

Reason for report:
COMPANY UPDATE

ARDELYX, INC.

Raising Our Price Target Following Positive Ph. 2b IBS Data

• **Bottom Line:** We are raising our valuation to \$36/shr (from \$32) following positive topline Ph. 2b data in constipation predominant irritable bowel syndrome. Overall, the data were strong evidencing a profile that may differentiate on magnitude of effect, tolerability and an ability to titrate the dose. As such - we are increasing our odds of success for the program to 60% (from 35%); part of our caution stems from the uncertainty regarding AZN's (MP) decision to advance the program into Ph. 3 but we're encouraged to see AZN launch other gastro products like Movantik + the Linzess launch validates blockbuster pot'l of IBS-C drugs. Next up we expect (1) company updates on Ph. 3 IBS-C program; (2) 1H'15 - topline Ph. 2b ESRD data; & (3) 2H'15 - topline Ph. 2a CKD data.

• **Tenapanor was well tolerated in pts at all dose levels; Diarrhea frequency of ~11% in the 50mg arm could be a key differentiator to Linzess.** Tenapanor demonstrated good tolerability in the study with the most common adverse events using the 50mg BID being diarrhea (11.2% vs. 0% for PBO). We view the 11.2% rate of diarrhea as encouraging but inconclusive. Relative to competitor products like linaclotide/plecanatide - those agents showed high single digit rates of diarrhea in Ph. 2 and linaclotide showed ~20% rates in its Ph. 3 trial. Importantly - rates of study discontinuation were low for tenapanor at 4.5% (3.3% for PBO) although causes of discontinuation were not disclosed. By comparison, ACT/IRWD's Linzess had a 5% discontinuation rate in Ph. 3 due to diarrhea (9% overall rate). In terms of efficacy, we are also encouraged by (1) signs of a positive dose response; and (2) the magnitude of benefit seen on the primary endpt - where tenapanor achieved ~25% placebo adj stat sig improvement on the bowel movement measurement which compares favorable to marketed alternatives (see pg.2).

• **Next steps with IBS development will come into view after ARDX meets with its partner.** ARDX plans to meet with its partner AZN (MP) to discuss the tenapanor data and next steps. The million dollar question is whether AZN is committed to advancing the IBS indication, given the high cost of development and marketing of the drug. Currently, the market for brand Rx constipation therapy is ~\$500-600m but innovator companies have been investing in DTC programs aimed at creating disease awareness. While we cannot predict AZN's next move, we are encouraged by the fact that (1) AZN will launch Movantik for treatment of opioid induced constipation in the 1H'15, which includes detailing gastroenterologists; (2) ACT/IRWD's Linzess has responded to DTC ads and the drug is tracking to exceed \$1B in peak US sales.

• **Positive data provides bump to our valuation:** Prior to today's topline IBS data, we forecast tenapanor 2025 sales of \$860m at a 35% probability of success. In our view, today's positive Phase 2 study warrants an improvement in our assigned POS to 60% (from 35%), which increases our contribution from the program to \$175m (from ~\$100m).

Key Stats: (NASDAQ:ARDX)

S&P 600 Health Care Index:	1,281.64
Price:	\$14.21
Price Target:	\$36.00 from \$32.00
Methodology:	Sum-of-the-parts DCF analysis, 15% discount rate
52 Week High:	\$21.60
52 Week Low:	\$11.37
Shares Outstanding (mil):	20.3
Market Capitalization (mil):	\$288.5
Book Value/Share:	\$0.00
Cash Per Share:	\$5.81
Net Debt to Total Capital:	0%
Dividend (ann):	\$0.00
Dividend Yield:	0.0%



Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	P/E
2013A	--	--	--	--	29.0	--	--	--	--	(0.65)	NM
2014E	8.6A	9.1A	6.5A	8.8A	33.0	(0.23)A	0.18A	(0.08)	(0.05)	(0.11)	NM
2015E	--	--	--	--	50.0	--	--	--	--	(0.02)	NM
2016E	--	--	--	--	60.0	--	--	--	--	0.40	35.5x

Source: Company Information and Leerink Partners LLC Research
Revenue in \$MM.

