IRONWOOD PHARMACEUTICALS (IRWD)

Second Linaclotide Phase III Trial Results Are Positive. Maintaining BUY Rating.

Investment Rating	BUY
Prior Rating	
Price Target	$15.00
Prior Target	
Price (November 1, 2010)	$10.57
52 Week Range	$8.90 - $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):

	Current	Prior
2010E	$39.1	
2009A	$36.1	

EPS:

	Current	Prior	P/E
2010E	($0.77)		NA
2009A	($10.00)		NA

Quarterly EPS*:

	Current	Prior
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; $33.27) and Almirall S.A. announced results from the second (of two) linaclotide pivotal trial in irritable bowel syndrome with constipation (IBS-C).

The results amply meet FDA and EMA criteria as well as the higher bar set by the planned statistical analysis in the US (see Tables 1 and 2). Similar to Study 31, the trial met all 16 primary and secondary endpoints.

The results confirm the strong findings seen in Study 31 (reported in September 2010). Noteworthy, the p-value for the abdominal pain endpoint (≥30% improvement for 9/12 weeks) was <0.0001 versus p= 0.0262 in Study 31 which, in our view, will likely alleviate concerns held by some people.

Importantly, although the primary endpoint was measured during the first 12 weeks, Study 302 followed patients through 26 weeks. The results showed linaclotide was superior to placebo in each of the 26 weeks in the treatment period in mean change from baseline in abdominal pain and CSBMs (p<0.0001). In our view, these results indicate there is not tachyphylaxis and linaclotide is likely to receive a label without limits to duration of therapy (for example, up to 12 weeks).

With two positive pivotal trials (Study 321 and Study 302) we believe the chances of linaclotide approval with a differentiating label in IBS-C (abdominal pain benefit) is high. The linaclotide NDA is expected to be filed in Q3 2011 and filing in Europe is expected a few months after.

Importantly, we continue to believe linaclotide could become a blockbuster drug (the basis of our investment thesis). In our analyses of available data, linaclotide has shown rapidly (within the first week) to have a profound effect in abdominal and bowel symptoms in IBS-C patients. In addition, the results are long-lasting and clinically relevant in the majority of patients. We believe linaclotide has the potential to become a $1.3 billion product in the US and a $300 million product between Europe and Asia.

The results showed extensive consistency among 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.

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 19.7% for linaclotide vs. 2.5% for placebo (Study 31 results were 19% for linaclotide versus 4% for placebo). However, 4.5% patients on linaclotide treatment discontinued due to diarrhea vs. 0.2% in placebo (Study 31 results were 6% for linaclotide vs. 0.3% for placebo).

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Table 1. Linaclotide Pivotal Trials: Results for U.S. Endpoints

	Study 31				Study 302		
U.S. Primary Endpoints	**Linaclotide**	**Placebo**	**p-value**		**Linaclotide**	**Placebo**	**p-value**
Endpoint A (complete responder 9/12 weeks)	12.10%	5.1%	p=0.0004		12.70%	3%	p<0.0001
Endpoint B (CSBM responder)	19.50%	6.3%	p<0.0001		18%	5%	p<0.0001
Endpoint C (abdominal pain responder)	34.30%	27.1%	p=0.0262		38.90%	19.60%	p<0.0001
Endpoint D (complete responder 6/12 weeks)	33.60%	21.0%	p<0.0001		33.70%	13.90%	p<0.0001

IRWD/FRX Press release, 9/13/10 and 11/1/10

Table 2. Linaclotide Pivotal Trials: Results for E.U. Endpoints

	Study 31				Study 302		
E.U. Primary Endpoints	**Linaclotide**	**Placebo**	**p-value**		**Linaclotide**	**Placebo**	**p-value**
Responders to Abdominal Pain* (30% improvement from baseline)	55%	42%	p=0.0002		54.10%	38.50%	p<0.0001
Responders to IBS Degree of Relief	37%	18%	p<0.0001		39.40%	16.60%	p<0.0001

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

Soure:Almirall Press releases, 9/13/10 and 11/1/10

Table 3. Linaclotide Pivotal Trials: Safety Results

	Study 31		Study 302	
Adverse events	**Linaclotide**	**Placebo**	**Linaclotide**	**Placebo**
Any SAE	0.5%	0.5%	NA	NA
Any AE	56%	53%	65%	57%
Diarrhea	19.0%	4.0%	19.7%	2.5%
Flatulence	5.0%	2.0%	3.7%	2.2%
Abdominal Pain	5.0%	3.0%	4.5%	4.0%
Headache	5.0%	4.0%	3.2%	2.7%
Discontinuation due to AE	8.0%	3.0%	10.2%	2.5%
Discontinuation due to Diahhrrea	6.0%	0.3%	4.5%	0.2%

