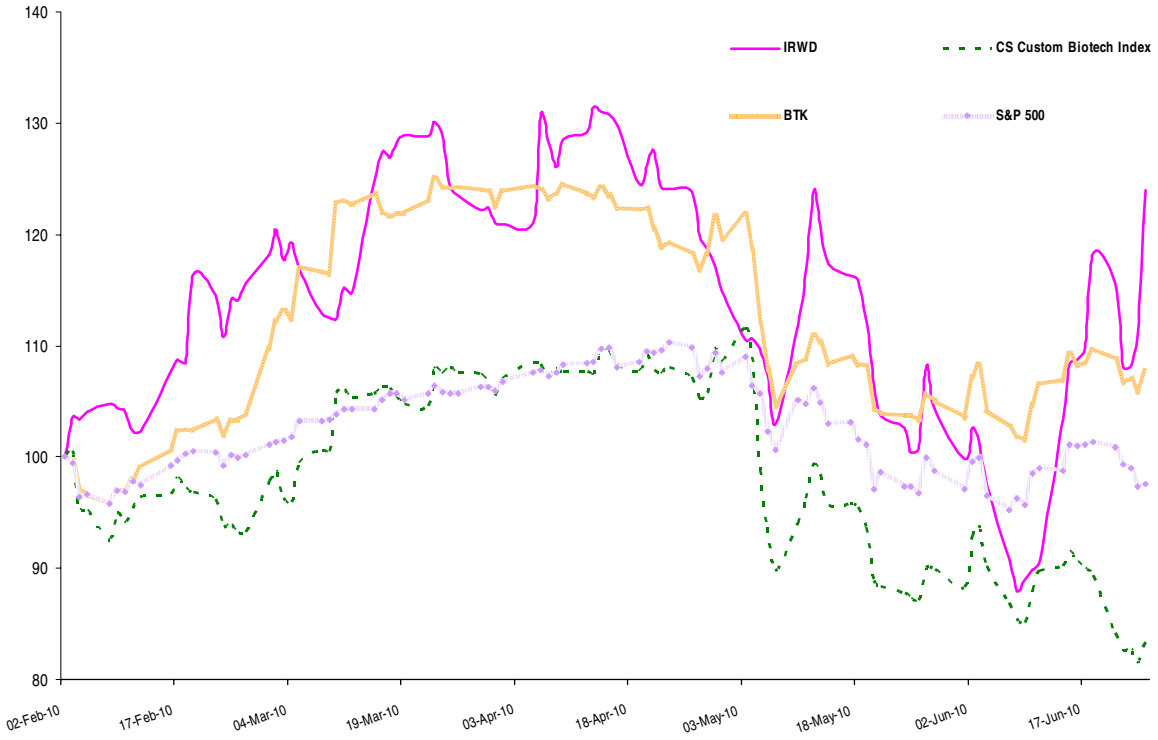
Source: Credit Suisse estimates.

Historical Stock Performance

Since the IPO on February 2, 2010, IRWD has outperformed the NYSE Biotech Index (tk: BTK) and S&P 500 by 12% and 22%, respectively (see Exhibit 70).

The short interest ratio for IRWD has reached 18 (per Bloomberg), the highest level since IPO. The upcoming lock up expiration date on August 1, 2010, may contribute to some weakness in the stock, but fundamentals view could also play a role (Exhibit 71). Nonetheless, it's possible that the ratio would decline with more float in the market.

Exhibit 70: Price Performance versus Credit Suisse Biotech Late-Stage Products Index, BTK, and S&P 500 (Since IPO)



Source: FactSet, Bloomberg, Credit Suisse estimates.

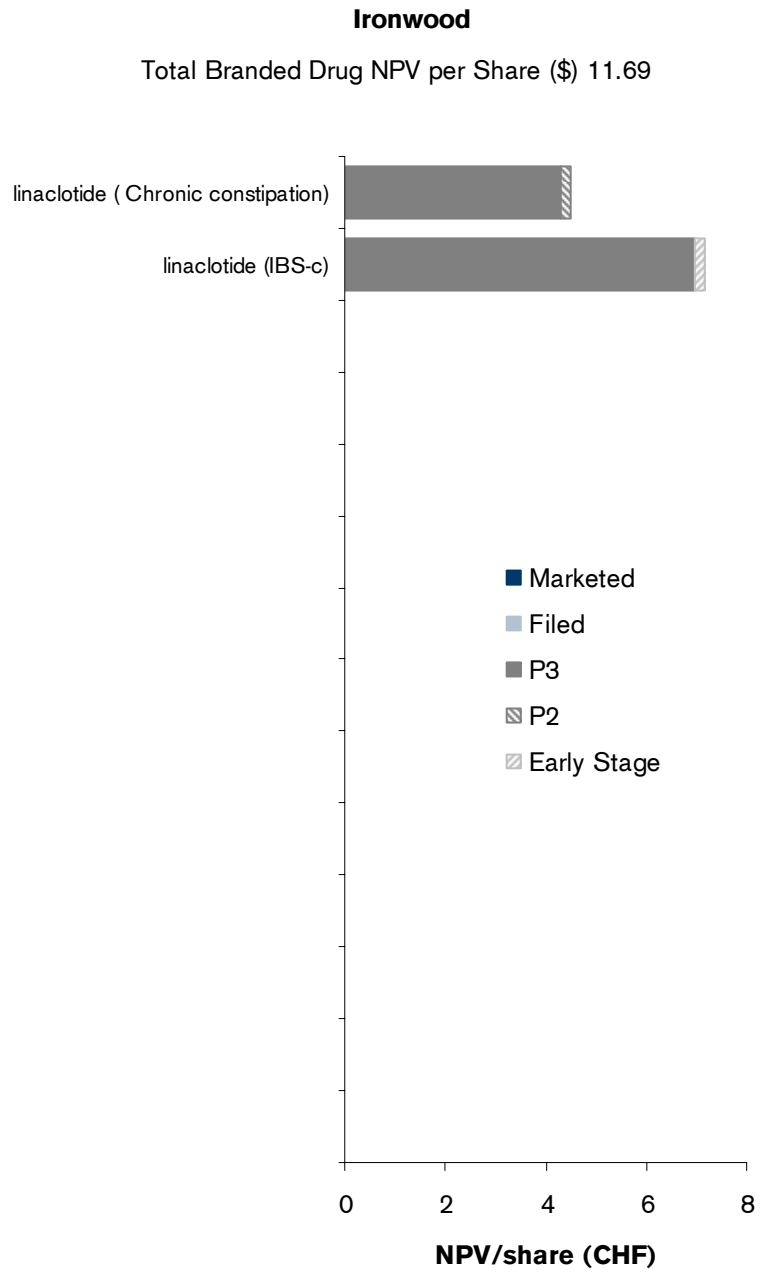
Exhibit 71: IRWD Short Interest Ratio, as of June 15, 2010

Source: Bloomberg. Short interest ratio is calculated by dividing the short interest by average 30-day daily volume. The ratio implies the number of days it takes to cover the outstanding short interest.

PharmaValues NPV Analysis

PharmaValues - a Credit Suisse proprietary valuation tool for the global pharmaceutical and biotechnology industry suggests a net present value (NPV) of $11.69 per share for Ironwood.

