

# IRONWOOD PHARMACEUTICALS (IRWD)

Unprecedented Results in IBS-C. First Down; One More to Go.  
Maintaining BUY Rating And Increasing PT to \$15.00 from \$14.00.

Investment Rating BUY  
Prior Rating

Price Target \$15.00  
Prior Target \$14.00

Price (September 13, 2010) \$9.74  
52 Week Range \$9.05 - \$15.03  
Shares Outstanding 97.6 MM  
Market Capitalization \$950.6 MM  
Cash (June 30, 2010) \$271.6 MM

Fiscal Year End December

Revenues (MM's):

	<u>Current</u>	<u>Prior</u>
2010E	\$39.1	
2009A	\$36.1	

EPS:

	<u>Current</u>	<u>Prior</u>	P/E
2010E	(\$0.77)		NA
2009A	(\$10.00)		NA

Quarterly EPS\*:

	<u>Current</u>	<u>Prior</u>
2010E		
Mar (A)	(\$0.25)	
Jun (A)	(\$0.18)	
Sep	(\$0.20)	
Dec	(\$0.16)	
2011E		
Mar	(\$0.15)	
Jun	(\$0.12)	
Sep	(\$0.10)	
Dec	(\$0.10)	

## Highlights

Ironwood, Forest Labs (NYSE: FRX; not rated; \$29.86) and Almirall S.A. announced results from the first (of two) linaclotide pivotal trials in irritable bowel syndrome with constipation (IBS-C).

In essence, the results met our high expectations and indicate linaclotide could potentially become a blockbuster drug (the basis of our investment thesis).

In addition, the results amply meet FDA and EMA criteria as well as the higher bar set by the US planned statistical analysis.

The results showed extensive consistency among the primary and secondary endpoint results for abdominal and bowel habit symptoms (the study met all 16 primary and secondary endpoints). Additionally, we see the level of pain response and improvement (1.9 point improvement versus baseline and a 1.1 point improvement vs. placebo) and CSBM improvements as unequivocally clinically relevant.

Importantly, the p-value for the abdominal pain endpoint ( $\geq 30\%$  improvement for 9/12 weeks) was 0.0262. These results may not seem as strong to some (relative to other p-values in the study), who may argue there is the possibility this endpoint might not be met in the second primary endpoint. We believe this is unlikely; however, if this were to be the case, we believe the results from the first trial and additional data will support the inclusion of an abdominal pain benefit in the drug's label.

Specifically, the trial amply met the FDA criteria for abdominal pain responders ( $p=0.0003$ ). In addition, the percentage of patients reaching 30% and 50% improvement (or any other level of pain improvement) was statistically significantly superior to placebo every single week including week 1. Finally, the mean improvement in pain versus placebo was 1.1 points, which is considered clinically significant for any chronic pain trial. For these reasons, we believe there is strong data supporting linaclotide's robust analgesic effects on abdominal pain and we believe the inclusion of this benefit in a future label is very likely.

On the safety front, the incidence of diarrhea was 19% versus 4% for placebo. Although this is higher than in the Phase IIb study (16% for linaclotide versus 1% for placebo) the delta versus placebo was maintained. However, 6% patients on linaclotide treatment discontinued due to diarrhea (vs. 0.3% for placebo), which is somewhat higher (although within expected variability) than the discontinuations seen in the Phase IIb IBS-C trial (1% for linaclotide versus 0% for placebo) and the Phase III trials in CC (4% for linaclotide versus 0.5% for placebo).

**What is next:** We expect data from the second pivotal trial in Q4 2010. Strong results from the first pivotal IBS-C trial strengthen our belief the probability of the second trial meeting all endpoints is very high.

Consequently, we have increased the probability of success of the linaclotide program which translates into a price target increase to \$15.00 from \$14.00.

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Disclosures and Analyst Certifications can be found in Appendix A.