INVESTMENT THESIS

We rate ARDX with an Outperform rating and a \$36 price target (from \$32) in 12 months. ARDX is partnered with AZN on its lead program, tenapanor, a small molecule inhibitor of NHE3, which is one of the main transporters of sodium in the GI tract. With emerging data suggesting maintenance of a low sodium diet can provide therapeutic benefit in kidney disease patients, tenapanor holds the promise of addressing an important unmet need in the multi-billion dollar kidney disease market, as well as potential utility in constipation predominant irritable bowel syndrome (IBS). While AZN owns WW commercialization rights on tenapanor, ARDX may receive up to ~\$225m in development milestones and tiered royalties (in “teens”). We are bullish ahead of Phase II data for tenapanor, which MEDACorp Key Opinion Leaders (KOL) believe will help establish tenapanor’s profile as a blockbuster drug, based on potential for: (1) efficacy similar to marketed phosphate binders; (2) reduction in sodium absorption; & (3) reduce the pill burden associated with current meds. Longer term, ARDX plans to invest in its proprietary drug discovery platform and develop wholly owned assets.

Changes to our Model

EPS & Total Sales Forecasts (2013-19E) (\$MM, except per share data)

Total Sales Forecasts 2014-19E							
	2013	2014E	2015E	2016E	2017E	2018E	2019E
New	29	33	50	60	60	94	33
Old	29	33	50	60	60	91	23
Difference	-	-	-	-	-	3.39	10.65
Total EPS Forecasts 2014-19E							
	2013	2014E	2015E	2016E	2017E	2018E	2019E
New	(\$0.65)	(0.11)	(0.02)	0.40	0.42	1.54	0.62
Old	(0.65)	(0.11)	(0.02)	0.40	0.42	1.42	0.29
Difference	-	-	-	-	-	0.11	0.33

Source: Leerink Partners, Company Information

Tenapanor Phase 2b Data

Tenapanor Phase 2b Data Comparison Chart

	ARDX	IRWD	
	tenapanor	Linzess (linaclotide)	
	Phase 2b (IBS-C)	Phase 3, Study 1 (IBS-C)	Phase 3, Study 2 (IBS-C)
total # of subjects	371 (n=93 on 50mg)	804 (n=401 on 290mcg)	800 (n=405 on 290mcg)
% CSBM responders	60.7% vs. 33.7% for PBO (p<0.001)	48.6% vs. 29.6% for PBO (p<0.0001)	47.6% vs. 22.6% for PBO (p<0.0001)
% abdominal pain responders	n/a	50.1% vs. 37.5% for PBO (p<0.0003)	48.9% vs. 34.5% for PBO (p<0.0001)
% combined responder	50% vs. 23.6% for PBO (p<0.001)	33.6% vs. 21.0% for PBO (p<0.0001)	33.7% vs. 13.9% for PBO (p<0.0001)
Adverse events			
Diarrhea	11.2% vs. 0% for PBO	19.7% vs. 2.5% for PBO	19.5% vs. 3.5% for PBO
UTI	5.6% vs. 4.4% for PBO	n/a	n/a
Discontinuation rate	4.5% vs. 3.3% for PBO	10.2% vs. 2.5% for PBO	7.9% vs. 2.8% for PBO

Source: Company Press releases

VALUATION

Our ~\$36/shr price target (from \$32) on ARDX shares is based on our risk-adjusted, sum-of-the-parts DCF analysis through 2025E. We used a 15% discount rate, and we estimate tenapanor will achieve market shares of 30%, 40%, and 5% in the ESRD-Pi, sodium, and fluid overload chronic kidney disease (CKD) and IBS-C indications, respectively.