Exhibit 72: IRWD PharmaValues NPV breakdown



Source: Company data, Credit Suisse estimates

Risks

Clinical Risks with Phase III IBS-C Trial and Long Term Safety Study

With the Phase III IBS-C trials ongoing, clinical risk exists ahead of the data to be top-lined in the second half of 2010. We expect the data to be statistically and clinically significant in terms of abdominal pain improvement and weekly CSBM increases based on the Ph II data. However, as with any responder analysis, the risk of an unusual placebo response must always be considered. While we believe efficacy should be rather straightforward, the risks associated with safety may be higher than efficacy as it will be the longest duration that patients will be on drug. We recognize the mechanism implies better safety than Zelnorm, but also highlight that concerns surrounding Zelnorm only emerged after a meta analysis of data from 29 clinical studies. The long-term safety study will dose patients on 266 mcg (the high dose in Phase III trials) for 18 months. Nonetheless, class history suggests a post-marketing safety surveillance program to be linked with approval.

Risk of Delay or Setback in Approval Process

As with any Phase III, regulatory risk exists with the FDA approval process. With Phase III IBS-C data expected in the second half of 2010, Ironwood plans to file an NDA for linaclotide in the first quarter of 2011 with approval in late 2011 and commercial launch in 2012. Any delay or setback in this the present value of our cash flow assumptions and our valuation.

Financing Risk

Having raised $203 million in net proceeds from the IPO, Ironwood has $299 million in cash on hand as of first quarter 2010. IRWD intends to use most of the cash resources to launch linaclotide in the United States along with partner Forest. The costs of launch will be significant, and we believe IRWD is likely targeting $100 million per year in marketing alone, which represents the cost for physician education, patient education, promotional materials, and sampling. In addition, we expect the U.S. sales force will consist of approximately 1,000 sales representatives with IRWD responsible for approximately 200 of these. These costs may turn out to be inadequate suggesting the potential of future financial burden on the company. With the additional roughly $200 million in pre-commercial milestones should help IRWD sustain its cash balance ahead of profitability. Last, our model does assume $150 million new equity issuance in 2014.

Commercial Risk—Competition

With the lackluster penetration of Amitiza and Zelnorm off the market, IRWD stands to benefit from the lack of current competition. However, the recent launch of Movetis' Resolor in the E.U. (in the first qaurter of 2010) brings a novel 5 HT-4 agonist (Zelnorm) to the constipation market without the cardiac safety risk. In addition, new agents are in development for constipation (e.g., Theravance's TD-5108) which, if approved, could put our commercial penetration rates of linaclotide at risk. In particular, SP-304, also a GC-C receptor agonist being developed by Synergy Pharmaceuticals to treat CC and IBS-C, has advanced into Phase IIa clinical development.

Assumed Market Size and Penetration Rates

As we discuss in more detail later in this report, estimates for the prevalence, and hence patient population, of chronic constipation are highly variable depending on the data source. Moreover, estimates of what proportion of chronic constipation patients visit their primary care physicians and are then referred to GI specialists are even more rudimentary. We have used a broad range of literature sources and conducted a number of calls with physician consultants to attempt to attain more granularity with respect to our modeling assumptions. We have erred on the side of caution, but nevertheless highlight that our modeling methodology remains subjective.

Slow Ramp Up in Sales

IRWD's launch globally will be staggered owing to industry-standard delays to market access owing to different reimbursement environments in each country. This may result in an initially slower sales ramp for linaclotide revenues. Further, constipation is a consumer driven market and adoption of linaclotide may turn out to be slower than our projections. Such a lack of visibility and/or extrapolation of initial launch revenues may be viewed negatively.

Company Overview

Profile

Located in Cambridge, MA, Ironwood is a pharmaceutical company that is developing linaclotide, a GC-C agonist that is being evaluated in a confirmatory Phase 3 program. for the treatment of irritable bowel syndrome with constipation (IBS-C) and chronic constipation. Ironwood completed its initial public offering on February 2, 2010. Ironwood has developed commercial alliances with Forest in the United States, Almirall in Europe, and Astellas in Asia, to achieve global exposure and maximize the value of linaclotide.

Management Team

IRWD's public history is relatively short, but management team (Exhibit 73) is well known in the investment community. Their success with linaclotide remains to be seen, but we are impressed with their interest in strategic and appropriate investment to build a sustainable pharmaceutical company. Conversations with management suggest that it is committed to enhance shareholder value. Management does not plan to issue quarterly or annual earnings guidance, but has maintained willingness to be transparent about the key elements of performance.

Nonetheless, dual class equity voting structure results in concentrated control within Class B common stockholders, among which IRWD's executive officers and directors as a group have 24.76% of total voting power. This means the direction of the company lies largely on the managements' ability to make prudent decisions.

IRWD's compensation structure seems also to be aligned with shareholders' interests, as executive officers and many of its employees have significant portion of their incentive compensation in milestone-based equity awards that accelerate upon achievement of major value-creating events which may occur many years from the date of the grant. Meanwhile, almost the company's entire CEO annual performance award is based on corporate objective achievements (Exhibit 74).

Exhibit 73: IRWD Senior Management Team

Name	Position	Start Date (Current Position)	Comment
Peter M. Hecht, Ph.D.	Chief Executive Officer	1998	Prior to founding Ironwood in 1998, Dr. Hecht was a research fellow at Whitehead Institute for BioMedical Research. He serves on the board of directors of Whitehead Institute and Microbia Inc. Dr. Hecht holds a B.S in mathematics and an M.S in biology from Stanford University apart from a Ph.D. in molecular biology from the University of California.
Michael J. Higgins	Chief Operating Officer and Chief Financial Officer	2003	Prior to joining in the current position in 2003, Mr. Higgins served in several senior positions at Genzyme Corporation, including vice president of corporate finance. He serves on the board of directors at Microbia. Mr. Higgins holds a B.S from Cornell University and an M.B.A from the Amos Tuck School of Business Administration.
Mark G. Currie, Ph.D.	Senior Vice President, R&D and Chief Scientific Officer	2002	Prior to joining Ironwood in 2002, Dr. Currie served as vice president of discovery research at Sepracor leading cardiovascular and central nervous system disease research. Prior to that, he led discovery pharmacology and was a director of arthritis and inflammation at Monsanto Company. Dr. Currie holds a B.S in biology and a Ph.D.in cell biology.
Thomas A. McCourt	Chief Commerical Officer and Senior Vice President, Marketing and Sales	2009	Before joining at this position in September 2009, Mr. McCourt led the US brand team for denosumab at Amgen Inc. Prior to that, he held various senior positions at Novartis AG between 2001 and 2008. Mr. McCourt holds a degree in pharmacy from the University of Wisconsin.

Source: Company data.

Exhibit 74: Management Compensation for Key Officers at Ironwood

Name	Position	Salary	Bonus	Option Awards	All Other Compensation	Total
Peter M. Hecht, Ph.D.	Chief Executive Officer	$100,000	$0	$465,684	$4,440	**$570,124**
Michael J. Higgins	Chief Operating Officer and Chief Financial Officer	$265,000	$5,000	$177,771	$4,440	**$452,211**
Mark G. Currie, Ph.D.	Senior Vice President, R&D and Chief Scientific Officer	$315,000	$8,000	$475,561	$4,440	**$803,001**
Thomas A. McCourt	Chief Commerical Officer and Senior Vice President, Marketing and Sales	$102,292	$0	$52,698	$2,639	**$157,629**

Source: Company data

Board of Directors

We believe IRWD currently has a strong composition of board members that bring various industry perspectives into the organization (Exhibit 75). Bryan E. Roberts will replace chairman and co-founder Joseph Cook as chairman of the board of directors (but will remain a director) in July 2010.

