July 14, 2014

OUTPERFORM

Jason M. Gerberry, JD
(617) 918-4549
Jason.Gerberry@Leerink.com

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Reason for report:

INITIATION

ARDELYX, INC.

Initiate at OP; Tenapanor's Blockbuster Pot'l Drives Our $32 Price Target

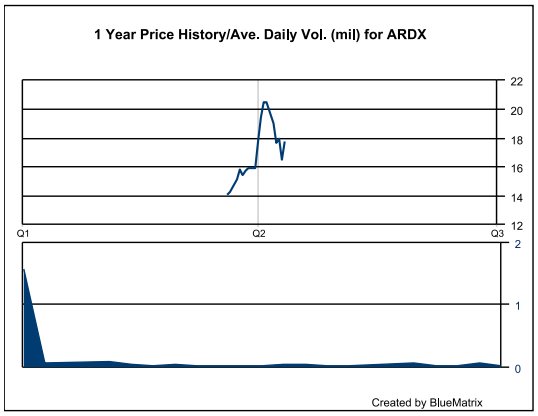
• **Bottom Line:** We are initiating coverage of ARDX with an Outperform rating and a $32 price target in 12 months. ARDX is partnered with AZN (MP) on its lead program, tenapanor, a small molecule inhibitor of NHE3, which is a transporter of sodium & phosphorous in the GI tract. With emerging data suggesting 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. 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 kidney disease 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) a reduction in the pill burden associated with current meds. Longer term, ARDX plans to invest in its proprietary drug discovery platform & develop wholly owned assets.

• **The commercial potential of ARDX's platform has been validated by both AZN and SNY (MP),** the former of which has agreed to fully fund the development of tenapanor, ARDX's lead product for kidney disease and IBS-C. In Phase I, tenapanor demonstrated a statistically significant increase in fecal sodium output, which has been linked to fluid overload that can cause lead to cardiovascular events in dialysis patients. To advance the ESRD program to Phase III, we believe ARDX and AZN are looking to see significant reductions in serum phosphorous & modest rates of diarrhea. Given the heavy pill burden associated with current standard of care phosphate binders (9 tablets), specialists view tenapanor's dosing profile as an important clinical advantage.

• **CKD and IBS indications offer potential to be major catalysts.** Tenapanor secondary indications include IBS and CKD (with comorbid diabetes), which have substantial end markets. In the US alone, there are ~2m CKD pts with stage 3 or 4 disease and comorbid diabetes representing a multi-billion dollar market. In addition to demonstrated ability to increase sodium output, recent studies demonstrate dietary restriction of sodium leads to a reduction of proteinuria and potentiates the efficacy of anti-hypertensive drugs in non-diabetic nephropathy pts. Interesting, Approximately 80% of our price target is derived from the AZN collaboration, with significant room for upside given each program is heavily risk adjusted (<35% POS).

• **Low burn rate + validated preclinical discovery engine a source of upside.** ARDX does have longer-term aspirations to take fully owned drugs to commercialization. With a low burn rate and pot'l non-dilutive cash flow from the AZN deal -- we believe ARDX's validated discovery engine has the potential to deliver upside over the next 1-2 years.

Key Stats:	**(NASDAQ:ARDX)**
S&P 600 Health Care Index:	**1,316.76**
Price:	**$17.75**
Price Target:	$32.00
Methodology:	Sum-of-the-parts DCF analysis
52 Week High:	$21.60
52 Week Low:	$14.05
Shares Outstanding (mil):	17.9
Market Capitalization (mil):	$317.7
Book Value/Share:	$0.00
Cash Per Share:	$4.08
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	5.0	5.5	5.0	24.0	(0.23)A	(0.20)	(0.15)	(0.15)	(0.72)	NM
2015E	--	--	--	--	50.0	--	--	--	--	(0.03)	NM
2016E	--	--	--	--	60.0	--	--	--	--	0.51	34.8x

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

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ARDX Initiation of Coverage Report

Jason Gerberry, JD
Director, Specialty/Generic Pharmaceuticals Analyst
(617) 918-4549
jason.gerberry@leerink.com

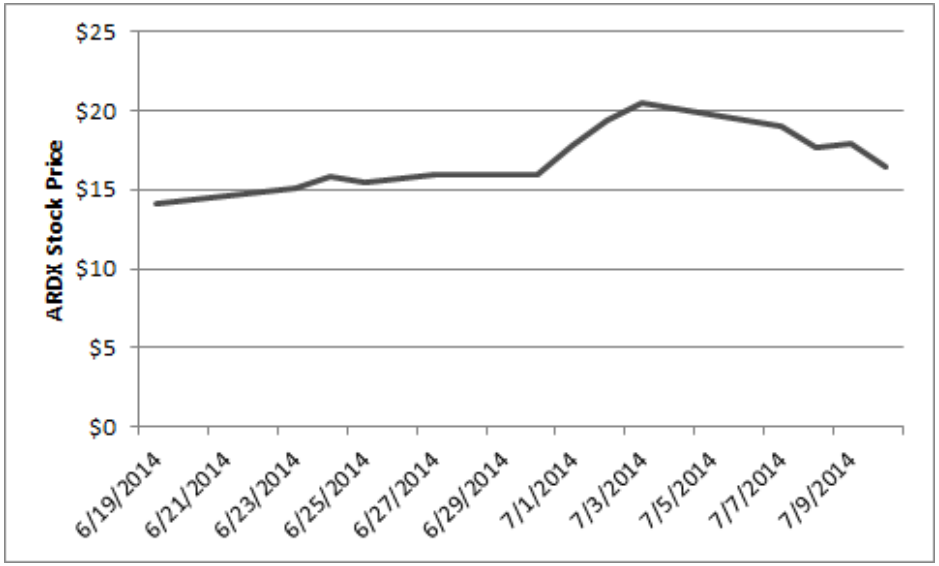
Ardelyx (ARDX): Outperform

Rating: Outperform

Current Price: $17.75

Leerink PT: $32.00

Market Cap: $318M



Source: FactSet

Leerink Estimates

LP Estimates	ARDX Revenue	GAAP EPS
2014	24	($0.72)
2015	50	($0.03)
2016	60	$0.51

Revenues in $MM.

Investment thesis: We are initiating coverage of ARDX with an Outperform rating and a $32 price target 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.

Valuation: Our ~$32/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.

Risks to Valuation: (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.