RISKS TO VALUATION

Risks include (1) tenapanor drives our valuation and clinical/regulatory failure would significantly impact our valuation; (2) AZN may not commit to funding all the currently envisioned indications, depending on strength of future data.

ARDX Sum of Parts (SOTP) DCF Valuation

In MM, except per share data

Shares Outstanding	17.9			
Net cash	73			
Discount Rate	15%			
ARDX	Valuation	Per shr	% of value	
AZN p/s (risk adj royalties + m'stones)	561	\$ 31	87%	
SNY p/s (milestones)	26	\$ 1	4%	
Cash (less near-term burn)	61	\$ 3	9%	
Total	648	\$ 36	100%	
Current market price	\$ 17.75			
Implied upside/downside	104%			

Source: Company info., Leerink Research est.

AZN Partnership - \$MM, except per share	Base
Tenapanor ESRD Pi peak share	30%
Tenapanor launch price/day	\$15
2025E tenap ESRD global sales	860
ESRD % POS	35%
Risk adj NPV tenapanor ESRD	102
Tenapanor CKD peak share	40%
Tenapanor launch price/day	\$15
2025E tenap CKD global sales	3005
CKD % POS	25%
Risk adj NPV tenapanor CKD	221
Tenapanor IBS peak share	5%
Tenapanor launch price/day	\$15
2025E tenap IBS US sales	950
IBS % POS	60%
Risk adj NPV tenapanor IBS	186
Risk Adj AZN Milestones	
Ph 2 b data, \$20m, 50% POS	10
start Ph 3 ESRD, \$50m, 50% POS	25
Est. approval milestone, \$100m, 35% POS	35
NDA filing, \$50m	18
All other, \$2.5m	1
Discounted, risk adj AZN milestones	52
Total NPV of AZN partnership	561
Total NPV of SNY p/s milestones	26

Source: Company info., Leerink Research est.

ARDX Annual P&L Summary (Adj. Basis)

ARDX Annual Product Summary

(figures in \$m, except per share data)