Exhibit 75: IRWD Board of Directors

Name	Position	Independent?
Joseph C. Cook, Jr. (1)	Chairman of the Board, Co-founder of Ironwood	No
Peter M. Hecht, Ph.D.	Chief Executive Officer and Founder of Ironwood	No
George H. Conrades	Executive Chairman of Akamai Technologies	Yes
David Ebersman	Chief Financial Officer of Facebook	Yes
Marsha H. Fanucci	Former Senior Vice President and Chief Financial Officer of Millennium Pharmaceuticals	Yes
Terrance G. McGuire	General Partner at Polaris Venture Partners	Yes
Gina Bornino Miller	Co-founder of Ironwood; Former President and General Manager for Quantum Corporation's Specialty Storage Products Group	Yes
Bryan E. Roberts, Ph.D. (2)	Partner at Venrock, a Venture Capital Investment Firm	Yes
David E. Shaw	Managing Director of Black Point Group LLC, a Private Equity Partnership; Partner at Venrock	Yes
Christopher T. Walsh, Ph.D.	Hamilton Kuhn Professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School	Yes

(1) Will step down as chairman of the board of directors in July 2010 but remain a director
(2) Will become chairman of the board of directors in July 2010

Source: Company data.

Institutional Ownership

Exhibit 76: Ironwood's Top Ten Holders as of March 31, 2010

Holder Name	March-31-2010 (% O/S)
Ridgeback Capital Management LLC	8.91
Morgan Stanley Investment Management, Inc.	5.03
Wellington Management Co. LLP	2.48
Putnam Investment Management, Inc.	1.31
Morgan Stanley & Co., Inc.	0.96
BVF, Inc.	0.86
Adage Capital Advisors LLC	0.84
AllianceBernstein LP	0.83
Maverick Capital Ltd.	0.76
Waddell & Reed Investment Management Co.	0.69
Total	**22.65**

Source: FactSet

Financial Statements

Exhibit 77: Ironwood Annual Income Statement

			2010														
			Mar-10	Jun-10	Sep-10	Dec-10											
	FY 2008	FY 2009	1QA	2QE	3QE	4QE	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018	FY 2019	FY 2020
Linaclotide Profit Share	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	57,604.92	140,584.13	196,356.33	244,259.14	300,600.53	328,831.30	346,507.17
Linaclotide ex-US Royalty Income	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1,500.00	4,500.00	8,500.00	14,000.00	21,000.00	31,500.00	43,470.00	54,868.80	66,391.25
Linaclotide API Reimbursement	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1,280.58	5,388.06	14,772.76	22,146.09	27,211.07	31,526.18	36,737.13	39,199.10	40,939.60
Milestones	18,383.00	34,321.00	8,838.00	9,153.33	8,047.56	10,561.48	36,600.37	50,350.00	133,959.00	23,550.00	45,550.00	15,000.00	115,000.00	0.00	0.00	0.00	0.00
Collaborative arrangements	18,383.00	34,321.00	8,838.00	9,153.33	8,047.56	10,561.48	36,600.37	50,350.00	136,739.58	33,438.06	126,427.68	191,730.22	359,567.40	307,285.32	380,807.66	422,899.19	453,838.01
Services	3,833.00	1,781.00	214.00	0.00	0.00	0.00	214.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Total Revenues	22,216.00	36,102.00	9,052.00	9,153.33	8,047.56	10,561.48	36,814.37	50,350.00	136,739.58	33,438.06	126,427.68	191,730.22	359,567.40	307,285.32	380,807.66	422,899.19	453,838.01
COGS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1,289.54	5,943.54	9,795.54	14,411.06	17,583.96	20,288.30	23,562.64	25,098.98	26,194.51
Gross Profit	22,216.00	36,102.00	9,052.00	9,153.33	8,047.56	10,561.48	36,814.37	50,350.00	135,450.05	27,494.52	116,632.14	177,319.16	341,983.44	286,997.02	357,255.02	397,800.21	427,643.50
R&D	59,809.00	84,892.00	18,637.00	18,934.14	19,026.34	19,130.07	75,727.56	67,753.24	56,141.64	50,124.81	45,860.06	41,275.39	39,571.86	38,105.03	38,138.54	35,672.38	35,706.56
SG&A	18,328.00	23,980.00	6,643.00	6,363.90	6,363.90	6,926.34	26,297.15	41,969.26	84,064.60	98,133.82	99,660.91	101,624.76	103,623.48	105,238.87	106,882.00	108,553.38	110,253.52
Collaboration Expense	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Operating Income (Loss)	(55,921.00)	(72,770.00)	(16,228.00)	(16,144.71)	(17,342.69)	(15,494.93)	(65,210.33)	(59,372.50)	(4,756.19)	(120,764.11)	(28,888.83)	34,419.02	198,788.10	143,653.11	212,234.47	253,574.46	281,683.43