To Date, ARDX Has Outperformed the Market & Recent Biopharma IPOs

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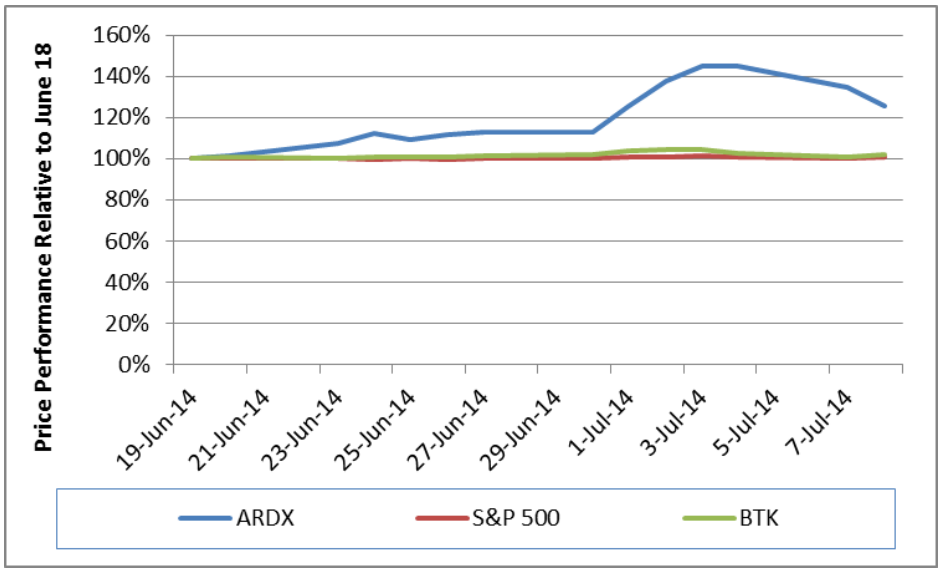
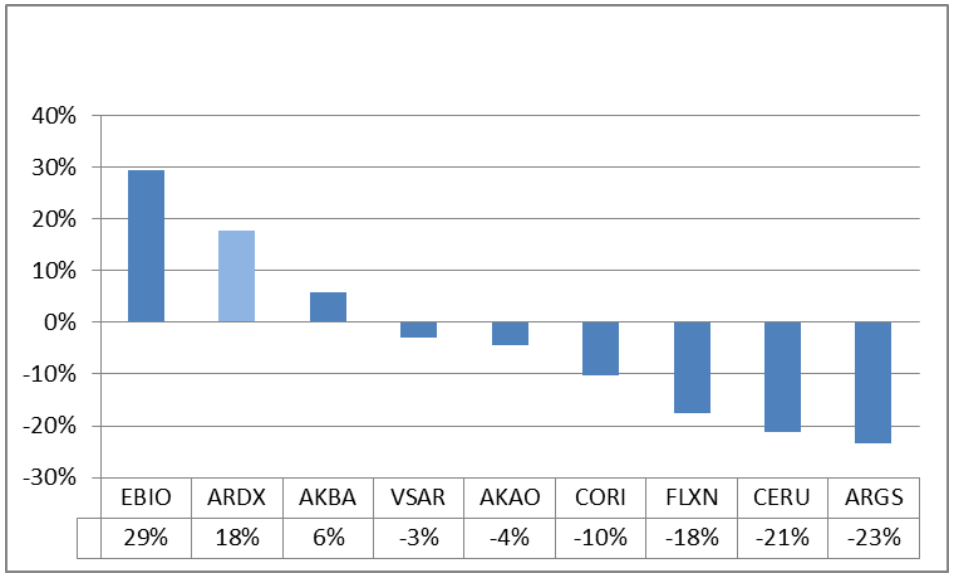
- On June 19th, shares of ARDX were listed on the NASDAQ Global Market . Pricing of 4.3m common shares IPO (initial public offering) was set at $14/shr. Since the IPO, ARDX shares have outpaced the market by ~25% and the biotech index by ~23%. ARDX 2014 relative performance to other biopharma IPOs has been favorable year-to-date.

ARDX stock performance post IPO



Source: FactSet

Performance Relative to Rest of 2014 IPO Class



Source: FactSet

ARDX Company Description

- **Company summary:** ARDX is a clinical-stage biopharmaceutical company that develops non-systemic, small molecule therapeutics that work exclusively in the GI tract to treat cardio-renal, GI, and metabolic diseases. ARDX's lead product candidate, tenapanor, has demonstrated an ability to reduce absorption of dietary sodium and phosphorous, both of which are key factors in progression of kidney disease. Tenapanor is partnered with AZN, which owns worldwide commercialization rights, in exchange for a royalty on net sales. Tenapanor is currently in Phase 2 for three indications: (1) end-stage renal disease – hyperphosphatemia; (2) late stage chronic kidney disease; (3) constipation predominant IBS.

- **History of ARDX:** ARDX was founded in 2007 as a corporation under the name Nteryx, Inc. The current CEO, Mike Raab, has served in his role since March 2009. ARDX entered into two major collaborations with large pharma partners: ARDX-AZN formed a collaboration for the worldwide development & commercialization of Tenapanor in 2012; and ARDX-SNY entered into an option and license agreement under which ARDX has granted SNY a WW license to conduct research utilizing its small molecule NaP2b inhibitors. ARDX has incurred operating losses of $9.8m and $6.6m in 2012 and 2013, respectively; the company currently depends on milestone payments from partners to offset its operating losses.

Knowledgeable Management Team

- Mike Raab (CEO since 2009)
  - Previously Mr. Raab was a partner at New Enterprise Associates (NEA), a venture capital firm specializing in healthcare investments. Prior to joining NEA, Mr. Raab spent 15 years in commercial and operating roles in the biotech and pharmaceutical industries. Notably, Mr. Raab was the Senior VP and General Manager of the Renal Division of Genzyme.

- Dominique Charmot (Co-founder and CSO since 2007)
  - Dr. Charmot started his career in 1982 at Rhone-Poulenc SA, a chemical company. In 2003, Dr. Charmot co-founded Ilypsa, a company developing polymeric drugs and worked there until the company was acquired by Amgen (MP).

- Mark Kaufman (CFO since May 2014)
  - Previously Mr. Kaufman served as ARDX's Chief Business Officer from 2011-14. Mr. Kaufman has 20 years of biopharma experience, most recently serving as CEO of Allostera, a preclinical company focused on autoimmune diseases.

Key Investment Issues

- **We expect ARDX shares to outperform the market over the next 12-months as:**
  - **Favorable risk/reward heading into readout of Phase II data**. At ARDX's current valuation, the Street is heavily risk adjusting the future cash streams associated with the tenapanor program. While tenapanor's current data sets are hypothesis-generating, we are highly encouraged to see consistent improvement in fecal sodium output coupled with studies demonstrating a low sodium diet is beneficial to kidney disease patients. Given the enormous size of the kidney disease markets & ARDX's ability to potentially collect royalties (max: high teens) plus a contractual provision to buy back as much as 1-3% of royalties depending on the quality of upcoming Phase 2 data, we view the risk/reward as highly favorable heading into the upcoming data read outs.
  - **CKD offers blockbuster potential in market with unmet needs.** The market for CKD stage 3/4 patients with comorbid diabetes is substantial with at least 2m US pts seeking pharmacotherapy and the unmet need remains high. KOLs believe emerging data may allow the FDA to lower the clinical hurdle for registration. Based on feedback from MEDACorp KOL specialists, tenapanor for treatment of CKD has the potential to become a blockbuster treatment given its: (1) ability to reduce sodium intake; & (2) data indicating low sodium diet, in line with guidance levels, helps potentiate the efficacy of antihypertensives.
  - **With a validated drug discovery platform, low cash burn + potentially non-dilutive financing next year, ARDX will look to advance more proprietary drugs into the clinic**. ARDX mgmt plans to develop and advance more therapeutics into the clinic and eventually become a commercial stage company. With several potential sources of non-dilutive financing in the way of partnership milestones + a validated drug discovery platform, we view ARDX as well positioned to evolve into a vertically integrated drug company.

- If all three tenapanor indications succeed, we forecast tenapanor could achieve 2025 global sales of ~$5B (to AZN); given the early stage nature of the tenapanor development program we risk adj sales estimates (ranging from 25% to 35% POS) in each indication and forecast risk adjusted royalties to ARDX of $140m. We believe the drug could be significantly larger in CKD if the data show a pristine safety profile and a clinically meaningful improvement in fecal sodium output. Currently, there is no sell-side consensus for ARDX sales.

Sum-of-Parts DCF Analysis Suggests a $32/shr Price Target for ARDX

Shares Outstanding	17.9				
Net cash	73				
Discount Rate	15%				
ARDX		**Valuation**		**Per shr**	**% of value**
AZN p/s (risk adj royalties + m'stones)		484	$	27	85%
SNY p/s (milestones)		26	$	1	4%
Cash (less near-term burn)		61	$	3	11%
Total		**570**	**$**	**32**	**100%**
Current market price	$ 17.75				
Implied upside/downside	80%				

Source: Company info., Leerink Research est.