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Table 1. Linacotide Trial Results for U.S. Endpoints

U.S. Primary Endpoints	Linacotide	Placebo	p-value
Endpoint A (complete responder 9/12 weeks)	12.10%	5.1%	p=0.0004
Endpoint B (CSBM responder)	19.50%	6.3%	p<0.0001
Endpoint C (abdominal pain responder)	34.30%	27.1%	p=0.0262
Endpoint D (complete responder 6/12 weeks)	33.60%	21.0%	p<0.0001

IRWD/FRX Press release, 9/13/10

Table 2. Linacotide Trial Results for E.U. Endpoints

E.U. Primary Endpoints	Linacotide	Placebo	p-value
Responders to Abdominal Pain* (30% improvement from baseline)	55%	42%	p=0.0002
Responders to IBS Degree of Relief	37%	18%	p<0.0001

\*Responder mean abdominal pain score or mean abdominal discomfort score exhibited improvement for 6/12 weeks

Source:Almirall Press release, 9/13/10

Table 3. Sum-of-Part Valuation (\$000s)

Amounts in \$000s	Peak Revenues (\$) (est. 2016-2017)	IRWD Net Profit / Royalties	Multiple	Valuation (Present Value)*	Probability**	Probability Adjusted	Per Estimated Fully Diluted Share
North American Market	1,284,256	477,996	9.0x	1,888,832	76%	1,443,980	12.26
European Market	236,346	59,086	8.0x	207,541	80%	165,620	1.41
Asia	70,000	12,600	8.0x	41,542	76%	31,758	0.27
Other						20,000	0.17
Cash Expected at Approval (Excludes approval milestone payment)						160,000	
<b>TOTAL</b>	<b>1,590,602</b>					<b>1,821,359</b>	
Outstanding Shares (Class A)						19,167	
Outstanding Shares (Class B)						78,839	
Options						98,006	
Future Dilution						15,227	
Estimated Fully-Diluted Shares						4,500	
						117,733	
<b>Valuation per Share</b>						<b>15.47</b>	

\* uses a 13.5% discount rate

\*\* refers to the probability of regulatory approval and reaching our revenue estimates