Interest, Other Income	2,124.00	843.00	68.00	597.14	578.43	533.83	1,777.40	4,109.84	5,007.94	3,137.81	1,177.07	4,717.35	8,955.76	11,829.70	16,670.62	23,772.49	32,441.07
Interest and Other Expense	(1,234.00)	(474.00)	(93.00)	(28.41)	(23.98)	(19.46)	(164.85)	(60.84)	(9.24)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Other income (expense), net	890.00	369.00	(25.00)	568.73	554.45	514.37	1,612.55	4,049.00	4,998.70	3,137.81	1,177.07	4,717.35	8,955.76	11,829.70	16,670.62	23,772.49	32,441.07
Pretax Income (Loss)	(55,031.00)	(72,401.00)	(16,253.00)	(15,575.99)	(16,788.24)	(14,980.56)	(63,597.78)	(55,323.51)	242.51	(117,626.30)	(27,711.76)	39,136.37	207,743.86	155,482.81	228,905.10	277,346.95	314,124.50
Provision For Income Taxes	0.00	911.00	0.00	0.00	0.00	0.00	0.00	0.00	4.85	0.00	0.00	782.73	4,154.88	3,109.66	4,578.10	5,546.94	86,830.26
Net Loss prior to noncontrolling interest	(55,031.00)	(73,312.00)	(16,253.00)	(15,575.99)	(16,788.24)	(14,980.56)	(63,597.78)	(55,323.51)	237.66	(117,626.30)	(27,711.76)	38,353.64	203,588.98	152,373.16	224,326.99	271,800.01	227,294.24
Net Loss attributable to noncontrolling interest	1,157.00	2,127.00	329.00	0.00	0.00	0.00	329.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Net Income (Loss)	(53,874.00)	(71,185.00)	(15,924.00)	(15,575.99)	(16,788.24)	(14,980.56)	(63,268.78)	(55,323.51)	237.66	(117,626.30)	(27,711.76)	38,353.64	203,588.98	152,373.16	224,326.99	271,800.01	227,294.24
Basic Shares Outstanding	6,889.82	7,116.77	89,357.33	89,841.69	90,412.84	91,086.34	91,759.85	95,399.75	96,087.35	97,008.13	107,350.38	109,001.59	111,212.77	114,173.81	118,139.04	123,448.97	130,559.66
Diluted Shares Outstanding	6,889.82	7,116.77	89,357.33	89,841.70	90,412.80	91,086.30	91,759.80	101,424.41	101,362.84	103,692.93	115,769.42	119,528.35	124,260.92	130,175.97	137,504.34	146,486.53	157,348.42
Earnings Per Share, Basic	(7.82)	(10.00)	(0.18)	(0.17)	(0.19)	(0.16)	(0.69)	(0.58)	0.00	(1.21)	(0.26)	0.35	1.83	1.33	1.90	2.20	1.74
Earnings Per Share, Diluted	(7.82)	(10.00)	(0.18)	(0.17)	(0.19)	(0.16)	(0.69)	(0.55)	0.00	(1.13)	(0.24)	0.32	1.64	1.17	1.63	1.86	1.44
Margin Analysis																	
Gross margin	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*99.1%*	*82.2%*	*92.3%*	*92.5%*	*95.1%*	*93.4%*	*93.8%*	*94.1%*	*94.2%*
R&D % sales	*269.2%*	*235.1%*	*205.9%*	*206.9%*	*236.4%*	*181.1%*	*205.7%*	*134.6%*	*41.1%*	*149.9%*	*36.3%*	*21.5%*	*11.0%*	*12.4%*	*10.0%*	*8.4%*	*7.9%*
SG&A % sales	*82.5%*	*66.4%*	*73.4%*	*69.5%*	*79.1%*	*65.6%*	*71.4%*	*83.4%*	*61.5%*	*293.5%*	*78.8%*	*53.0%*	*28.8%*	*34.2%*	*28.1%*	*25.7%*	*24.3%*
Operating margin	*(251.7%)*	*(201.6%)*	*(179.3%)*	*(176.4%)*	*(215.5%)*	*(146.7%)*	*(177.1%)*	*(117.9%)*	*(3.5%)*	*(361.2%)*	*(22.9%)*	*18.0%*	*55.3%*	*46.7%*	*55.7%*	*60.0%*	*62.1%*
Pre-tax margin	*(247.7%)*	*(200.5%)*	*(179.6%)*	*(170.2%)*	*(208.6%)*	*(141.8%)*	*(172.8%)*	*(109.9%)*	*0.2%*	*(351.8%)*	*(21.9%)*	*20.4%*	*57.8%*	*50.6%*	*60.1%*	*65.6%*	*69.2%*
Actual Tax rate	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*2.0%*	*0.0%*	*0.0%*	*2.0%*	*2.0%*	*2.0%*	*2.0%*	*2.0%*	*27.6%*
Net margin	*(242.5%)*	*(197.2%)*	*(175.9%)*	*(170.2%)*	*(208.6%)*	*(141.8%)*	*(171.9%)*	*(109.9%)*	*0.2%*	*(351.8%)*	*(21.9%)*	*20.0%*	*56.6%*	*49.6%*	*58.9%*	*64.3%*	*50.1%*
Year/Year Changes																	
Sales	*112.3%*	*62.5%*	*73.0%*	*38.5%*	*(48.6%)*	*22.8%*	*2.0%*	*36.8%*	*171.6%*	*(75.5%)*	*278.1%*	*51.7%*	*87.5%*	*(14.5%)*	*23.9%*	*11.1%*	*7.3%*
Gross profit										*360.9%*	*64.8%*	*47.1%*	*22.0%*	*15.4%*	*16.1%*	*6.6%*	*4.4%*
R&D	*4.5%*	*41.9%*	*(5.0%)*	*(3.4%)*	*(3.0%)*	*(26.6%)*	*(10.8%)*	*(10.5%)*	*(17.1%)*	*(10.7%)*	*(8.5%)*	*(10.0%)*	*(4.1%)*	*(3.7%)*	*0.1%*	*(6.5%)*	*0.1%*
SG&A	*69.2%*	*30.8%*	*15.1%*	*10.3%*	*10.3%*	*3.8%*	*9.7%*	*59.6%*	*100.3%*	*16.7%*	*1.6%*	*2.0%*	*2.0%*	*1.6%*	*1.6%*	*1.6%*	*1.6%*
Net income	*2.1%*	*32.1%*	*(11.4%)*	*(15.3%)*	*54.0%*	*(37.4%)*	*(11.1%)*	*(12.6%)*	*(100.4%)*	*(49593.4%)*	*(76.4%)*	*(238.4%)*	*430.8%*	*(25.2%)*	*47.2%*	*21.2%*	*(16.4%)*
Earnings per share	*(1.2%)*	*27.9%*	*(93.1%)*	*(93.4%)*	*(87.9%)*	*(95.0%)*	*(93.1%)*	*(20.9%)*	*(100.4%)*	*(48481.2%)*	*(78.9%)*	*(234.0%)*	*410.6%*	*(28.6%)*	*39.4%*	*13.7%*	*(22.1%)*