Source: Leerink Research ests

The AZN collaboration is the primary driver of our sum-of-parts valuation

AZN Partnership	Base
Tenapanor ESRD Pi peak share	30%
Tenapanor launch price/day	$15
2025 tenap ESRD global sales	860
ESRD % POS	35%
Risk adj NPV tenapanor ESRD	**102**
Tenapanor CKD peak share	40%
Tenapanor launch price/day	$15
2025 tenap CKD global sales	3005
CKD % POS	25%
Risk adj NPV tenapanor CKD	**221**
Tenapanor IBS peak share	5%
Tenapanor launch price/day	$15
2025 tenap IBS US sales	950
IBS % POS	35%
Risk adj NPV tenapanor IBS	**109**
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	**484**
Total NPV of SNY p/s milestones	**26**

Source: Leerink Research ests

ARDX Pipeline & Upcoming Events

Program	Target	Partner	Indication	Current status	Next milestone	Timing
tenapanor	NHE3	AZN	ESRD - Phosphate	Ph. 2b	Ph. 2b data	1H'15
			IBS-C	Ph. 2b	top-line data	4Q'14
			Chronic fluid overload - ESRD	Ph. 1		
			Chronic fluid overload - CKD	Ph. 2a	Ph. 2a data	2H'15
undisclosed	NaP2b	SNY	ESRD - Phoshate	Pre-clinical		
	TGR5 agonists	none	diabetes	Pre-clinical		
			Irritable bowel disease	Pre-clinical		
RDX013	undisclosed	none	Hyperkalemia	Pre-clinical		
RDX020	DRA inhibitor	none	Fluid overload - CKD and CHF	Pre-clinical		

ESRD = end-stage renal disease
CKD = chronic kidney disease
IBS-C = constipation predominant irritable bowel syndrome
Source: ARDX S-1 statement

ARDX's key catalysts will be top-line Phase 2 data for lead drug tenapanor

Tenapanor for ESRD

Tenapanor Is Believed to Work Via Dual Blockade of Sodium & Phosphorous Absorption

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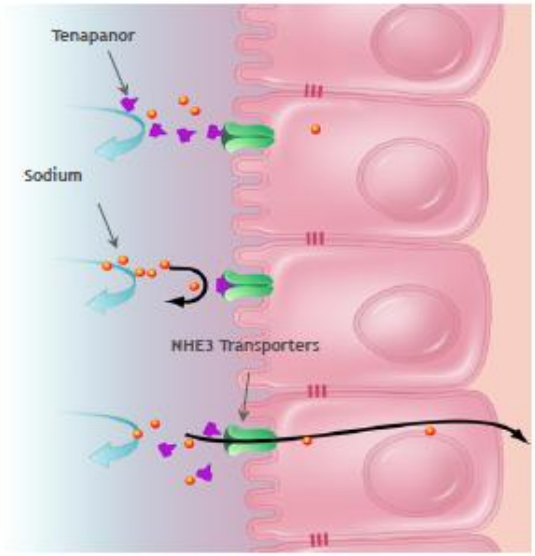
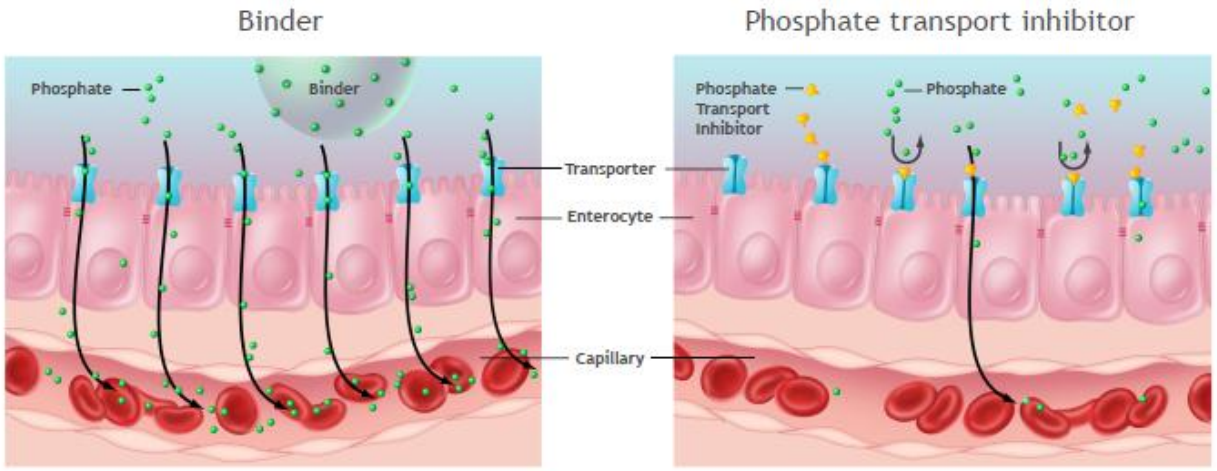
Sodium Diversion



Sodium Diversion



- **Intestinal absorption of dietary sodium and phosphorous are widely recognized as key factors in the progression of kidney disease.** Normal functioning kidneys remove extra phosphorous from the patient's blood, while subjects with kidney disease experience high phosphorous levels that cause damage to the body, including bone weakness (hyperparathyroidism) and dangerous vascular calcifications. Patients with kidney disease are recommended to be on a low sodium diet, since the kidneys cannot eliminate excess sodium and fluid from the body, which can lead to high blood pressure, further exacerbating damage to the kidneys, and other complications may include edema and/or heart failure.

Pathway: Tenapanor is believed to divert sodium away from systemic circulation emulating benefits of a low sodium diet; benefits of low sodium diet, which has poor compliance rates, include reduced blood pressure; theoretical benefit of low sodium diet may mitigate effects of sodium induced cardiac and renal damage.

Source: ARDX company presentation

So Far, Tenapanor Has Shown a Pretty Clean Safety Profile

- **Tenapanor is non-systemic**
  - Supportive animal studies: When radiolabeled & administered orally to rats, ARDX saw ~98% of the administered dose detected unchanged in the feces, indicating no substantial metabolism occurred.
  - Supportive human studies: When orally administered, tenapanor was detected in the blood in only 0.7% of more than 2000 collected serum samples; in those samples, drug levels were very low (<1.5ng/mL).

- **Clinical experience** – tenapanor has been administered to 765 subjects to date, including 291 healthy volunteers. Tenapanor has been dosed as high as 900mg (single dose) and for a period of 3 months (100mg/day).
  - Dose limiting side effects were due to exaggerated pharmacology of the drug, mainly related to gastroenterology symptoms.
  - All serious adverse events (AEs) thus far have been assessed as unrelated to tenapanor by study investigators.

