Research Note

Biotechnology / Biopharmaceuticals

Ironwood Pharmaceuticals, Inc. (IRWD)

September 14, 2010

IRWD Announces Positive Phase III Results for Linaclotide in Patients with IBS with Constipation

- **Ironwood along with its US (Forest Labs) and EU (Almirall) partners has announced the results of the first of two Phase III studies for linaclotide.** The company reports that linaclotide met all 16 US and EU primary and secondary endpoints, and has now achieved a total of 48/48 endpoints in the first 3 Phase III IBS-C and two Phase III CC trials.
- **The US study achieved all four co-primary endpoints including: (1) patients achieving both a ≥30% reduction in abdominal pain relative to baseline for at least 9 of the 12 weeks, and ≥3 CSBMs and an increase ≥1 CSBM per week over baseline for at least 9 of the 12 weeks (2) patients achieving ≥3 CSBMs per week and ≥1 CSBM per week over baseline for at least 9 of the 12 weeks (3) patients achieving both a ≥30% reduction in abdominal pain relative to baseline for at least 9 of the 12 weeks, (4) patients achieving both a ≥30% reduction in abdominal pain relative to baseline for at least 6 of the 12 weeks.** The primary co-endpoint 1, was met for 12.1% of the linaclotide group vs. 5.1% for the placebo group, p=0.0004, 19.5% vs. 6.3%, P<0.0001 for the second co-endpoint, 34.3% vs 27.1%, p=0.0262 for the 3rd co-primary endpoint and 33.6% vs. 21%, p<0.0001 for the 4th co-primary endpoint. The combined responder endpoints (the CSBM responder and the abdominal pain responder) were evaluated sequentially and all 4 endpoints are >95% powered to demonstrate statistical significance.
- **The EU study achieved its co-primary endpoints of: (1) patients achieving both a ≥30% reduction in mean abdominal pain or mean abdominal discomfort score for at least 6 of the 12 weeks, (2) degree of relief response of either "considerably relieved" or "completely relieved" for at least 6 of the 12 weeks.** Results showed a greater proportion of patients on linaclotide responded 55% vs. 42% on placebo, p=0.0002 for the first endpoint and on linaclotide 37% vs. 18% on placebo, p<0.0001, responded for the second endpoint. Additionally, secondary endpoints were statistically significant for linaclotide vs. placebo.
- **Linaclotide displayed good safety results consistent with past trials, diarrhea was the most common AE.** Additional AEs included flatulence, abdominal pain, and headache. 19% of the linaclotide group vs. 4% in the placebo group experienced diarrhea. AEs caused discontinuation in 8% of the linaclotide group vs. 3% for the placebo. While some may focus on these numbers its important to note that the AE rates are not informative to the longer term experience with linaclotide, and that its the prevalence of these observations, not incidence, that predicts the likelihood a patient will stay on therapy. We view the efficacy and tolerability results as superior to existing IBS-C treatments and expect the real-world efficacy and tolerability results for patients to improve upon that of the Phase III study as patients titrate their treatment to optimize their CSBM frequency and pain relief while minimizing side effects.

FYE Dec	2009E	2010E			2011E		
REV. ($m)	ACTUAL	CURR.	PREV.	CONS.	CURR.	PREV.	CONS.
Q1 Mar	--	$9.1	--	NA	$14.5	--	NA
Q2 Jun	--	$11.0	--	NA	$14.5	--	NA
Q3 Sep	--	$9.8	--	NA	$14.5	--	NA
Q4 Dec	--	$9.8	--	NA	$14.5	--	NA
Year*	**$36.8**	**$39.5**	**--**	**NA**	**$58.0**	**--**	**NA**
Change	NA	NA	NA	NA	NA	NA	NA
	2009E	2010E			2011E		
EPS	ACTUAL	CURR.	PREV.	CONS.	CURR.	PREV.	CONS.
Q1 Mar	--	(0.25)	--	NA	(0.04)	--	NA
Q2 Jun	--	(0.18)	--	NA	(0.06)	--	NA
Q3 Sep	--	(0.11)	--	NA	(0.10)	--	NA
Q4 Dec	--	(0.06)	--	NA	(0.12)	--	NA
Year*	**($0.84)**	**(0.55)**	**--**	**NA**	**(0.32)**	**--**	**NA**
P/E	NA	NA	NA	NA	NA	NA	NA
Change	NA	NA	NA	NA	NA	NA	NA