Source: Company data, Credit Suisse estimates.

Exhibit 78: Ironwood Balance Sheet-Forecast

			2010														
			Mar-10	Jun-10	Sep-10	Dec-10											
	FY 2008	FY 2009	1QA	2QE	3QE	4QE	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018	FY 2019	FY 2020
ASSETS																	
Cash and cash equivalents	67,722	123,145	76,338	66,985	44,685	41,315	41,315	88,167	54,661	36,624	155,015	296,295	392,093	553,457	790,186	1,079,139	1,330,917
Available for sale securities	22,045	-	222,230	222,230	222,230	222,230	222,230	162,230	102,230	22,230	2,230	2,230	2,230	2,230	2,230	2,230	2,230
Accounts receivable	4	12	192	183	161	211	211	265	1,367	1,115	1,920	2,343	3,273	4,071	5,010	5,481	5,775
Related party accounts receivable	7,117	5,222	4,531	4,531	4,531	4,531	4,531	4,531	4,531	4,531	4,531	4,531	4,531	4,531	4,531	4,531	4,531
Prepaid expenses and other assets	2,498	3,069	3,107	1,831	1,610	2,112	2,112	2,654	5,470	1,338	2,304	5,623	7,854	9,770	12,024	13,153	13,860
Forward purchase contract	8,700	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Inventory	-	-	-	-	-	-	-	1,062	2,735	669	1,440	3,515	4,909	6,106	7,515	8,221	8,663
Total current assets	**108,086**	**131,448**	**306,398**	**295,760**	**273,216**	**270,399**	**270,399**	**258,909**	**170,993**	**66,505**	**167,440**	**314,537**	**414,890**	**580,166**	**821,496**	**1,112,755**	**1,365,976**
Marketable securities, available for sale	-																
Restricted cash	7,968	8,431	8,162	8,162	8,162	8,162	8,162	8,162	8,162	8,162	8,162	8,162	8,162	8,162	8,162	8,162	8,162
Property and equipment, net	24,596	22,551	23,540	23,382	23,072	23,012	23,012	21,842	23,190	25,874	25,969	27,258	27,691	28,726	28,956	29,347	29,785
Intangible Assets/Goodwill		-					-	-	-	-	-	-	-	-	-	-	-
Forward purchase contract	-	-	-	-	-	-	-	-									
Other assets	73	21	30	110	97	127	127	265	684	167	288	703	982	1,221	1,503	1,644	1,733
TOTAL ASSETS	**140,723**	**162,451**	**338,130**	**327,414**	**304,547**	**301,700**	**301,700**	**289,179**	**203,029**	**100,708**	**201,860**	**350,660**	**451,725**	**618,275**	**860,117**	**1,151,908**	**1,405,655**
LIABILITIES AND SHAREHOLDERS' EQUITY																	
Accounts payable	6,086	4,944	5,116	6,317	6,342	6,520	6,520	7,790	6,676	4,872	4,906	4,970	5,083	5,175	5,337	5,359	5,451
Accrued research and development costs	9,653	12,401	8,426	11,360	11,416	11,478	11,478	10,211	8,421	7,519	6,879	6,191	5,936	5,716	5,721	5,351	5,356
Accrued expenses	4,341	4,899	4,326	18,952	19,026	19,559	19,559	23,369	26,705	29,231	29,437	29,820	30,497	31,051	32,023	32,156	32,705
Current portion of long-term debt	943	1,310	1,166	1,073	988	904	904	706	154	-	-	-	-	-	-	-	-
Current portion of capital lease obligations	117	143	147	147	147	147	147	147	147	147	147	147	147	147	147	147	147
Current portion of deferred rent	166	180	196	196	196	196	196	196	196	196	196	196	196	196	196	196	196
Current portion of deferred revenue	17,846	32,560	35,607	18,609	10,561	50,350	50,350	133,959	23,550	45,550	15,000	115,000	-	-	-	-	-
Total current liabilities	**39,152**	**56,437**	**54,984**	**56,655**	**48,676**	**89,153**	**89,153**	**176,378**	**65,850**	**87,514**	**56,566**	**156,324**	**41,859**	**42,285**	**43,423**	**43,209**	**43,855**
Long-term debt, net of current portion	872	1,764	1,529	1,312	1,086	860	860	154	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Capital lease obligations, net of current portion	189	112	74	74	74	74	74	74	74	74	74	74	74	74	74	74	74
Deferred rent, net of current portion	9,313	10,486	10,703	10,703	10,703	10,703	10,703	10,703	10,703	10,703	10,703	10,703	10,703	10,703	10,703	10,703	10,703
Deferred revenue, excl. current portion	48,208	93,642	82,038	83,409	83,409	53,059	53,059	-	15,550	-	-	-	-	-	-	-	-
Total liabilities	**97,734**	**162,441**	**149,328**	**152,152**	**143,948**	**153,849**	**153,849**	**187,309**	**92,176**	**98,291**	**67,343**	**167,101**	**52,636**	**53,062**	**54,200**	**53,986**	**54,632**
Convertible preferred stock	273,400	298,350					-	-	-	-	-	-	-	-	-	-	-
Class A common stock	-	-	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19
Class B common stock	7	8	79	79	79	79	79	79	79	79	79	79	79	79	79	79	79
Additional paid-in capital	7,594	12,999	516,403	518,439	520,564	522,797	522,797	532,139	540,884	550,075	709,887	720,575	732,517	746,267	762,643	782,849	808,656
Accum. other comprehensive income (loss)	(243,374)	-	(99)	(99)	(99)	(99)	(99)	(99)	(99)	(99)	(99)	(99)	(99)	(99)	(99)	(99)	(99)
Accum. deficit	23	(314,559)	(330,483)	(346,059)	(362,847)	(377,828)	(377,828)	(433,151)	(432,914)	(550,540)	(578,252)	(539,898)	(336,309)	(183,936)	40,391	312,191	539,485
Total stockholders' equity	**37,650**	**(3,202)**	**185,919**	**172,379**	**157,716**	**144,968**	**144,968**	**98,987**	**107,970**	**(466)**	**131,634**	**180,676**	**396,206**	**562,330**	**803,033**	**1,095,039**	**1,348,140**
Noncontrolling interest	5,339	3,212	2,883	2,883	2,883	2,883	2,883	2,883	2,883	2,883	2,883	2,883	2,883	2,883	2,883	2,883	2,883
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	**140,723**	**162,451**	**338,130**	**327,414**	**304,547**	**301,700**	**301,700**	**289,179**	**203,029**	**100,708**	**201,860**	**350,660**	**451,725**	**618,275**	**860,117**	**1,151,908**	**1,405,655**

Source: Company data, Credit Suisse estimates.