Ongoing Phase 2 trials are looking at tenapanor doses as high as 60mg twice daily

Tenapanor (ESRD-Pi) Opportunity: Cheat Sheet

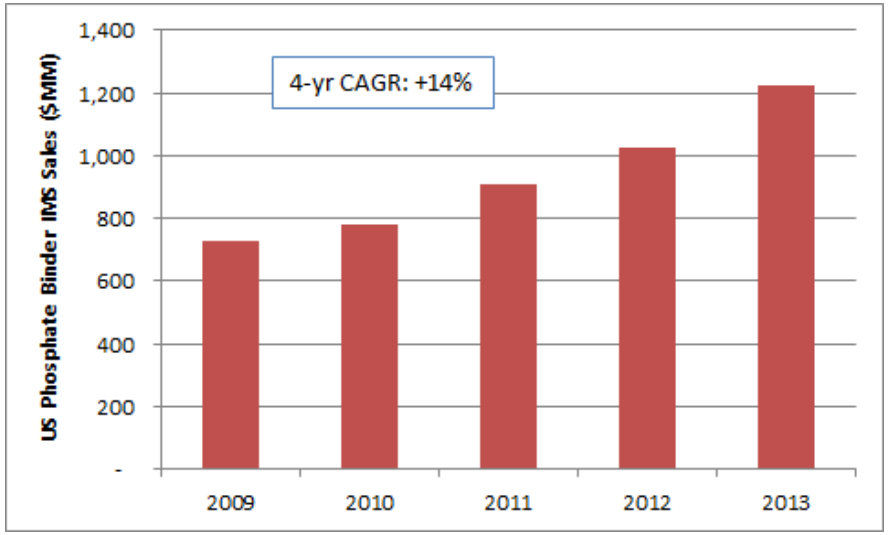
Background

- **Product description**: Tenapanor is a non-systemic small molecule inhibitor of NHE3, a sodium transporter present on the epithelia of the GI tract. Tenapanor is administered as a single tablet two times a day and has a lower pill burden than the currently marketed phosphate binders used for patients with ESRD-Pi.
- **Product history**: In several Ph. 1 studies, tenapanor has consistently demonstrated the ability to inhibit the absorption of dietary phosphorus. Based on these studies, ARDX partnered with AZN in 2012 and together have initiated a Ph. 2b trial to evaluate tenapanor in patients with ESRD-Pi. We expect top-line results of the Ph. 2b trial in 1H15.
- **ESRD-Pi market:** The lead indication for tenapanor is for the treatment of hyperphosphatemia in ESRD patients in the US. Approximately ~300K dialysis patients in the US are taking phosphate binders and we expect this population to increase due to: (1) increase in obesity/diabetes – two causes of ESRD; (2) aging population. The US market in 2013 for phosphate binders was approximately ~$1 billion (net sales). There are significant unmet needs in this market. Current marketed products have many unwanted side effects such as: (1) GI issues; (2) hypercalcemia leading to vascular calcification; (3) pill burden – patients are required to take ~9-10 phosphate binders a day.
- **Intellectual property**: At present, Ardelyx has an issued patent (U.S. Patent No. 8,541,448) on tenapanor covering the composition of matter. The issued US patent is currently predicted to expire in 2029, and two additional pending US patent applications cover methods of using tenapanor. ARDX has patent applications in most major markets which would also expire in 2029.
- **Development stage label expansion opportunities**: ARDX is exploring additional indications for tenapanor including chronic kidney disease and IBS-C.

How Tenapanor Works

- **Description of mechanism**: Tenapanor acts as an inhibitor of the sodium-proton exchanger (NHE3), which is a transporter of sodium in the GI tract. It is orally administered, non-systemic which selectively inhibits sodium uptake in the intestines limiting the amount absorbed from food, thereby reducing the level of sodium in the body. This drug's ability to block sodium & phosphorous absorption may make it useful in the treatment of chronic kidney disease which is exacerbated by excess sodium in the diet.

US Phosphate Binder market (IMS Sales)



Source: IMS

Background on ESRD-Pi

- ESRD is the final stage of chronic kidney disease (CKD). When the patient progresses to ESRD, hyperphosphatemia has been shown to increase the risk of morbidity and mortality in those patients.
  - **Symptoms:** ESRD-Pi is a serious condition and without treatment, patient outcomes are poor. Uncontrolled hyperphosphatemia leads to hyperparathyroidism, severe vascular calcifications, and increased vascular mortality in patients with ESRD.
  - **Goals of pharmacotherapy:** The overall goal of ESRD treatment is to reduce the accumulation of toxins in the blood once the kidneys have failed. To do this, patients will begin hemodialysis and/or peritoneal dialysis at least three times a week for up to five hours a session. Most toxins are removed during this process, but phosphorus is not and requires phosphate binding agents to be used in combination to remove the accumulated phosphorus from the bloodstream. Physicians will also put patients on dietary restrictions to limit dietary phosphate and sodium, but adherence to such strict diet regimens is low among patients.
  - **Most common outcome indicators:** Physicians are able to measure the amount of phosphorus through: (1) bloods tests on serum, normal range = 2.4-4.1mg/dL. Any result >5.0mg/dL is considered hypophosphatemia and toxic to patients, although MEDACorp specialists we spoke with viewed 6.0 mg/dL as the clinically relevant cutoff. (2) Urinary and fecal phosphorus can also be measured.

Comparison of Therapeutic Approaches

Current Treatment Options					
Drug	**Company**	**Drug Class**	**Dosing**	**Pros**	**Cons**
Renvela (sevelamer carbonate)	SNY	Calcium free/metal-free binder	3tabs/ 3x daily	• Reformulated Renagel to reduce incidence of acidosis; also available in powder form	• GI side effects • Pill burden
Renagel (sevelamer HCL)	SNY	Calcium free/metal-free binder	4tabs/3x daily	• Does not increase aluminum/calcium load	• GI side effects; linked to worsening of metabolic acidosis • Pill burden
Velphoro	FMS	Calcium free/iron based binder	3x/day	• Chew only pills	• Mild GI side effects
Fosrenol (lanthanum carbonate)	SHPG	Calcium free/metal-free binder	2tabs/ 3x daily	• Can be crushed and chewed if needed	• In 6 mo ext. study, 23% of patients discontinued because of AEs • Physician concerns around long-term toxicity from metal absorption
Phoslyra (calcium acetate)	FMS	Calcium based binder	10-20ml/ 3x daily	• Only approved liquid binder	• GI issues, hypercalcemia, long-term vascular calcification

Source: Product package Inserts

Numerous Follow-On Phosphate Binders in the Development Pipeline

Review of ESRD/Hyperphosphatemia Late Stage Pipeline

Drug (Company)	Drug Class	Stage of Development	Comments
Zerenex (Keryx Biopharmaceuticals)	Phosphate binder	Phase 3	Keryx completed a US based Ph.3 program conducted pursuant to a SPA agreement with the FDA; PDUFA date: Sept. 7th, 2014.
SBR759 (NVS)	Phosphate binder	Phase 3	SBR759 is a polynuclear iron (III) starch/saccharose complex that binds selectively to phosphate irons through chelation. It was acquired from SeBo GmbH.
Alpharen (Opko Health)	Phosphate binder	Phase 3	Currently in Ph. 3 in the US and EU. Available data have shown similar results to currently marketed products w/o metal accumulation & ~40% reduction in pill burden.
PT20 (Shield Therapeutics)	Phosphate binder	Phase 2	Pivotal trials of PT20 are expected to commence during 2014.
RenaZorb (Spectrum Pharma)	Phosphate binder	Phase 2	RenaZorb binds to phosphates and forms an insoluble lanthanum phosphate complex which is expected to reduce serum phosphate levels in ESRD patients.

Source: BioMedTracker

The US ESRD-Pi Market Is an Attractive Commercial Opportunity

- **The US market for ESRD-Pi drugs is measured by:** (1) the ~300K dialysis pts who get a phosphate binder; (2) commercial market – ARDX comments in its S-1 that worldwide phosphate binder sales were ~$1.5B in 2011 and trending to $2.3B by 2015. According to IMS – US gross sales for the phosphate binders was $1.2B in 2013, and we est net sales are likely closer to $1.0-1.1B and ~30% of phosphate binder use is off-label in CKD pts. Over 700,000 patients in the US, EU, and Japan on hemodialysis are receiving phosphate binders with about half these patients in the US. This patient population will continue to grow due to: (1) increased prevalence in obesity/diabetes, a leading cause of CKD/ESRD; (2) growing elderly population.

