Research Note

Biotechnology / Biopharmaceuticals

Ironwood Pharmaceuticals, Inc. (IRWD)

November 2, 2010

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

- **Ironwood along with Forest Labs announced positive results from the second of the two Phase III studies for linaclotide in IBS-C.** The study met all 4 primary and all of the secondary endpoints, and has now achieved all primary endpoints in its Phase III IBS-C trials.
- **The MCP-103-302 study achieved success for 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 (1) 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 12.7% of the linaclotide group vs. 3.0% for the placebo group, p<0.0001, 18.0% vs. 5.0%, p<0.0001 for the second co-endpoint, 38.9% vs 19.6%, p<0.0001 for the 3rd co-primary endpoint and 33.7% vs. 13.9%, p<0.0001 for the 4th co-primary endpoint.
- **Linaclotide displayed good safety results consistent with past trials, diarrhea was the most common AE.** Additional AEs included flatulence, abdominal pain, and headache. The most common AE, diarrhea, was experienced by 19.7% of the linaclotide group vs. 2.5% in the placebo group experienced diarrhea, however, 4.5% of patients discontinued treatment due to diarrhea. Overall, AEs caused discontinuation in 10.2% of the linaclotide group vs. 2.5% for the placebo. 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.
- **Ironwood expects the timing of the NDA for linaclotide to be Q3:11**. We are adjusting our estimate of the approval for linaclotide to Q3:12 from Q1:12. We expect the European launch to also occur in the Q3:12 timeframe as the Company and European regulators have agreed that the EMEA analysis of US data would support registration.
- **We reiterate our OUTPERFORM rating and adjusting our price target to $20/share price target from $24/share.** With our change to our estimate of the timing of linaclotide's approval, we are also adjusting our price target to $20 from $24. 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 regulatory risk associated with potential approvals in US and other markets and failure to achieve meaningful sales penetration of linaclotide in the IBS-C and/or CC settings.

FYE Dec	2009E	2010E			2011E		
REV. ($m)	ACTUAL	CURR.	PREV.	CONS.	CURR.	PREV.	CONS.
Q1 Mar	--	$9.1	--	$9.1	$14.5	--	$10.7
Q2 Jun	--	$11.0	--	$11.0	$14.5	--	$18.4
Q3 Sep	--	$9.8	--	$9.3	$14.5	--	$20.3
Q4 Dec	--	$9.8	--	$9.5	$14.5	--	$11.7
Year*	**$36.8**	**$39.5**	**--**	**$38.8**	**$58.0**	**--**	**$67.6**
Change	NA	NM	NM	NM	NM	NM	NM
	2009E	2010E			2011E		
EPS	ACTUAL	CURR.	PREV.	CONS.	CURR.	PREV.	CONS.
Q1 Mar	--	($0.18)	--	($0.25)	($0.04)	--	($0.12)
Q2 Jun	--	($0.18)	--	($0.18)	($0.05)	--	($0.11)
Q3 Sep	--	($0.11)	--	($0.19)	($0.06)	--	($0.01)
Q4 Dec	--	($0.06)	--	($0.17)	($0.06)	--	($0.14)
Year*	**($0.84)**	**($0.52)**	**--**	**($0.75)**	**($0.21)**	**--**	**($0.36)**
P/E	NA	NM	NM	NM	NM	NM	NM
Change	NA	NM	NM	NM	NM	NM	NM

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

Price (intraday 11/2/10)
$10.85

Rating
OUTPERFORM

Price target
$20 (from $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.	$1.1 B
ST/LT Debt	$1.3 M / $1.7 M
Debt/Capital	0.3%
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

IBS-C Phase III IBS-C Trial and Results

Topline Efficacy Results (MCP-103-301 and -302)