*Consensus estimates are from Thomson First Call. * Numbers may not add up due to rounding.*

Price (close 09/13/10)
$9.74

Rating
OUTPERFORM

Price target
$24

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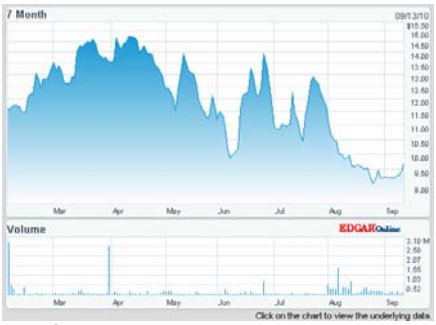
Company Information

52-Week Range	$8.90 - $15.03
Shares/Diluted	98.0M / 119.8M
Cash (Q2)	$271.6 M
FY:10 Burn	$60.4 M
Market Cap.	$952 M
ST/LT Debt	$1.3 M / $1.7 M
Debt/Capital	1.3%
ROE	NM
Cash & Inv/Share	$2.78
Book Value/Share	$1.75

Company Description

Ironwood is developing linaclotide, an agonist of guanylate cyclase type-C receptors that line the intestinal tract, for the treatment of chronic constipation (CC) and irritable bowel syndrome with constipation (IBS-C).



Nasdaq.com

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- **This primary endpoint data may be included in a potential linaclotide label, making potential comparisons future IBS-C products much more straightforward.**
- **Results from the 26-week second Phase III pivotal trial of linaclotide in IBS-C are expected in Q4:10**. Ironwood also expects that following these results an NDA could be filled in the US by mid-year 2011.
- **IRWD expects to finish 2010 with about $220 million in cash and equivalents.**
- **We reiterate our OUTPERFORM rating and our $24/share price target.** We estimate that US linaclotide sales will peak at approximately $2.4 billion in 2019 in the CC and IBS-C settings. We arrive at our valuation by discounting back the product of the net present value of losses and profits through 2015 plus 18X 2016 linaclotide royalties and US revenues (25% discount rate, estimated current diluted share count of 119.8 million).
- Risks to the attainment of our price target include potential negative data from the IBS-C Phase III studies, regulatory risk associated with the NDA expected to be filed with the FDA and failure to achieve meaningful sales penetration of linaclotide in the IBS-C and/or CC settings.

IBS-C Phase III IBS-C Trial and Results

Topline Efficacy Results (US Study)

Primary Endpoints	Responder Rates (%)		
	266 mcg	Placebo	P-value
Composite responder 1 (abdominal pain 30, CSBM 3+1, 9/12)	12	5	0.0004
CSBM responder 1 (CSBM 3+1, 9/12)	20	6	<0.0001
Abdominal pain responder 1 (abdominal pain 30, 9/12)	34	27	0.0262
Composite responder 2 (abdominal pain 30, CSBM +1, 6/12)	34	21	<0.0001
Secondary Endpoints			
CSBM+1 responder 2 (CSBM+1, 6/12)	49	30	<0.0001
Abdominal pain responder 2 (abdominal pain 30, 6/12)	50	37	0.0003
Abdominal pain (12-week)		Yes	<0.0001
Percent of abdominal pain-free days (12-week)		Yes	0.0014
Abdominal discomfort (12-week)		Yes	<0.0001
Bloating (12-week)		Yes	<0.0001
CSBM frequency rate (12-week)		Yes	<0.0001
SBM frequency rate (12-week)		Yes	<0.0001
Stool consistency (12-week)		Yes	<0.0001
Severity of straining (12-week)		Yes	<0.0001