- **Pill burden is a major factor for patients**, the number of phosphate pills taken by a patient averages 9 a day
  - As most ESRD patients are also taking medications for diabetes and hypertension, a patient's total pill burden could reach 10-14 pills a day
  - Non-compliance has a detrimental impact on patients and has been associated with an increased risk of mortality

- **Tenapanor pricing expected to be ~$2-$3K/annually per patient.** We estimate tenapanor being priced on par with phosphate binders, on a 2018 inflation adj basis $15/day. Medicare bundling for ESRD treatments does not include oral-only therapies (such as phosphate binders), and a recently passed bill ensures that nephrologists and dialysis care providers will be able to continue billing (under Part D) for the drugs through 2024.

- **Upcoming trial data**: According to MEDACorp physician specialists, in order for tenapanor to gain traction in the ESRD market the drug will need to: (1) maintain serum phosphorous on par with existing phosphate binders; (2) show improvement on weight gain between dialysis; (3) increase fecal sodium output somewhere in the 10-20% range; (4) show above benefits with lower pill count regimen and no major safety issues, e.g., specialists don't want to see excessive rates of diarrhea, volume depleted pts, and electrolyte imbalance.

The ESRD Market for Phosphate Binders Limited by Niche Market Size + Limited Compliance

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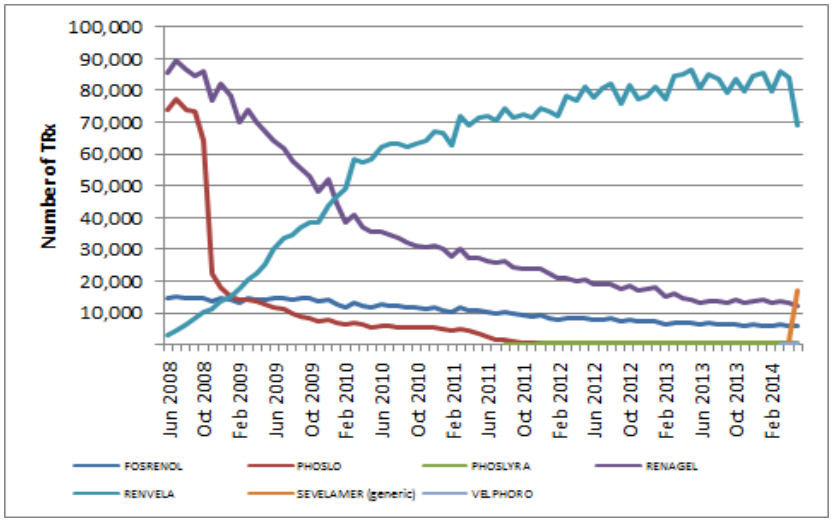
Background

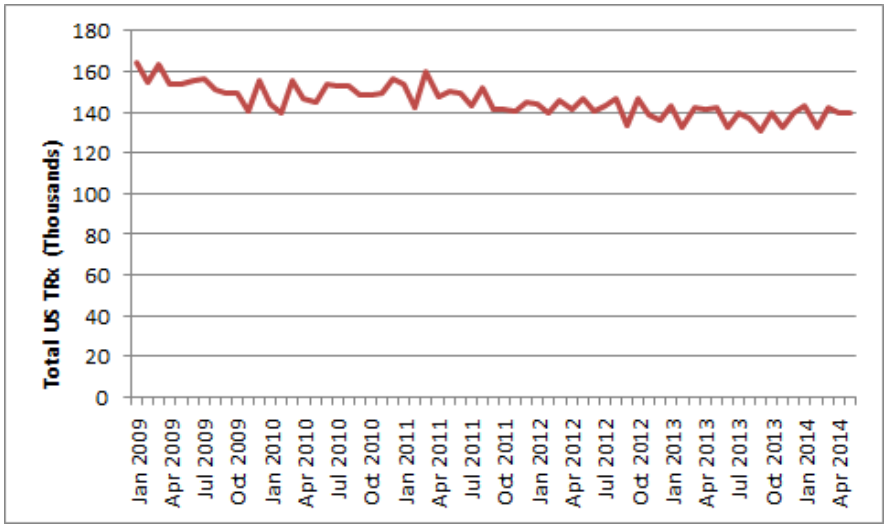
- **Market Size**: We est the WW phosphate binder market to be approx. ~$2B, with ~$1B sales occurring in the US. In the US, phosphate binders are approved for treatment of kidney disease in dialysis pts. Currently there are ~400k patients on dialysis in the US and an est ~300k of these patients require phosphate binders.
- **Non-compliance a major issue:** Due to the pill burden and the side effects associated with current treatments, patients taking phosphate binders discontinue treatment frequently. Physician specialists have indicated that approx. ~50% of patients are non-compliant with their phosphate binder prescriptions.
- **Current Trends in TRx:** The overall trend in TRx for phosphate binders in the US is relatively stable as patients need these drugs to survive. Renvela, the market leader, recently has gone generic. We do not see this as a threat to tenapanor as the generic will continue to suffer from the same shortcomings as the branded drug.

Market Share of Phosphate Binders



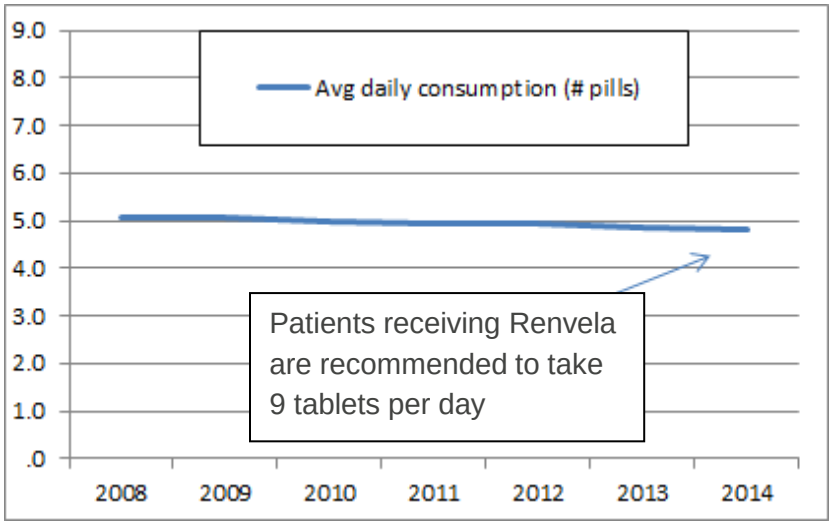
Source: IMS

Phosphate Binder: Total Prescription Volume



Source: IMS

Compliance is Limitation with Renvela



Source: Leerink estimates

Tenapanor for Treatment of ESRD-Pi

- Based on reported preclinical and clinical data, tenapanor may offer the following benefits to pts with kidney disease:
  - Lower pill burden
  - Emulates a low sodium diet
  - Reduces serum phosphate
  - Very safe due to the drug's non-systemic nature

- **Summary of reported clinical data:** In ESRD, the most advanced study was a Phase 2a exploratory study in ESRD patients (n=88) on hemodialysis designed to compare the effect of tenapanor vs. placebo on reduction of interdialytic weight gain (IDWG) in pts with ESRD. Important data from the study included tenapanor pts showed a benefit: (1) in increased sodium stool excretion; (2) a decrease in serum phosphate (trend), but no effect on IDWG. It's important to note the study was not designed to show phosphorous effects as most pts did not have phosphorous levels above 6.0 mg/dL and they were taking phosphate binders during the study. The ongoing Phase 2b (n=140-150) will assess:

  - **Primary endpoint will be change in serum phosphate –** patients enrolled in the study will have ESRD, with hypophosphatemia while on hemodialysis.