Exhibit 79: Ironwood Cash Flow Statement Forecast

			2010														
			Mar-10	Jun-10	Sep-10	Dec-10											
	FY 2008	FY 2009	1QA	2QE	3QE	4QE	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018	FY 2019	FY 2020
CASH FLOWS FROM OPERATING ACTIVITIES																	
Net Income (Loss)	(55,031.0)	(73,312.0)	(16,253.0)	(15,576.0)	(16,788.2)	(14,980.6)	(63,597.8)	(55,323.5)	237.7	(117,626.3)	(27,711.8)	38,353.6	203,589.0	152,373.2	224,327.0	271,800.0	227,294.2
Net income from discontinued operations																	
Depreciation and amortization	2,849.0	5,250.0	1,303.0	1,164.8	1,195.0	1,221.6	4,884.5	5,198.0	2,754.6	3,000.7	2,784.8	2,928.8	2,511.8	2,629.6	2,776.1	2,896.4	3,027.9
Loss (gain) on disposal of property and equipment	(1.0)	80.0	5.0	0.0	0.0	0.0	5.0	0.0									
Impairment loss on long-lived assets		890.0	0.0														
Remeasurement of forward purchase contracts	900.0	(600.0)	0.0														
Share-based compensation expense	2,794.0	5,244.0	1,608.0	1,608.0	1,608.0	1,608.0	6,432.0	6,594.4	7,969.9	8,049.6	8,130.1	8,211.4	8,293.5	8,376.5	8,460.2	8,544.8	8,630.3
Accretion of discount/premium on investment securities	(368.0)	240.0	98.0				98.0	0.0									
Change in assets and liabilities:																	
Accounts receivable	18,387.0	(465.0)	511.0	8.9	22.1	(50.3)	491.8	(54.2)	(1,102.0)	252.8	(805.6)	(422.9)	(929.5)	(798.4)	(939.0)	(470.5)	(294.6)
Restricted cash	(5,008.0)	(463.0)	269.0	0.0	0.0	0.0	269.0	0.0									
Prepaid expenses and other current assets	(768.0)	(571.0)	(38.0)	1,276.3	221.2	(502.8)	956.7	(542.0)	(2,815.3)	4,132.1	(966.7)	(3,319.2)	(2,230.9)	(1,916.1)	(2,253.7)	(1,129.2)	(707.0)
Inventory	0.0	0.0		0.0	0.0	0.0	0.0	(1,061.7)	(1,673.1)	2,066.0	(771.4)	(2,074.5)	(1,394.3)	(1,197.6)	(1,408.5)	(705.8)	(441.9)
Other assets	(45.0)	52.0	(9.0)	(79.8)	13.3	(30.2)	(105.7)	(138.7)	(418.3)	516.5	(120.8)	(414.9)	(278.9)	(239.5)	(281.7)	(141.2)	(88.4)
Accounts payable and accrued expenses	2,357.0	1,574.0	(1,622.0)	15,827.4	98.3	710.6	15,014.3	5,080.9	2,222.2	720.8	241.2	446.5	790.1	646.3	1,133.4	155.6	640.4
Accrued research and development costs	4,615.0	2,748.0	(3,975.0)	2,934.5	55.3	62.2	(923.0)	(1,267.3)	(1,789.5)	(902.5)	(639.7)	(687.7)	(255.5)	(220.0)	5.0	(369.9)	5.1
Deferred rent	(8,338.0)	1,187.0	233.0	0.0	0.0	0.0	233.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Deferred revenue	9,462.0	54,148.0	(8,557.0)	(15,627.3)	(8,047.6)	9,438.5	(22,793.4)	30,550.4	(94,859.4)	6,450.4	(30,550.0)	100,000.0	(115,000.0)	0.0	0.0	0.0	0.0
Net cash provided by (used in) operating activities	**(28,195.0)**	**(3,998.0)**	**(26,427.0)**	**(8,463.2)**	**(21,622.5)**	**(2,522.9)**	**(59,035.6)**	**(10,963.7)**	**(89,473.1)**	**(93,339.9)**	**(50,409.7)**	**143,021.2**	**95,095.2**	**159,653.9**	**231,818.8**	**280,580.2**	**238,066.0**
CASH FLOWS FROM INVESTING ACTIVITIES																	
Purchase of available-for-sale securities	(82,613.0)	(26,673.0)	(222,427.0)	0.0	0.0	0.0	(222,427.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sales and maturities of available-for-sale securities	90,465.0	48,455.0	0.0	0.0	0.0	0.0	0.0	60,000.0	60,000.0	80,000.0	20,000.0	0.0	0.0	0.0	0.0	0.0	0.0
Purchases of property and equipment	(22,934.0)	(4,045.0)	(1,063.0)	(1,006.9)	(885.2)	(1,161.8)	(4,116.9)	(4,028.0)	(4,102.2)	(5,684.5)	(2,880.2)	(4,217.5)	(2,945.3)	(3,663.9)	(3,006.0)	(3,288.3)	(3,465.1)
Proceeds from the sale of property and equipment	9.0	21.0	1.0	0.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net cash used in investing activities	**(15,073.0)**	**17,758.0**	**(223,489.0)**	**(1,006.9)**	**(885.2)**	**(1,161.8)**	**(226,542.9)**	**55,972.0**	**55,897.8**	**74,315.5**	**17,119.8**	**(4,217.5)**	**(2,945.3)**	**(3,663.9)**	**(3,006.0)**	**(3,288.3)**	**(3,465.1)**
CASH FLOWS FROM FINANCING ACTIVITIES																	
Proceeds from issuance of preferred stock, net	49,598.0	40,250.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Proceeds from exercise of stock options and issuance of restricted stock	179.0	272.0	354.0	427.9	517.2	625.1	1,924.1	2,747.9	774.9	1,141.4	1,681.3	2,476.7	3,648.2	5,374.0	7,916.1	11,660.8	17,176.8
Proceeds from issuance of common stock, net		0.0	203,168.0	0.0	0.0	0.0	203,168.0	0.0	0.0	0.0	150,000.0	0.0	0.0	0.0	0.0	0.0	0.0
Proceeds from sale of noncontrolling interest in subsidiary	1.0							0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Proceeds from borrowings	465.0	2,642.0					0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Payments on borrowings	(1,680.0)	(1,501.0)	(413.0)	(310.3)	(310.3)	(310.3)	(1,344.0)	(904.0)	(706.0)	(154.0)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net cash provided by financing activities	**48,563.0**	**41,663.0**	**203,109.0**	**117.5**	**206.8**	**314.8**	**203,748.1**	**1,843.9**	**68.9**	**987.4**	**151,681.3**	**2,476.7**	**3,648.2**	**5,374.0**	**7,916.1**	**11,660.8**	**17,176.8**
Net increase (decrease) in cash and cash equivalents	**5,295.0**	**55,423.0**	**(46,807.0)**	**(9,352.5)**	**(22,300.9)**	**(3,369.9)**	**(81,830.3)**	**46,852.2**	**(33,506.4)**	**(18,037.0)**	**118,391.3**	**141,280.3**	**95,798.1**	**161,364.0**	**236,728.9**	**288,952.7**	**251,777.7**
Cash and cash equivalents at beginning of year	62,427.0	67,722.0	123,145.0	76,338.0	66,985.5	44,684.5	123,145.0	41,314.7	88,166.9	54,660.5	36,623.5	155,014.9	296,295.2	392,093.3	553,457.4	790,186.3	1,079,139.0
Cash and cash equivalents at end of year	**67,722.0**	**123,145.0**	**76,338.0**	**66,985.5**	**44,684.5**	**41,314.7**	**41,314.7**	**88,166.9**	**54,660.5**	**36,623.5**	**155,014.9**	**296,295.2**	**392,093.3**	**553,457.4**	**790,186.3**	**1,079,139.0**	**1,330,916.7**
Cash paid for interest	333.0	412.0	96.0	96.0	96.0	96.0	384.0	384.0	384.0	384.0	384.0	384.0	384.0	384.0	384.0	384.0	384.0
Marketable Securities																	
Cash and marketable securities																	
Free Cash Flow																	
EBIT	(55,921.0)	(72,770.0)	(16,228.0)	(16,144.7)	(17,342.7)	(15,494.9)	(65,210.3)	(59,372.5)	(4,756.2)	(120,764.1)	(28,888.8)	34,419.0	198,788.1	143,653.1	212,234.5	253,574.5	281,683.4
Less: Taxes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3
Earnings before interest	(55,921.0)	(72,770.0)	(16,228.0)	(16,144.7)	(17,342.7)	(15,494.9)	(65,210.3)	(59,372.5)	(4,661.1)	(120,764.1)	(28,888.8)	33,730.6	194,812.3	140,780.1	207,989.8	248,503.0	203,820.5
Plus: Depreciation & amortization	2,849.0	5,250.0	1,303.0	1,164.8	1,195.0	1,221.6	4,884.5	5,198.0	2,754.6	3,000.7	2,784.8	2,928.8	2,511.8	2,629.6	2,776.1	2,896.4	3,027.9
Less: Capital expenditures	22,934.0	4,045.0	1,063.0	1,006.9	885.2	1,161.8	4,116.9	4,028.0	4,102.2	5,684.5	2,880.2	4,217.5	2,945.3	3,663.9	3,006.0	3,288.3	3,465.1
Less: Change in working capital	20,662.0	58,210.0	(13,188.0)	4,340.0	(7,637.3)	9,628.1	(6,857.3)	32,567.4	(100,435.2)	13,236.0	(33,612.9)	93,527.3	(119,299.1)	(3,725.3)	(3,744.5)	(2,661.0)	(886.4)
Free Cash Flow	**(55,344.0)**	**(13,355.0)**	**(29,176.0)**	**(11,646.8)**	**(24,670.2)**	**(5,807.0)**	**(71,300.0)**	**(25,635.1)**	**(106,443.9)**	**(110,211.8)**	**(62,597.2)**	**125,969.3**	**75,079.7**	**136,020.5**	**204,015.4**	**245,450.1**	**202,496.9**

Source: Company data, Credit Suisse estimates.