Source: Ladenburg Thalmann &amp; Co. estimates

**Table 4. Quarterly Financial Model (\$000s)**

	2009A	Q1 '10A	Q2 '10A	Q3 '10E	Q4 '10E	2010E	Q1 '11E	Q2 '11E	Q3 '11E	Q4 '11E	2011E
Collaborative Agreement Services	\$34,321 1,781	\$8,838 214	\$9,188 1,771	\$9,341 200	\$9,341 200	\$36,708 2,385	9,341 300	9,341 300	9,341 300	9,341 300	\$37,363 1,200
<b>Total Revenues</b>	<b>36,102</b>	<b>9,052</b>	<b>10,959</b>	<b>9,541</b>	<b>9,541</b>	<b>39,093</b>	<b>9,641</b>	<b>9,641</b>	<b>9,641</b>	<b>9,641</b>	<b>38,563</b>
<b>R&amp;D</b>	84,892	18,637	20,953	21,000	17,000	77,590	15,000	12,000	10,000	10,000	47,000
<b>SG&amp;A</b>	23,980 1,207	6,643	7,325	8,400	8,400	30,768	9,000	9,500	9,600	9,500	37,600
<b>Operating Expense</b>	<b>110,079</b>	<b>25,280</b>	<b>28,278</b>	<b>29,400</b>	<b>25,400</b>	<b>108,358</b>	<b>24,000</b>	<b>21,500</b>	<b>19,600</b>	<b>19,500</b>	<b>84,600</b>
<b>Operating Income/Loss</b>	<b>(73,977)</b>	<b>(16,228)</b>	<b>(17,319)</b>	<b>(19,859)</b>	<b>(15,859)</b>	<b>(69,265)</b>	<b>(14,359)</b>	<b>(11,859)</b>	<b>(9,959)</b>	<b>(9,859)</b>	<b>(46,037)</b>
<b>Other Income</b>											
Interest Income	243	68	189	140	110	507	100	90	95	80	365
Interest Expense	(474)	(93)	(79)	(90)	(90)	(352)	(80)	(80)	(80)	(80)	(320)
Other	600					-					-
Net Loss Attributable to Non-Controlling Interest	2,127	329	73			402					-
<b>Net Non-Operating Income</b>	<b>2,496</b>	<b>304</b>	<b>183</b>	<b>50</b>	<b>20</b>	<b>557</b>	<b>20</b>	<b>10</b>	<b>15</b>	<b>-</b>	<b>45</b>
<b>Pretax Income</b>	<b>(71,481)</b>	<b>(15,924)</b>	<b>(17,136)</b>	<b>(19,809)</b>	<b>(15,839)</b>	<b>(68,708)</b>	<b>(14,339)</b>	<b>(11,849)</b>	<b>(9,944)</b>	<b>(9,859)</b>	<b>(45,992)</b>
<b>Taxes</b>											
Provision for Income Taxes	296	-	-	-	-	-	-	-	-	-	-
<b>Net Income/Loss</b>	<b>(71,185)</b>	<b>(15,924)</b>	<b>(17,136)</b>	<b>(19,809)</b>	<b>(15,839)</b>	<b>(68,708)</b>	<b>(14,339)</b>	<b>(11,849)</b>	<b>(9,944)</b>	<b>(9,859)</b>	<b>(45,992)</b>
<b>Earnings/ (Loss) Per Share</b>	<b>(\$10.00)</b>	<b>(\$0.25)</b>	<b>(\$0.18)</b>	<b>(\$0.20)</b>	<b>(\$0.16)</b>	<b>(\$0.77)</b>	<b>(\$0.15)</b>	<b>(\$0.12)</b>	<b>(\$0.10)</b>	<b>(\$0.10)</b>	<b>(\$0.47)</b>
<b>Shares Outstanding (MM)*</b>	<b>7,117</b>	<b>63,958</b>	<b>97,642</b>	<b>97,740</b>	<b>98,300</b>	<b>89,410</b>	<b>98,500</b>	<b>98,650</b>	<b>98,800</b>	<b>98,950</b>	<b>98,725</b>

Source: Corporate Reports and Ladenburg Thalmann &amp; Co estimates.