  - **IDWG –** unlikely to carry much weight with physician specialists as it's viewed as a challenging endpoint to measure, which is exacerbated by the fact that pts are highly variable

  - **Determination of Phase 3 dose –** in the ongoing Phase 2b study 5 dose strengths (3 & 30mg QD; 1, 3, 10, 30mg BID); the study will include 20 patients per dose group

MEDACorp Physician Specialists' Comments on Tenapanor for ESRD

- **Target product profile:**
  - **Base case:** (1) effectively limit serum phosphorous in the 0.5-1.0 mg/dL range; (2) establish efficacy in pivotal trials with a 2-4 tablet/day regimen; (3) increase stool sodium ~10%; (4) safety is important – specialists don't want to see excessive diarrhea & electrolyte imbalance
  - **Bull case:** In addition to the above base case profile, the specialists would like to see a greater increase in stool sodium in the 10-20% range, which would make tenapanor more of a first line therapy option

- **Unmet need in ESRD market:** (1) most dialysis pts are on phosphate binder but compliance rates are poor, which specialists attribute to pill burden that pts dislike; (2) the efficacy of phosphate binders was viewed by the specialists as "adequate at best" and not as good as clinical trial data would suggest, partly due to compliance issues; (3) specialists indicated it would be very desirable to have a drug that limits sodium intake in the majority of their pts

- **Thoughts on tenapanor preclinical/clinical data & mechanism of action:** (1) specialists like the idea of a dual sodium/phosphate blocker, but specialist excitement is really around the potential impact on sodium diversion**;** (2) specialists were split on the relevance of tenapanor's inability to show an improvement in IDWG, with the bear view that tenapanor may not have an incredibly potent effect limiting salt intake while the more optimistic view was that IDWG is a very difficult endpoint to measure & the missed endpt may not be relevant; (3) elimination of fecal sodium in Phase I is encouraging, but the specialists want to see this signal in a larger study to ensure there is no excessive diarrhea or other side effects typically seen with drugs in this category

Source: MEDACorp Physician KOL calls

Tenapanor ESRD Market Model

ESRD, hyperphosphatemia	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
ESRD pts, US	705	706	708	709	711	712	714	715	716	718	719	721	722
% growth	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%
%	55%	55%	55%	55%	55%	55%	55%	55%	55%	55%	55%	55%	55%
ESRD, hemodialysis	388	389	389	390	391	392	392	393	394	395	396	396	397
% share													
phosphate binders	65%	63%	60%	58%	57%	57%	57%	57%	57%	57%	57%	57%	57%
tenapanor	6%	12%	18%	24%	30%	30%	30%	30%	30%	30%	30%	30%	30%
Other (including no treatment)	29%	25%	22%	18%	13%	13%	13%	13%	13%	13%	13%	13%	13%
% total share	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Total treated patients (000's)													
Phosphate binders	252	245	234	226	223	223	224	224	225	225	225	226	226
Tenapanor	23	47	70	94	117	117	118	118	118	118	119	119	119
Pricing assumptions:													
Avg days of therapy	160	160	160	160	160	160	160	160	160	160	160	160	160
Cost per day	15	16	17	17	18	18	19	19	20	20	21	22	22
Avg annual cost	2400	2520	2646	2725	2807	2891	2978	3067	3159	3254	3352	3452	3556
Tenapanor ESRD, Pi US Sales	56	117	185	255	329	340	351	362	373	385	398	411	424
% POS	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
Tenapanor ESRD, Pi US Sales (risk adj)	**20**	**41**	**65**	**89**	**115**	**119**	**123**	**127**	**131**	**135**	**139**	**144**	**148**
Ex-US sales (risk adj)	35	70	105	140	175	175	175	175	175	175	175	175	175
% royalty to Ardelyx (tiered, double digit)	8%	8%	10%	13%	13%	13%	13%	13%	15%	15%	15%	15%	15%
Total ESRD royalties (risk adj)	**4**	**8**	**17**	**29**	**36**	**37**	**37**	**38**	**46**	**46**	**47**	**48**	**48**

Source: Leerink Research estimates

Tenapanor Clinical Trial Summary

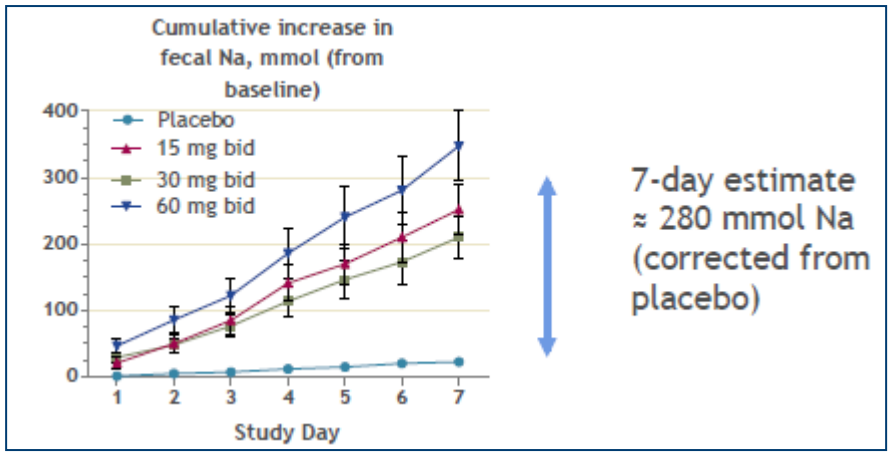
Trial	Phase	Subjects (Active/ Placebo)	Indication	Objectives	Summary of Results
RDX5791-201 (Ardelyx)	Phase 2a	186 (139/47)	IBS-C; Completed	• Safety, tolerability, and pharmacodynamics of tenapanor for the treatment of constipation predominant irritable bowel syndrome (IBS-C) • Dosing: 10mg, 30mg, 100mg QD	• Tenapanor was generally safe and well tolerated when administered once a day for 4 weeks at doses of 10 mg, 30mg, and 100 mg; the results of this study provide preliminary evidence of the ability of tenapanor at doses of 30 mg and 100 mg to alleviate symptoms associated with IBS-C.
D5610C00001 (Ardelyx)	Phase 2a	140 (70/70)	CKD – Na & Fluid; Ongoing	• Safety, tolerability, and pharmacodynamics of tenapanor in CKD patients with T2DM and albuminuria • Dosing: 5mg, 15mg, 30mg, 60mg BID titration	• Pre-specified primary analysis: To compare the effect of tenapanor versus placebo on the changes in urine albumin-to-creatinine ratio (UACR) from Baseline to week 12
D5611C00001 (Ardelyx)	Phase 2a	88 (45/43)	ESRD-Fluid; Completed	• Safety, tolerability, and pharmacodynamics of tenapanor in ESRD-HD patients with elevated interdialytic weight gain (IDWG) • Dosing: 5mg, 15mg, 30mg, 60mg BID titration	• Tenapanor was generally safe and well tolerated when administered for 4 weeks at doses between 5 and 45 mg BID; no effect on IDWG; increase in stool sodium excretion; decrease in serum phosphate; minimal to no systemic exposure
D5613C00001 (AstraZeneca)	Phase 2b	140 (120/20)	ESRD-Pi; Ongoing	• Efficacy and safety of tenapanor for the treatment of hyperphosphatemia in ESRD-HD patients; determination of Phase 3 dose(s) • 3mg, 30mg QD; 1mg, 3mg, 10mg, 30mg BID	• Pre-specified primary analysis: The change in serum phosphate levels from the end of wash out (pre-randomization value) to end of treatment
D5612C00001 (Ardelyx)	Phase 2b	360 expected (270/90); 371 enrolled	IBS-C Ongoing; enrollment completed	• Efficacy and safety of tenapanor for the treatment of constipation predominant irritable bowel syndrome (IBS-C); determination of Phase 3 dose(s) • Dosing 5mg, 20mg, 50mg BID	• Pre-specified primary analysis: Percent CSBM responders (weekly responders for 6/12 weeks; ≥ 1 CSBM from baseline) vs. placebo