Exhibit 80: Probability Adjusted Europe and Japan Linaclotide Revenue and Royalty Income NPV Forecasts

PROBABILITY- ADJUSTED	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Probability			*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*
EU Revenue			20	60	100	140	168	202	232	267	293	323	355	373	391	403
YoY Revenue Growth			*na*	*200.0%*	*66.7%*	*40.0%*	*20.0%*	*20.0%*	*15.0%*	*15.0%*	*10.0%*	*10.0%*	*10.0%*	*5.0%*	*5.0%*	*3.0%*
Prob. Adjusted Revenue			15	45	75	105	126	151	174	200	220	242	266	279	293	302
EU Royalty			2	5	8	11	15	23	31	40	48	56	64	70	76	82
EU Royalty Rate (post-tax)			*10%*	*10%*	*10%*	*10%*	*12%*	*15%*	*18%*	*20%*	*22%*	*23%*	*24%*	*25%*	*26%*	*27%*
NPV of Cash Flows	**0**	**0**	**1**	**3**	**5**	**6**	**7**	**10**	**12**	**14**	**15**	**15**	**15**	**15**	**15**	**14**
Probability-Adjusted NPV ($MM)	**$146**															

JAPAN PROBABILITY- ADJUSTED	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Probability			*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
Japan Sales			0	0	20	70	98	118	135	149	164	172	180	186	191	197
YoY Sales Growth					*na*	*250.0%*	*40.0%*	*20.0%*	*15.0%*	*10.0%*	*10.0%*	*5.0%*	*5.0%*	*3.0%*	*3.0%*	*3.0%*
Prob. Adjusted Revenue			0	0	10	35	49	59	68	74	82	86	90	93	96	99
Japan Royalty			0	0	1	4	6	9	12	15	18	20	22	23	25	27
Japan Royalty Rate (post-tax)			*10%*	*10%*	*10%*	*10%*	*12%*	*15%*	*18%*	*20%*	*22%*	*23%*	*24%*	*25%*	*26%*	*27%*
NPV of Cash Flows	**0**	**0**	**0**	**0**	**1**	**2**	**3**	**4**	**5**	**5**	**5**	**5**	**5**	**5**	**5**	**5**
Probability-Adjusted NPV ($MM)	**$49**															

Source: Company data, Credit Suisse estimates

Exhibit 81: Ironwood- Base Case Probability Adjusted NPV Summary

Drug	Peak Sales ($ millions)	Stage	(Estimated) Launch	Probability of Reaching Market	Economics	Probability Adjusted NPV	Per Share Value	% of Total Value
Pipeline								
Linaclotide Franchise								
Linaclotide US Collaboration	$1,202	Phase III	2012	75%	50/50 Profit Split w/ FRX	$813	$9.10	64.0%
Linaclotide EU Royalty	$403	Phase III	2012	75%	Tiered Royalty w/ Almirall	$146	$1.63	11.5%
Linaclotide Japan Royalty	$197	Phase III	2014	50%	Tiered Royalty w/ Astellas	$49	$0.55	3.9%
Total						**$1,008**	**$11.29**	**79.4%**
Other								
Net Cash (Cash/Equivalents - Debt)						$262	$2.93	20.6%
Other Costs NPV (not directly accounted for in programs above)						$0	$0.00	0.0%
Total Other						**$262**	**$2.93**	**20.6%**
Total						**$1,270**	**$14.21**	**100.0%**

Source: Company data, Credit Suisse estimates

Exhibit 82: Ironwood-Forest Linaclotide Collaboration Profit-Share Model

	Contribution	FY 2010	FY 2011	FY 2012	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017	FY 2018	FY 2019	FY 2020
Product Revenue			0.0	32.0	134.7	369.3	553.7	680.3	788.2	918.4	980.0	1,023.5
COGS	100%	**0.6**	**2.9**	3.8	18.9	25.9	38.8	47.6	55.2	64.3	68.6	71.6
% of Sales				*12.0%*	*14.0%*	*7.0%*	*7.0%*	*7.0%*	*7.0%*	*7.0%*	*7.0%*	*7.0%*
SG&A												
Cost per Rep (in 000s)		125.0	126.3	127.5	128.8	130.1	131.4	132.7	134.0	135.4	136.7	138.1
IRWD Reps & MSLs Headcount	20%	0.0	0.0	100.0	200.0	200.0	200.0	200.0	200.0	200.0	200.0	200.0
IRWD Sales Force Costs		0.0	0.0	12.8	25.8	26.0	26.3	26.5	26.8	27.1	27.3	27.6
IRWD Sales Force Contribution	67%	0.0	0.0	8.5	17.3	17.4	17.6	17.8	18.0	18.1	18.3	18.5
FRX Reps & MSLs Headcount	80%	0.0	0.0	400.0	800.0	800.0	800.0	800.0	800.0	800.0	800.0	800.0
FRX Sales Force Costs		0.0	0.0	51.0	103.0	104.1	105.1	106.2	107.2	108.3	109.4	110.5
FRX Sales force Contribution	67%	0.0	0.0	34.2	69.0	69.7	70.4	71.1	71.8	72.6	73.3	74.0
Total Sales Force Costs Fully Loaded		0.0	0.0	63.8	128.8	130.1	131.4	132.7	134.0	135.4	136.7	138.1
Total Sales Force Cost Allocated to the Deal		0.0	0.0	42.7	86.3	87.2	88.0	88.9	89.8	90.7	91.6	92.5
% of Sales				*133.4%*	*64.1%*	*23.6%*	*15.9%*	*13.1%*	*11.4%*	*9.9%*	*9.3%*	*9.0%*
Marketing	100%	10.0	25.0	100.0	100.0	102.0	104.0	106.1	108.2	110.4	112.6	114.9
% of Sales				*312.4%*	*74.2%*	*27.6%*	*18.8%*	*15.6%*	*13.7%*	*12.0%*	*11.5%*	*11.2%*
G&A	100%	8.6	8.8	9.0	9.2	9.3	9.5	9.7	9.9	10.1	10.3	10.5
% of Sales		*na*	*na*	*28.0%*	*6.8%*	*2.5%*	*1.7%*	*1.4%*	*1.3%*	*1.1%*	*1.1%*	*1.0%*
Total SG&A		18.6	33.8	151.7	195.4	198.5	201.6	204.7	207.9	211.2	214.5	217.9
% of Sales				*473.8%*	*145.1%*	*53.7%*	*36.4%*	*30.1%*	*26.4%*	*23.0%*	*21.9%*	*21.3%*
R&D	100%	65.0	45.0	25.0	20.0	15.0	10.0	8.0	5.0	5.0	0.0	0.0
% of Sales				*78.1%*	*14.8%*	*4.1%*	*1.8%*	*1.2%*	*0.6%*	*0.5%*	*0.0%*	*0.0%*
Total Operating Expenses		84.2	81.7	180.5	234.3	239.3	250.3	260.4	268.1	280.5	283.1	289.5
US Pre Tax Profit		**(84.2)**	**(81.7)**	**(148.5)**	**(99.6)**	**130.0**	**303.3**	**419.9**	**520.0**	**637.9**	**696.9**	**734.0**
Operating Margin				*-463.9%*	*-73.9%*	*35.2%*	*54.8%*	*61.7%*	*66.0%*	*69.5%*	*71.1%*	*71.7%*
Detailing Reimbursement	0%	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
API Reimbursement (based on sales)	4%	0.0	0.0	1.3	5.4	14.8	22.1	27.2	31.5	36.7	39.2	40.9
Adjusted US Pre Tax Profit		(84.2)	(81.7)	(149.8)	(105.0)	115.2	281.2	392.7	488.5	601.2	657.7	693.0
Ironwood profit share	50%	**(42.1)**	**(40.8)**	**(74.9)**	**(52.5)**	**57.6**	**140.6**	**196.4**	**244.3**	**300.6**	**328.8**	**346.5**
Ironwood detailing reimbursement		0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ironwood API reimbursement		0.0	0.0	1.3	5.4	14.8	22.1	27.2	31.5	36.7	39.2	40.9
Total Ironwood share		(42.1)	(40.8)	(73.6)	(47.1)	72.4	162.7	223.6	275.8	337.3	368.0	387.4