Source: Ironwood Pharmaceuticals and Wedbush PacGrow Life Sciences

Topline Efficacy Results (EU Study)

Primary Endpoints	Responder Rates (%)		
	266 mcg	Placebo	P-value
12-week abdominal pain / abdominal discomfort responder	55	42	0.0002
12-week IBS degree of relief responder	37	18	<0.0001
Secondary Endpoints			
Bloating (12-week)		Yes	<0.0001
CSBM frequency rate (12-week)		Yes	<0.0001
Stool consistency (12-week)		Yes	<0.0001
Severity of straining (12-week)		Yes	<0.0001

Source: Ironwood Pharmaceuticals and Wedbush PacGrow Life Sciences

Common Adverse Events

	266 mcg N=406	Placebo N=396
AnySAE	0.50%	0.50%
Any AE	56%	53%
Diarrhea	19%	4%
Mild	9%	2%
Moderate	8%	1%
Severe	2%	0.30%
Abdominal pain	5%	3%

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Flatulence	5%	2%
Headache	5%	4%
Discontinued due to diarrhea	6%	0.30%

Source: Ironwood Pharmaceuticals and Wedbush PacGrow Life Sciences

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9/13/2010

WEDBUSH PACGROW LIFESCIENCES

Ironwood Pharmaceuticals, Inc.
Annual Financial Results & Projections
($ in thousands except per share data)
Ticker: IRWD (Nasdaq)

	FY:07A	FY:08A	FY:09E	FY:10E	FY:11E	FY:12E	FY:13E	FY:14E
Revenue:								
US profit share	0	0	0	0	0	0	0	17,766
Royalties	0	0	0	0	0	0	6,143	37,815
Contracts and grants	10,464	22,216	36,798	39,511	58,000	133,000	17,000	41,000
Total Revenues	**$10,464**	**$22,216**	**$36,798**	**$39,511**	**$58,000**	**$133,000**	**$23,143**	**$96,581**
Cost and Expenses:								
Research and development	57,246	59,809	78,235	64,590	50,000	48,020	56,863	43,532
Sales, general, and administrative	10,833	18,328	23,020	25,968	42,000	127,712	161,176	82,606
Cost of goods	0	0	0	0	0	0	0	0
Total Costs and Expenses	**$68,079**	**$78,137**	**$101,255**	**$90,558**	**$92,000**	**$175,732**	**$218,039**	**$126,138**
Other Income (Expense):	600	(900)	(133)	1,586	2,417	2,092	1,093	152
Income before taxes	(57,015)	(56,821)	(64,590)	(49,461)	(31,583)	(40,640)	(193,803)	(29,405)
Provision for income taxes (expense)	0	0	(203)	0	0	948	0	800
Net loss	**(57,015)**	**(56,821)**	**(64,797)**	**(49,461)**	**(31,583)**	**(40,640)**	**(193,803)**	**(30,205)**
GAAP EPS	**(0.77)**	**(0.76)**	**(0.84)**	**(0.52)**	**(0.32)**	**(0.42)**	**(1.98)**	**(0.31)**
Basic weighted shares outstanding	74,500	75,000	77,038	95,672	97,483	97,583	97,683	97,783
Fully diluted shares outstanding	74,500	75,000	77,038	119,823	119,923	120,023	120,123	120,223

Source: Wedbush PacGrow Life Sciences

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I, Gregory Wade, certify that the views expressed in this report accurately reflect my personal opinion and that I have not and will not, directly or indirectly, receive compensation or other payments in connection with my specific recommendations or views contained in this report.