Source: ARDX company presentation

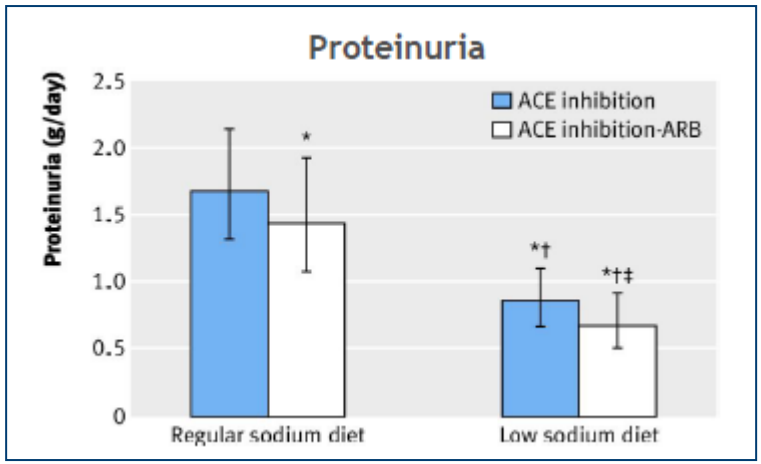
Tenapanor for Chronic Kidney Disease

Rationale for Using Tenapanor in CKD

Coupled with clinical data showing tenapanor increases fecal sodium output in healthy volunteers, recent studies (non-diabetic nephropathy pts) showing low sodium potentiates the efficacy of anti-hypertensive medications was a catalyst for CKD development



Source: ARDX company presentation



Source: ARDX company presentation

Background on Sodium and Fluid Overload in CKD

- Tenapanor is also being evaluated in earlier stage kidney disease patients, specifically CKD (chronic kidney disease) stage III and IV patients. In those patients, the kidneys are less efficient at blood filtration and sodium elimination resulting in sodium overload. This occurs frequently in patients with CKD and correlates with the rapid decline in kidney function.
  - **Symptoms:** Sodium & fluid overload can lead to serious issues such as: (1) high blood pressure, (2) worsening in kidney function, (3) heart disease, and (4) edema/dyspnea. All these issues ultimately lead to poorer survival and increased mortality.
  - **Goals of pharmacotherapy:** While reducing the amount of sodium is the main goal, this has been very difficult for patients and physicians. Patients are generally put on a restrictive diet which has shown to have high non-compliance rates. Physician specialists noted the use of diuretics to inhibit sodium uptake in CKD patients, but as kidney function declines they become less effective.
  - **Most common outcome indicators:** The most common indicators are the measurement of a patient's blood pressure and albuminuria. These two measures are key indicators that kidney function is improving/worsening.

MEDACorp Physician Specialists' Comments on Tenapanor for CKD Stage III/IV

LEERINK

- **Target product profile:** The specialists we spoke with generally believe that if tenapanor shows a benefit on kidney function, that would be sufficient to gain significant usage in CKD, while any longer-term data showing a benefit on hard CV outcomes measures would clearly be a homerun for the drug commercially

- **Unmet need:** CKD indication was viewed as having the biggest unmet need relative to the disease states being targeted by tenapanor. Specialists were particularly excited about tenapanor's theoretical promise to reduce sodium absorption and lessen the pts' dietary sodium restrictions

- **Tenapanor usage would become widespread if target product profile gets validated in clinical study.**
  - The specialists indicated a 1-2 year pivotal trial showing a 30% change in creatinine would be a sufficient for registration purposes and convince specialists that the drug benefits these pts, as long as there is a Phase 4 commitment showing preservation of kidney function and/or some hard outcomes measurements
  - **Upcoming Phase 2a wasn't viewed as a major de-risking event:** The specialists generally believe the UACR endpoint is the only short endpoint to gauge whether the drug has activity, but by itself (and absent data showing improvement in kidney function) the specialists believe the Phase 2a data won't significantly derisk tenapanor in CKD. Said differently, albuminuria is not an approvable endpoint but does provide an early signal of drug activity
  - **Risks** – some specialists raise the concern that changes in blood pressure could lead to compensatory mechanisms negating benefit of the drug over time & want longer-term safety data

Source: MEDACorp Physician KOL calls

Tenapanor for Treatment of CKD Stage III/IV

- Based on reported preclinical and clinical data, tenapanor may offer the following benefits to pts with kidney disease: Lower pill burden, emulates a low sodium diet, reduces serum phosphate & provides a very safe alternative due to the drug's non-systemic nature

- **Summary of reported clinical data:** In CKD, the decision to advance tenapanor into the clinic was based on two hypothesis generating data points: (1) tenapanor has demonstrated an ability to increase fecal sodium output; and (2) in a 52-patient study, adherence to a low sodium diet was shown to be more effective than ACE-I or ARB blockade for reduction of proteinuria and blood pressure in non-diabetic nephropathy patients. According to MEDACorp KOL specialists, it is reasonable to assume lowering sodium would produce a similar albumin lowering effect in non-diabetic nephropathy pts and type 2 diabetics

- The ongoing Phase 2a (n=140) will assess:

  - **Primary endpoint will be change in UACR** (urine albumin-to-creatinine ratio) – UACR is a surrogate endpoint intended to assess proteinuria, or leakage of protein in the urine which is a byproduct of an unhealthy kidney; according to ARDX, UACR is the only short-term endpoint available to assess drug activity.

  - **What is an approvable endpoint?**
    - Historically, drugs being developed for CKD stage III-IV had to show a 50% change in creatinine in a 3-year study. Estimated glomerular filtration rate (eGFR) has long been considered as a predictor of progression to ESRD. Based on emerging data, some KOLs are suggesting the optimal level of eGFR decline is closer to 30% over a 2-year time frame, which would make for a less strict endpoint

    - Phase 2a data on the UACR endpoint is perceived as a good first step for tenapanor, but by itself still won't evidence improvement in kidney function. According to the specialists – a 2-year trial wherein tenapanor shows at least a 30% change in proteinuria was viewed as a good compromise vs. the current FDA recommended pivotal study protocols

Tenapanor Market Assumptions for CKD Stage III/IV

- **Market Size:** There are ~2m patients in the US with CKD stage III/IV and co-morbid diabetes, the potential market for patients who could benefit from long-term sodium control. These are patients with some renal function, but not yet on dialysis.

- **Current management:** (1) low sodium diet generally required for all CKD patients; (2) pharmacotherapy is aimed at slowing progression of kidney disease by controlling blood pressure, reducing urinary protein excretion, and decreasing fluid retention. Diuretics are prescribed to inhibit sodium re-uptake in the kidney and increased urinary sodium excretion, while ACE inhibitor ARBs and mineral corticoid receptor blockers also reduce blood pressure associated with fluid overload, which in turn slow the rate of progression of CKD.

- **Tenapanor market share –** we forecast tenapanor CKD sales based on assumption that the drug demonstrates a reduction in serum phosphate, increased fecal sodium output, and launches with a BID dosing profile. Based on physician specialist feedback, they would prescribe tenapanor to most of their CKD stage III and IV patients with comorbid diabetes. We forecast 40% penetration and assume a 25% cumulative probability of clinical/commercial success.

- **Duration of therapy**: We forecast tenapanor patients receiving chronic therapy for mgmt of CKD and model a 160-day duration of therapy

- **Pricing & price increases**: We forecast tenapanor being priced on par with the current phosphate binders, which are priced at ~$12/day; we adjust this price to reflect cost inflation between now and launch timing.