Source: Company data, Credit Suisse estimates

Exhibit 83: **Exhibit 84: Linaclotide Revenues – Base Case**

U.S. Rx Model	2010E	2011E	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
Total Rx	27,678,008	28,231,568	29,643,147	32,607,461	36,520,357	40,537,596	44,591,355	48,158,664	50,566,597	52,083,595	53,125,267	54,187,772
Absolute Growth	542,706	553,560	1,411,578	2,964,315	3,912,895	4,017,239	4,053,760	3,567,308	2,407,933	1,516,998	1,041,672	1,062,505
YoY growth %	2%	2%	5%	10%	12%	11%	10%	8%	5%	3%	2%	2%
Laxatives/Fecal Softeners	26,501,693	26,961,148	27,864,558	29,672,790	32,137,914	35,267,708	38,571,522	41,657,244	43,487,273	44,791,892	45,422,103	46,330,545
% of Market	*96%*	*96%*	*94%*	*91%*	*88%*	*87%*	*87%*	*87%*	*86%*	*86%*	*86%*	*86%*
Branded Rx	1,176,315	1,270,421	1,778,589	2,934,672	4,382,443	5,269,887	6,019,833	6,501,420	7,079,324	7,291,703	7,703,164	7,857,227
Absolute Growth	58,048	94,105	508,168	1,156,083	1,447,771	887,445	749,946	481,587	577,904	212,380	411,460	154,063
YoY growth %	*5.2%*	*8.0%*	*40.0%*	*65.0%*	*49.3%*	*20.3%*	*14.2%*	*8.0%*	*8.9%*	*3.0%*	*5.6%*	*2.0%*
% of Market	4%	5%	6%	9%	12%	13.0%	13.5%	13.5%	14.0%	14.0%	14.5%	14.5%
Zelnorm	0	0	0	0	0	0	0	0	0	0	0	0
% of Prescription Rx Market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Amitiza (+ generic lubiprostone)	1,176,315	1,270,421	1,600,730	2,054,270	2,410,344	2,371,449	2,407,933	2,275,497	2,194,590	2,041,677	2,002,823	1,964,307
% of Prescription Rx Market	100%	100%	90%	70%	55%	45%	40%	35%	31%	28%	26%	25%
Linaclotide	0	0	177,859	733,668	1,972,099	2,898,438	3,491,503	3,965,866	4,530,767	4,739,607	4,852,993	4,792,908
% of Prescription Rx Market	0%	0%	10%	25%	45%	55%	58%	61%	64%	65%	63%	61%
Resolor	0	0	0	0	0	0	0	0	0	0	0	0
% of Prescription Rx Market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Other (TD-5108,	0	0	0	146,734	0	0	120,397	260,057	353,966	510,419	847,348	1,100,012
% of Prescription Rx Market	0%	0%	0%	5%	0%	0%	2%	4%	5%	7%	11%	14%
Cost per Rx												
Zelnorm												
Amitiza	$187.51	$191.26	$195.09	$198.99	$202.97	$207.03	$211.17	$215.39	$219.70	$224.09	$228.57	$233.14
Linaclotide			$180.00	$183.60	$187.27	$191.02	$194.84	$198.73	$202.71	$206.76	$210.90	$215.12
Resolor			$180.00	$183.60	$187.27	$191.02	$194.84	$198.73	$202.71	$206.76	$210.90	$215.12
Revenues												
Zelnorm (from Novartis)												
Amitiza (from IMS)	221	243	312	409	489	491	508	490	482	458	458	458
Linaclotide ($ Millions)			**32.0**	**134.7**	**369.3**	**553.7**	**680.3**	**788.2**	**918.4**	**980.0**	**1,023.5**	**1,031.0**
Resolor			0	0	0	0	0	0	0	0	0	0
Other												

Source: Company data, Credit Suisse estimates

Companies Mentioned *(Price as of 29 Jun 10)*
Adolor Corporation (ADLR, $1.10)
Amgen Inc. (AMGN, $54.12)
Amylin Pharmaceuticals (AMLN, $18.92, OUTPERFORM [V], TP $32.00)
Astellas Pharma (4503, ¥2,990, NEUTRAL, TP ¥3,000, MARKET WEIGHT)
AstraZeneca (AZN.L, 2947.00 p, NEUTRAL, TP 3100.00 p, OVERWEIGHT)
Epix Medical, Inc. (EPIX, $.01)
Forest Laboratories Inc. (FRX, $27.68, NEUTRAL, $27.00)
Genzyme Corp. (GENZ, $51.58)
GlaxoSmithKline (GSK.L, 1123.00 p, UNDERPERFORM, TP 1225.00 p, OVERWEIGHT)
Ironwood Pharmaceuticals (IRWD, $12.62, NEUTRAL, TP $14.00)
Johnson & Johnson (JNJ, $59.24, NEUTRAL, TP $69.00)
Movetis (MOVET.BR, Eu8.80, OUTPERFORM [V], TP Eu17.50, OVERWEIGHT)
Novartis (NOVN.VX, SFr52.20, NEUTRAL, TP SFr59.00, OVERWEIGHT)
Progenics Pharmaceuticals (PGNX, $5.24)
Roche (ROG.VX, SFr149.80, OUTPERFORM, TP SFr200.00, OVERWEIGHT)
Sanofi-Aventis (SASY.PA, Eu48.68, OUTPERFORM, TP Eu62.00, OVERWEIGHT)
Sucampo Pharmaceuticals (SCMP, $3.48)
Takeda Pharmaceutical (4502, ¥3,820, NEUTRAL, TP ¥3,900, MARKET WEIGHT)
Theravance, Inc. (THRX, $12.79, NEUTRAL [V], TP $17.00)

Disclosure Appendix

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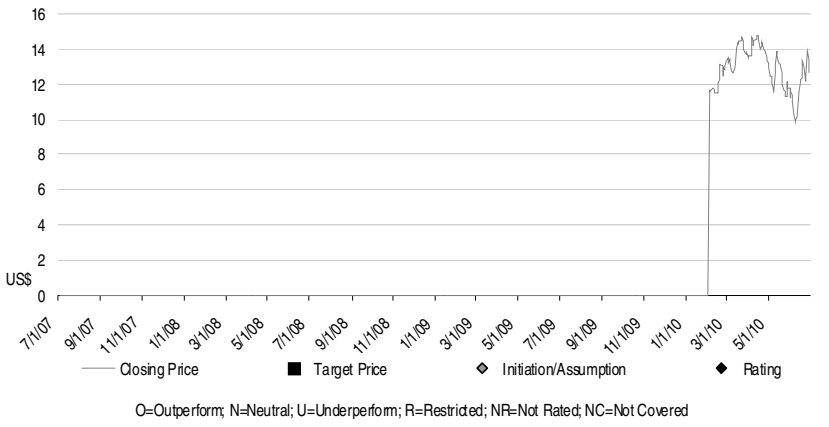
3-Year Price, Target Price and Rating Change History Chart for IRWD

IRWD Date	Closing Price (US$)	Target Price (US$)	Rating	Initiation/ Assumption



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Price Target: (12 months) for (IRWD)
Method: Our $14 target price for IRWD is based on a probability weighted net present value (NPV) analysis. We have used a 12% WACC (weighted average cost of capital) for our analysis. Major sources of cash inflow for Ironwood include: (1) Future US linaclotide profit share income, (2) linaclotide ex-US royalty income, and (3) milestones-based revenues.
Risks: Risk to our $14 target price include: (1) Regulatory risks related to linaclotide approval, (2) single product risk. (3) unexpected change in competitive landscape, and (4) the company's financing risk, due to the potential need to raise additional funds to fund spend related to linaclotide launch.

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