	2012A	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	19-23E
Tenapanor ESRD	-	-	-	-	-	-	4	8	17	29	36	37	24%
Tenapanor CKD	-	-	-	-	-	-	-	10	27	51	70	90	37%
Tenapanor IBS	-	-	-	-	-	-	5	15	25	46	62	65	23%
Total tenapanor royalties	-	-	-	-	-	-	9	33	69	126	168	191	28%
Licensing revenue	3	8	15	5	-	-	-	-	-	-	-	-	na
Collaborative development revenue	2	21	18	35	35	35	35	-	-	-	-	-	na
AZN milestones	-	-	-	10	25	25	50	-	-	-	-	-	na
Total Revenue (MM)	5	29	33	50	60	60	94	33	69	126	168	191	28%
% y/y growth	na	na	na	na	na	nm	57%	-65%	107%	83%	33%	14%	
COGS	-	-	-	-	-	-	-	-	-	-	-	-	na
% of sales	0	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	na
Gross Income	5.4	28.9	33.0	50.0	60	60	94	33	69	126	168	191	28%
% of net sales	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	
Discovery research	6.3	7.7	9.4	9.5	9.5	8.0	8.0	8.0	8.0	8.0	8.0	8.0	0%
Clinical development expense - tenapanor	2.0	-	-	-	-	-	-	-	-	-	-	-	na
AZN collaboration dev expense	1.9	20.3	18.0	35	35	35	35	-	-	-	-	-	na
Total R&D	10.2	28.1	27.4	44.5	44.5	43.0	43.0	8.0	8.0	8.0	8.0	8.0	0%
% of sales	188%	nm	83%	89%	74%	72%	46%	24%	12%	6%	5%	4%	
G&A	4.0	3.7	5.2	7.0	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	0%
% of sales	75%	13%	16%	14%	12%	12%	8%	23%	11%	6%	4%	4%	
Selling & Marketing	-	-	-	-	-	-	-	-	-	-	-	-	na
Total operating expenses	14.2	31.8	32.6	51.5	52.0	50.5	50.5	15.5	15.5	15.5	15.5	15.5	0%
Operating (loss)/gain	(8.8)	(2.9)	0.4	(1.5)	8.0	9.5	43.8	17.7	53.4	110.4	152.4	175.5	39%
% of sales	-163%	nm	1%	-3%	13%	16%	46%	53%	77%	88%	91%	92%	
Net financial expense	(1.0)	(3.6)	(2.6)	1.0	1.3	1.5	2.1	2.3	2.6	3.4	4.3	5.3	13%
Pre-tax Income	(9.8)	(6.4)	(2.2)	(0.5)	9.3	11.0	45.9	20.0	56.0	113.8	156.7	180.8	37%
% Pre-tax Margin	nm	nm	nm	nm	nm	18.4%	48.7%	60.2%	81.3%	90.4%	93.3%	94.7%	
Taxes (benefit)	-	0.1	-	-	-	-	4.6	3.0	11.2	28.4	47.0	63.3	55%
% Tax rate	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	10.0%	15.0%	20.0%	25.0%	30.0%	35.0%	
Net Income/(loss) (MM)	(10)	(7)	(2.2)	(1)	9	11	41	17	45	85	110	118	32%
% of net sales	NM	NM	NM	nm	15.6%	18.4%	43.8%	51.1%	65.1%	67.8%	65.3%	61.5%	
Diluted EPS	(\$1.26)	(\$0.65)	(\$0.11)	(\$0.02)	\$0.40	\$0.42	\$1.54	\$0.62	\$1.60	\$2.99	\$3.77	\$3.96	30%
Y/Y	NM	NM	NM	NM	NM	5%	267%	-60%	159%	87%	26%	5%	
Weighted Avg Diluted Shares (MM)	7.8	10.2	19.9	22.9	23.3	26.4	26.9	27.4	28.0	28.6	29.1	29.7	1%
% growth	NM	31%	96%	15%	2%	13%	2%	2%	2%	2%	2%	2%	

Source: Leerink Partners, LLC estimates and company reports

Disclosures Appendix

Analyst Certification

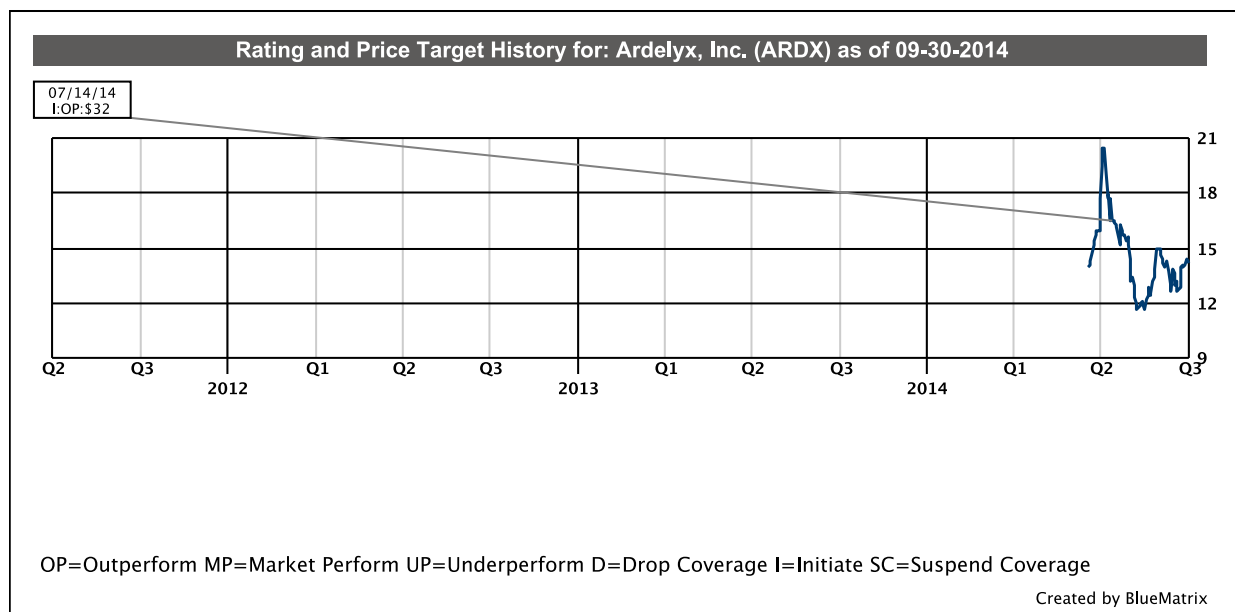
I, Jason M. Gerberry, JD, certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