Soure: Ironwood/Forest and Ironwood/Almirall Press release, 9/13/10, 11/1/10

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	$34,321	$8,838	$9,188	$9,341	$9,341	$36,708	9,341	9,341	9,341	9,341	$37,363
Services	1,781	214	1,771	200	200	2,385	300	300	300	300	1,200
Total Revenues	**36,102**	**9,052**	**10,959**	**9,541**	**9,541**	**39,093**	**9,641**	**9,641**	**9,641**	**9,641**	**38,563**
R&D	84,892	18,637	20,953	21,000	17,000	77,590	15,000	12,000	10,000	10,000	47,000
SG&A	23,980	6,643	7,325	8,400	8,400	30,768	9,000	9,500	9,600	9,500	37,600
	1,207										
Operating Expense	**110,079**	**25,280**	**28,278**	**29,400**	**25,400**	**108,358**	**24,000**	**21,500**	**19,600**	**19,500**	**84,600**
Operating Income/Loss	**(73,977)**	**(16,228)**	**(17,319)**	**(19,859)**	**(15,859)**	**(69,265)**	**(14,359)**	**(11,859)**	**(9,959)**	**(9,859)**	**(46,037)**
Other Income											
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					-
Net Non-Operating Income	2,496	304	183	50	20	557	20	10	15	-	45
Pretax Income	**(71,481)**	**(15,924)**	**(17,136)**	**(19,809)**	**(15,839)**	**(68,708)**	**(14,339)**	**(11,849)**	**(9,944)**	**(9,859)**	**(45,992)**
Taxes											
Provison for Income Taxes	296	-	-	-	-	-	-	-	-	-	-
Net Income/Loss	**(71,185)**	**(15,924)**	**(17,136)**	**(19,809)**	**(15,839)**	**(68,708)**	**(14,339)**	**(11,849)**	**(9,944)**	**(9,859)**	**(45,992)**
Earnings/ (Loss) Per Share	**($10.00)**	**($0.25)**	**($0.18)**	**($0.20)**	**($0.16)**	**($0.77)**	**($0.15)**	**($0.12)**	**($0.10)**	**($0.10)**	**($0.47)**
Shares Outstanding (MM)*	7,117	63,958	97,642	97,740	98,300	89,410	98,500	98,650	98,800	98,950	98,725

Source: Corporate Reports and Ladenburg Thalmann & Co estimates.

Table 5. Annual Financial Model ($000s)

	2010E	2011E	2012E	2013E	2014E	2015E	2016E	2017E	2018E
Sales/ Royalties									
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 Reimbursment 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
Astella 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
Total Sales/Royalties									
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					
Total Revenues	39,093	38,563	99,054	105,364	109,746	249,506	458,805	678,680	770,282
% Change		-1.4%	156.9%	6.4%	4.2%	127.3%	83.9%	47.9%	13.5%
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									
Operating Expenses	108,358	84,600	168,349	208,014	220,628	229,021	239,387	250,636	261,178
Operating Income/Loss	(69,265)	(46,037)	(69,295)	(102,650)	(110,882)	20,484	219,418	428,044	509,104
Other Income									
Interest Income	507	365	300	1,000	1,500	1,800	1,800	2,000	2,500
Interest Expense	(352)	(320)	-	-	-	-	-	-	-
Other	-	-	-	-	-	-	-	-	-
	402								
Net Non-Operating Income	$557	45	300	1,000	1,500	1,800	1,800	2,000	2,500
Pretax Income	(68,708)	(45,992)	(68,995)	(101,650)	(109,382)	22,284	221,218	430,044	511,604
Income Tax Paid/(Benefit)	-	-	-	-	-	5,571	66,365	129,013	153,481
Non-Operating Income / (Charge)	-	-	-	-	-	-	-	-	-
Net Income/ (Loss)	**(68,708)**	**(45,992)**	**(68,995)**	**(101,650)**	**(109,382)**	**16,713**	**154,852**	**301,031**	**358,123**
Earnings/ (Loss) Per Share	**(0.77)**	**(0.47)**	**(0.69)**	**(1.01)**	**(1.08)**	**0.16**	**1.51**	**2.92**	**3.45**
Growth Rate									
Shares Outstanding (MM)*	89,410	98,725	100,150	100,750	101,350	101,950	102,550	103,150	103,750
Earnings/ (Loss) - Diluted						**0.16**	**1.43**	**2.77**	**3.28**
Fully Diluted Shares Out (MM)			105,150	105,850	106,550	107,250	107,950	108,650	109,350

Source: Corporate Reports and Ladenburg Thalmann & 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 1010.

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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 10/31/10)

Buy	70%	(27% are banking clients)
Neutral	30%	(16% 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), 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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