**Table 5. Annual Financial Model (\$000s)**

	2010E	2011E	2012E	2013E	2014E	2015E	2016E	2017E	2018E
<b>Sales/ Royalties</b>									
US Linaclotide Total Revenues	-	-	15,406	147,896	315,081	563,950	893,419	1,284,256	1,453,852
IRWD Profit Share at 50%	-	-	-	-	-	113,428	280,442	477,996	555,062
SG&A and COGS Reimbursement from FRX	-	-	69,390	95,404	97,514	102,110	108,529	115,675	121,952
		-	69,390	95,404	97,514	215,537	388,971	593,670	677,015
Almirall Royalties	-	-	-	1,697	7,989	25,865	52,011	59,086	67,344
Astellia Royalties	-	-	-	-	-	2,700	8,100	12,600	12,600
Other Royalties	-	-	-	-	1,000	2,160	6,480	10,080	10,080
		-	69,390	97,101	106,503	246,262	455,562	675,437	767,039
<b>Total Sales/Royalties</b>									
Collaborative Arrangement (Forest)	-	25,000	16,300	-	-	-	-	-	-
Collaborative Arrangement (Almirall)	-	9,120	9,120	4,520	-	-	-	-	-
Collaborative Arrangement (Astellas)	-	3,243	3,243	3,243	3,243	3,243	3,243	3,243	3,243
	36,708	37,363	28,663	7,763	3,243	3,243	3,243	3,243	3,243
Services	2,385	1,200	1,000	500					
<b>Total Revenues</b>	<b>39,093</b>	<b>38,563</b>	<b>99,054</b>	<b>105,364</b>	<b>109,746</b>	<b>249,506</b>	<b>458,805</b>	<b>678,680</b>	<b>770,282</b>
<b>% Change</b>		<b>-1.4%</b>	<b>156.9%</b>	<b>6.4%</b>	<b>4.2%</b>	<b>127.3%</b>	<b>83.9%</b>	<b>47.9%</b>	<b>13.5%</b>
COGS	-	-	-	-	-	-	-	-	-
R&D	77,590	47,000	49,000	53,900	56,595	57,444	58,306	59,180	60,068
SG&A			43,240	45,402	47,672	50,056	52,558	55,186	57,946
COGS+SG&A (linaclotide)			76,109	108,712	116,361	121,522	128,523	136,269	143,164
Total SG&A	30,768	37,600	119,349	154,114	164,033	171,578	181,082	191,456	201,110
Other									
<b>Operating Expenses</b>	<b>108,358</b>	<b>84,600</b>	<b>168,349</b>	<b>208,014</b>	<b>220,628</b>	<b>229,021</b>	<b>239,387</b>	<b>250,636</b>	<b>261,178</b>
<b>Operating Income/Loss</b>	<b>(69,265)</b>	<b>(46,037)</b>	<b>(69,295)</b>	<b>(102,650)</b>	<b>(110,882)</b>	<b>20,484</b>	<b>219,418</b>	<b>428,044</b>	<b>509,104</b>
<b>Other Income</b>									
Interest Income	507	365	300	1,000	1,500	1,800	1,800	2,000	2,500
Interest Expense	(352)	(320)	-	-	-	-	-	-	-
Other	-	-	-	-	-	-	-	-	-
	402								
<b>Net Non-Operating Income</b>	<b>\$557</b>	<b>45</b>	<b>300</b>	<b>1,000</b>	<b>1,500</b>	<b>1,800</b>	<b>1,800</b>	<b>2,000</b>	<b>2,500</b>
<b>Pretax Income</b>	<b>(68,708)</b>	<b>(45,992)</b>	<b>(68,995)</b>	<b>(101,650)</b>	<b>(109,382)</b>	<b>22,284</b>	<b>221,218</b>	<b>430,044</b>	<b>511,604</b>
Income Tax Paid/(Benefit)	-	-	-	-	-	5,571	66,365	129,013	153,481
<b>Non-Operating Income / (Charge)</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>
<b>Net Income/ (Loss)</b>	<b>(68,708)</b>	<b>(45,992)</b>	<b>(68,995)</b>	<b>(101,650)</b>	<b>(109,382)</b>	<b>16,713</b>	<b>154,852</b>	<b>301,031</b>	<b>358,123</b>
<b>Earnings/ (Loss) Per Share</b>	<b>(0.77)</b>	<b>(0.47)</b>	<b>(0.69)</b>	<b>(1.01)</b>	<b>(1.08)</b>	<b>0.16</b>	<b>1.51</b>	<b>2.92</b>	<b>3.45</b>
<i>Growth Rate</i>									
<b>Shares Outstanding (MM)*</b>	<b>89,410</b>	<b>98,725</b>	<b>100,150</b>	<b>100,750</b>	<b>101,350</b>	<b>101,950</b>	<b>102,550</b>	<b>103,150</b>	<b>103,750</b>
<b>Earnings/ (Loss) - Diluted</b>						<b>0.16</b>	<b>1.43</b>	<b>2.77</b>	<b>3.28</b>
<b>Fully Diluted Shares Out (MM)</b>			<b>105,150</b>	<b>105,850</b>	<b>106,550</b>	<b>107,250</b>	<b>107,950</b>	<b>108,650</b>	<b>109,350</b>

Source: Corporate Reports and Ladenburg Thalmann &amp; Co estimates.

## APPENDIX A: IMPORTANT RESEARCH DISCLOSURES

### ANALYST CERTIFICATION

I, Juan Sanchez attest that the views expressed in this research report accurately reflect our personal views about the subject security and issuer. Furthermore, no part of our compensation was, is, or will be directly or indirectly related to the specific recommendation or views expressed in this research report.

The research analyst(s) primarily responsible for the preparation of this research report have received compensation based upon various factors, including the firm's total revenues, a portion of which is generated by investment banking activities.