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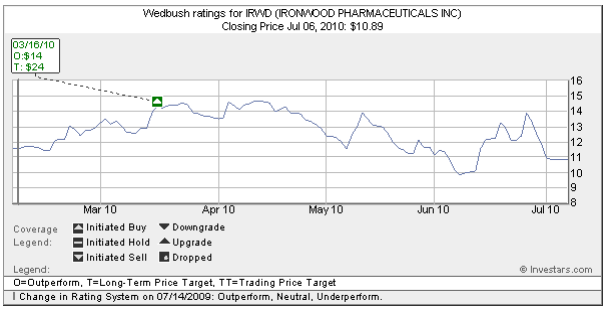

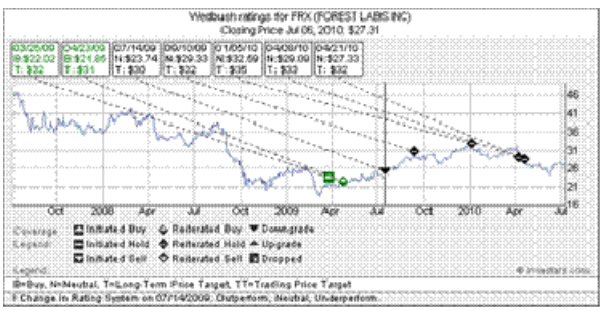

Disclosure information regarding historical ratings and price targets is available at
http://www.wedbush.com/ResearchDisclosure/DisclosureQ210.pdf

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OUTPERFORM – Expect the total return of the stock to outperform relative to the median total return of the analyst's (or the analyst's team) coverage universe over the next 6-12 months.

NEUTRAL – Expect the total return of the stock to perform in-line with the median total return of the analyst's (or the analyst's team) coverage universe over the next 6-12 months.

UNDERPERFORM – Expect the total return of the stock to underperform relative to the median total return of the analyst's (or the analyst's team) coverage universe over the next 6-12 months.

The Investment Ratings are based on the expected performance of a stock (based on anticipated total return to price target) relative to the other stocks in the analyst's coverage universe (or the analyst's team coverage).*

DISTRIBUTION OF RATINGS (as of June 30, 2010)

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NEUTRAL – 38% (1% of this rating category were investment banking clients within the last 12 months).

UNDERPERFORM – 11% (0% of this rating category were investment banking clients within the last 12 months).

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WS co-managed a public offering of securities for BioMimetic Therapeutics (BMTI), Clinical Data (CLDA), Delcath Systems (DCTH), Ironwood Pharmaceuticals (IRWD) and ZymoGenetics (ZGEN) within the last 12 months.

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WS provided investment banking services to BioMimetic Therapeutics (BMTI), Clinical Data (CLDA), CombinatoRx (CRXX), Delcath Systems (DCTH), Emergent BioSolutions (EBS), Ironwood Pharmaceuticals (IRWD), Pharmacyclics (PCYC) and ZymoGenetics (ZGEN) within the last 12 months.

WS is acting as financial advisor to Emergent BioSolutions (EBS) and Pharmacyclics (PCYC).

WS expects to receive compensation for investment banking services from BioMimetic Therapeutics (BMTI), Emergent BioSolutions (EBS) and Pharmacyclics (PCYC) within the next 3 months.

Greg Wade, the analyst providing research coverage of Adolor (ADLR), BioMimetic (BMTI), Cubist (CBST), CombinatoRx (CRXX), OncoGenex Pharmaceuticals (OGXI) and ZymoGenetics (ZGEN), maintains long positions in the common stocks.

Jeremiah Shepard, the associate providing research coverage of Ironwood Pharmaceuticals (IRWD) and Xenoport (XNPT) maintains a long position in the common stocks.

* WS changed its rating system from (Strong Buy/Buy/Hold/Sell) to (Outperform/ Neutral/Underperform) on July 14, 2009.

Please access the attached hyperlink for WS' Coverage Universe: http://www.wedbush.com/inside/CapitalMarkets/CoverageList.asp

Applicable disclosure information is also available upon request by contacting Ellen Kang in the Research Department at (213) 688-4529, by email to ellen.kang@wedbush.com, or the Business Conduct Department at (213) 688-8090. You may also submit a written request to the following: Business Conduct Department, 1000 Wilshire Blvd., Los Angeles, CA 90017.

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