Primary Endpoints	Responder Rates (%)					
	301 – 266 mcg linaclotide	Placebo (301)	P-value	302 – 266 mcg linaclotide	Placebo (302)	P-value
Composite responder 1 (abdominal pain 30, CSBM 3+1, 9/12)	12	5	0.0004	13	3	<0.0001
CSBM responder 1 (CSBM 3+1, 9/12)	20	6	<0.0001	18	5	<0.0001
Abdominal pain responder 1 (abdominal pain 30, 9/12)	34	27	0.0262	39	20	<0.0001
Composite responder 2 (abdominal pain 30, CSBM +1, 6/12)	34	21	<0.0001	34	14	<0.0001
Secondary Endpoints						
CSBM+1 responder 2 (CSBM+1, 6/12)	49	30	<0.0001	49	35	<0.0001
Abdominal pain responder 2 (abdominal pain 30, 6/12)	50	37	0.0003	48	23	<0.0001
Abdominal pain (12-week)	Yes		<0.0001	Yes		<0.001
Percent of abdominal pain-free days (12-week)	Yes		0.0014	Yes		<0.001
Abdominal discomfort (12-week)	Yes		<0.0001	Yes		<0.001
Bloating (12-week)	Yes		<0.0001	Yes		<0.001
CSBM frequency rate (12-week)	Yes		<0.0001	Yes		<0.001
SBM frequency rate (12-week)	Yes		<0.0001	Yes		<0.001
Stool consistency (12-week)	Yes		<0.0001	Yes		<0.001
Severity of straining (12-week)	Yes		<0.0001	Yes		<0.001

Source: Ironwood Pharmaceuticals and Wedbush PacGrow Life Sciences

Common Adverse Events

	266 mcg - 301	Placebo - 301	266 mcg - 302	Placebo - 302
Diarrhea	19%	4%	20%	3%
Abdominal pain	5%	3%	5%	4%
Flatulence	5%	2%	4%	2%
Viral Gastroenteritis			4%	2%
Headache	5%	4%	3%	3%
Discontinued due to diarrhea	6%	0.30%	5%	0.2%

Source: Ironwood Pharmaceuticals and 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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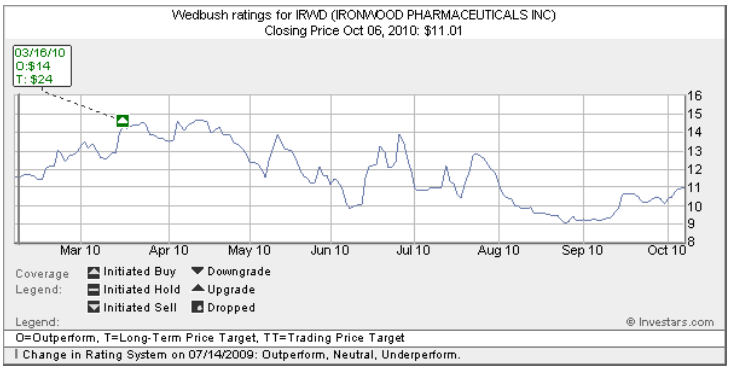

Disclosure information regarding historical ratings and price targets is available at
http://www.wedbush.com/ResearchDisclosure/DisclosureQ310.pdf

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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.
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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).*

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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), OncoGenex Pharmaceuticals (OGXI) and ZymoGenetics (ZGEN) within the last 12 months.

WS has received compensation for investment banking services from BioMimetic Therapeutics (BMTI), Clinical Data (CLDA), CombinatoRx (CRXX), Delcath Systems (DCTH), Emergent BioSolutions (EBS), Ironwood Pharmaceuticals (IRWD), OncoGenex Pharmaceuticals (OGXI) and ZymoGenetics (ZGEN) within the last 12 months.
WS provided investment banking services to BioMimetic Therapeutics (BMTI), Clinical Data (CLDA), CombinatoRx (CRXX), Delcath Systems (DCTH), Emergent BioSolutions (EBS), Ironwood Pharmaceuticals (IRWD), OncoGenex Pharmaceuticals (OGXI), 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), OncoGenex Pharmaceuticals (OGXI) 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), SIGA Technologies (SIGA) and ZymoGenetics (ZGEN), maintains long positions in the common stocks.
* WS changed its rating system from (Strong Buy/Buy/Hold/Sell) to (Outperform/ Neutral/Underperform) on July 14, 2009.
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