Valuation

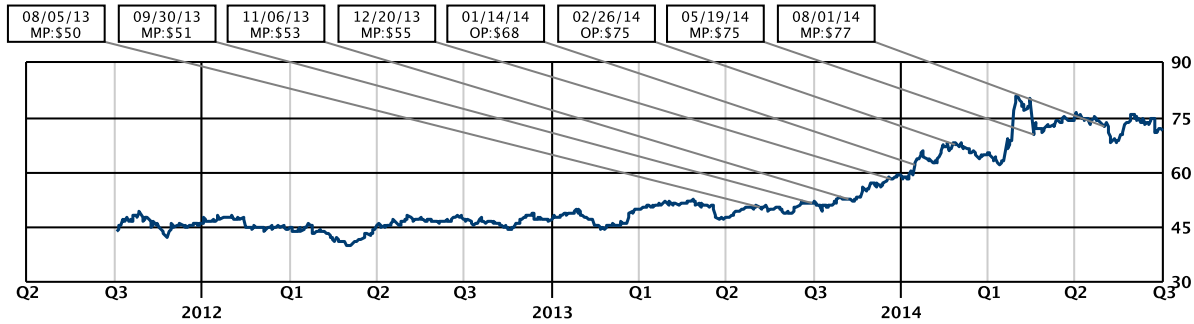
Our ~\$36/shr price target on ARDX shares is based on our risk-adjusted, sum-of-the-parts DCF analysis through 2025E. We used a 15% discount rate, and we estimate tenapanor will achieve market shares of 30%, 40%, and 5% in the ESRD-Pi, sodium, and fluid overload chronic kidney disease (CKD) and IBS-C indications, respectively.

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Rating and Price Target History for: AstraZeneca PLC (AZN) as of 09-30-2014

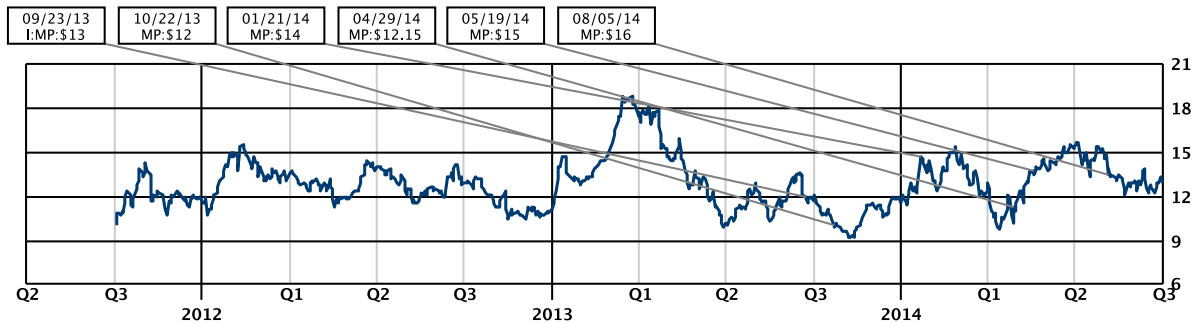


Leerink Swann initiated coverage of AZN with a Market Perform rating on Sept. 30, 2009. On June 11, 2013, Leerink Swann began a transition to specific price targets for the stocks under its coverage, replacing valuation ranges.

OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

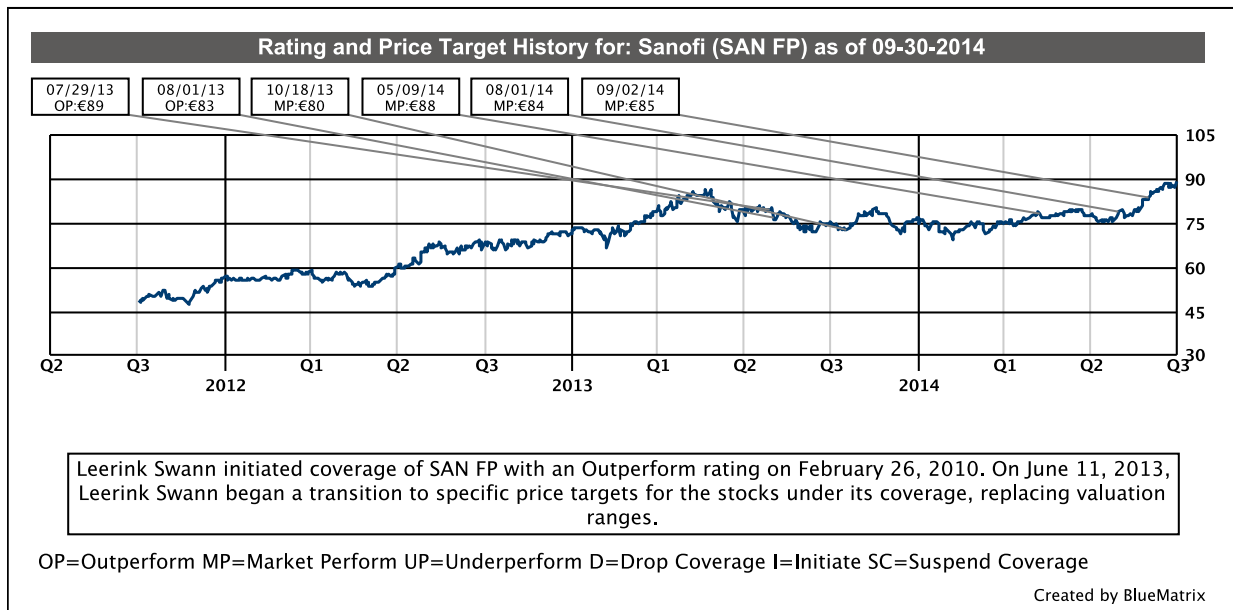
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Rating and Price Target History for: Ironwood Pharmaceuticals, Inc. (IRWD) as of 09-30-2014



OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

Created by BlueMatrix



Distribution of Ratings/Investment Banking Services (IB) as of 06/30/14				
Rating	Count	Percent	IB Serv./Past 12 Mos.	
			Count	Percent
BUY [OP]	138	69.00	50	36.20
HOLD [MP]	62	31.00	2	3.20
SELL [UP]	0	0.00	0	0.00

Explanation of Ratings

Outperform (Buy): We expect this stock to outperform its benchmark over the next 12 months.

Market Perform (Hold/Neutral): We expect this stock to perform in line with its benchmark over the next 12 months.

Underperform (Sell): We expect this stock to underperform its benchmark over the next 12 months. The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.

For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than \$2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over \$2 billion.

Important Disclosures

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Leerink Partners LLC is willing to sell to, or buy from, clients the common stock of AstraZeneca PLC and Sanofi on a principal basis.

Leerink Partners LLC has acted as the manager for a public offering of Ardelyx, Inc. in the past 12 months.

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