### COMPANY BACKGROUND

IRWD is a biopharmaceutical company primarily focused on developing and commercializing of linaclotide for the treatment of IBS-C and CC. Linaclotide is partnered with FRX in the US and Phase III results in IBS-C are expected in Q4 2010.

### VALUATION METHODOLOGY

We use a risk-adjusted sum-of-the-parts analysis to value linaclotide.

### RISKS

**Clinical Risk:** Linaclotide is in two pivotal clinical trials for the treatment of IBS-C. The FDA requires two positive clinical trials to prove efficacy and there is a risk linaclotide may fail to demonstrate efficacy in one or both of the studies. Results are expected in 4Q 2010 for the Phase III trials.

**Regulatory Risk:** IRWD plans to file the NDA for linaclotide in 2H 2011. Assuming positive Phase III trials, we believe the regulatory risk for this program is low given the need for a safe and efficacious drug in IBS-C.

**Commercial Risk:** IBS-C has traditionally been a difficult indication for prescription medicines. The availability of over the counter medicines coupled with the suboptimal commercial success of existing prescription therapies handicap the market potential of a new entrant Linaclotide may also fail to obtain a label for abdominal pain which could also impede initial sales. Therefore, linaclotide's market penetration could be lower than our estimates.

**Partner Risk:** FRX is responsible for North American commercialization of linaclotide. FRX does not have experience at commercializing major gastro-intestinal drugs which may require direct to consumer advertisement. Almirall is responsible for the European commercialization of linaclotide. Almirall's sales and marketing efforts may fall short or prove ineffective in promoting the adoption of linaclotide, which would result in royalty revenues below estimates.

**Reimbursement Risk:** Linaclotide may be unable to obtain favorable formulary placement by third party payers, which could limit initial uptake and patient use.both of the studies. Data from the Phase III program is expected in 4Q 2010.

**Commercial Risk:** IBS-C has traditionally been a difficult indication for prescription medicines. The availability of over the counter medicines coupled with the suboptimal commercial success of existing prescription therapies handicap the market potential of a new entrant Linaclotide may also fail to obtain a label for abdominal pain which could also impede initial sales. Therefore, linaclotide's market penetration could be lower than our estimates.

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**Reimbursement Risk.** Linaclotide may be unable to obtain favorable formulary placement by third party payers.

**Financial Risk:** We believe IRWD is unlikely to incur dilution in the near term. However, IRWD could need additional cash to fund its portion of the detailing of linaclotide in the United States.

### STOCK RATING DEFINITIONS

Buy: The stock's return is expected to exceed 15% over the next twelve months.

Neutral: The stock's return is expected to be plus or minus 15% over the next twelve months.

Sell: The stock's return is expected to be negative 15% or more over the next twelve months.

Investment Ratings are determined by the ranges described above at the time of initiation of coverage, a change in risk, or a change in target price. At other times, the expected returns may fall outside of these ranges because of price movement and/or volatility. Such interim deviations from specified ranges will be permitted but will become subject to review.

**RATINGS DISPERSION AND BANKING RELATIONSHIPS (as of 8/31/10)**

Buy	70%	(28% are banking clients)
Neutral	30%	( 17% are banking clients)
Sell	0%	( 0% are banking clients)

**BIOTECHNOLOGY & HEALTHCARE SECTOR STOCKS UNDER AUTHOR ANALYST COVERAGE ("The Universe")**

AMAG Pharmaceuticals (AMAG), Cadence Pharmaceuticals (CADX), Chelsea Therapeutics (CHTP), Corcept Therapeutics Inc. (CORT), Cypress Bioscience Inc. (CYPB), Ironwood Pharmaceuticals (IRWD), Micromet Inc. (MITI), Micrus Endovascular Corp (MEND), NeurogesX (NGSX), NeuroMetrix Inc. (NURO), Optimer Pharmaceuticals (OPTR), pSivida (PSDV), Raptor Pharmaceutical Corp. (RPTP), Targacept Inc. (TRGT), Valeant Pharmaceuticals (VRX), XenoPort, Inc. (XNPT), Harris & Harris Group, Inc (TINY).

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