Source: Leerink research ests

We Forecast Significant Penetration into CKD Market

CKD	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
CKD stage 3-4, plus diabetes	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.9	1.9
% growth	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%
% share													
tenapanor		8%	16%	24%	32%	40%	40%	40%	40%	40%	40%	40%	40%
Total tenapanor pts		0.1	0.3	0.4	0.6	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
Avg days of therapy		160	160	160	160	160	160	160	160	160	160	160	160
Cost per script/mo		16	17	17	18	18	19	19	20	20	21	22	22
Avg annual cost		2520	2646	2725.4	2807	2891.4	2978.1	3067	3159	3254	3352	3452	3556
Tenapanor CKD US Sales		366	770	1192	1640	2115	2183	2253	2325	2400	2477	2556	2638
% POS		25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
Tenapanor CKD Sales (risk adj)	-	**91**	**192**	**298**	**410**	**529**	**546**	**563**	**581**	**600**	**619**	**639**	**660**
Ex-US sales (risk adj)	0	37.5	75	112.5	150	187.5	187.5	187.5	187.5	187.5	187.5	187.5	187.5
% royalty to Ardelyx (tiered, double digit)	8%	8%	10%	13%	13%	13%	13%	13%	15%	15%	15%	15%	15%
Total CKD royalties	-	**10**	**27**	**51**	**70**	**90**	**92**	**94**	**115**	**118**	**121**	**124**	**127**

Source: Leerink Research estimates

Tenapanor for IBS-C

Background on Constipation

- Constipation predominant IBS (irritable bowel syndrome) and CC (chronic constipation) are both chronic functional disorders characterized by frequent and bothersome symptoms that affect patients' daily lives.
  - **Symptoms**: (1) IBS-C symptoms include abdominal pain, discomfort or bloating and constipation; (2) CC symptoms primarily characterized by constipation
  - **Goals of pharmacotherapy**: Treatment is usually predicated on the pts most bothersome symptoms & treatment decisions are largely based on frequency and severity of constipation. Marketed treatments have generally demonstrated therapeutic gain over placebos of 7-15% in clinical trials, although cross-trial comparison of drugs is difficult given a lack of conformity in study designs used by marketed products
  - **Most common outcome indicators**: (1) in practice, feedback from specialists suggests primary care practitioners are focused on managing symptoms while GI (gastroenterology) specialists are focused on managing disease syndrome; (2) in the clinical trial setting, IBS-C drugs are generally evaluated on bowel movement frequency and reduction in abdominal pain, while CC studies focused on bowel movement frequency
- **Specialists generally manage IBS & CC the same**, with: (1) mild pts – diet and exercise and possibly a laxative; (2) mild to moderate – treatment with a laxative and/or branded pro-secretory agent [ACT's (OP) Linzess & SCMP/Takeda's Amitiza]; and (3) more severe pts with abdominal pain get Linzess and/or antidepressant, while for severe CC pts surgery may be an option.

Constipation Markets & Treatment Options

Current Treatment Options

Drug Class	Treatments	Appropriate to treat	Pros	Cons
Diet & exercise	Fiber-rich food,fiber supplements	IBS-C (without pain) & CC	Safe, modestly effective in mild patients lacking abdominal pain	compliance is poor due to side effects, including flatulence, distension, bloating and unpleasant taste
Laxatives	PEG, Miralax	IBS-C & CC	Fast onset (stimulant), increases intestinal motility	May cause abdominal cramps, no benefit on pain or bloating; possible dehydration
GC-C agonist	linaclotide, plecanatide	IBS-C & CC	Effective, reduces pain/bloating	Diarrhea side effect, reportedly goes away after first month of treatment
Chloride type-2 channel activator	Amitiza	IBS-C, CC, OIC, pediatric constipation	Effective, long post-market safety record, broad label	Physician perception that drug is only modestly effective, nausea, no benefit on IBS-C abdominal pain
Anti-depressants	SSRI's	IBS-C	Improves pain	No benefit on bloating or stool frequency/consistency
Amitiza 5% withdrawal rate in Ph 3 due to AE's				

OIC = Opioid Induced Constipation; SSRI = Selective Serotonin Re-uptake Inhibitor
Source: Product Package inserts, Journal of Gut and Liver (2011)

Constipation Pipeline Is Not Very Crowded

Background

- The clinical trial design for marketed IBS-C drugs has varied, although the last FDA guidance has remained in place since March 2010 and will likely be followed by all the companies in late-stage development. For IBS-C, applicants will need to conduct two 12-week safety and efficacy studies looking at a co-primary endpoint of: (1) intestinal motility – CSBM; and (2) abdominal pain. In addition to the 12-week studies, applicants will also need to conduct a 52-week open label safety study. The typical study design for the chronic constipation indication is two randomized/controlled studies looking at intestinal motility as the primary endpoint.

LS Outlook

- The pipeline for IBS-C & chronic idiopathic constipation (CIC) drugs includes a couple of mid to late stage competitive threats. The most advanced threat is SGYP's (NR) plecanatide, which has the same mechanism as Linzess and is being positioned as an alternative with a better side effect profile (less diarrhea). Early data on plecanatide's tolerability are inconclusive. With lead pipeline agent plecanatide targeting a '16 timeline to market, the competitive threats from the pipeline are still several yrs away and, in the view of the KOL specialists with whom we've spoken, the pipeline agents don't offer "game changing" differentiation vs. Linzess.

Clinical Development Pipeline

Drug	Active/MOA	Company	Status	Theoretical Differentiation	Comments
Tenapanor	NHE3 inhibitor	ARDX/AZN	Phase 2b	Pot'l less SE"s & titratable	Ph 2b data in 4Q14; 30% reduction in pain
A3309	IBAT inhibitor	Albireo/Ferring	Phase 2b	New MOA, pot'l less SE's	
SGYP	GCC agonist	SGYP	Phase 3	Less diarrhea vs. Linzess, titratable	
KWA0711	Unknown	Kissei	Phase 2	Inhibits water absorption in GI	Initiated May '12

Source: Medtrack

Linzess Scripts Are Starting to Accelerate Driven by Start of New DTC Promotional Initiatives

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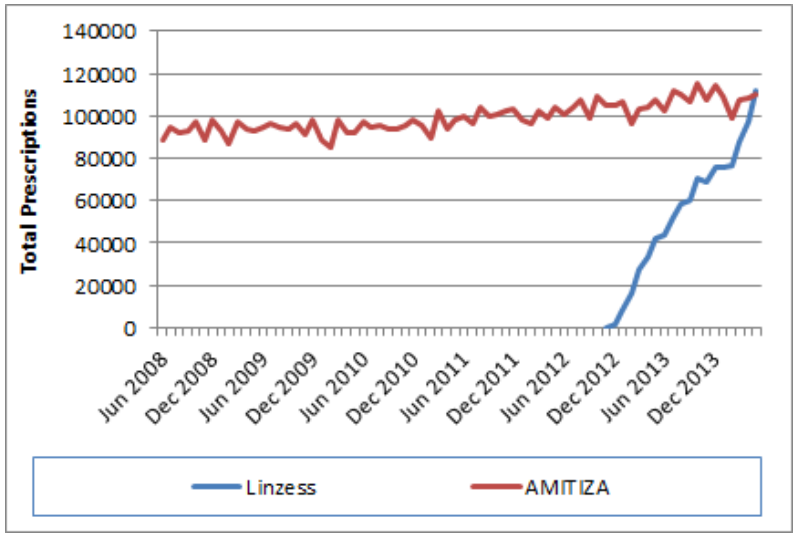
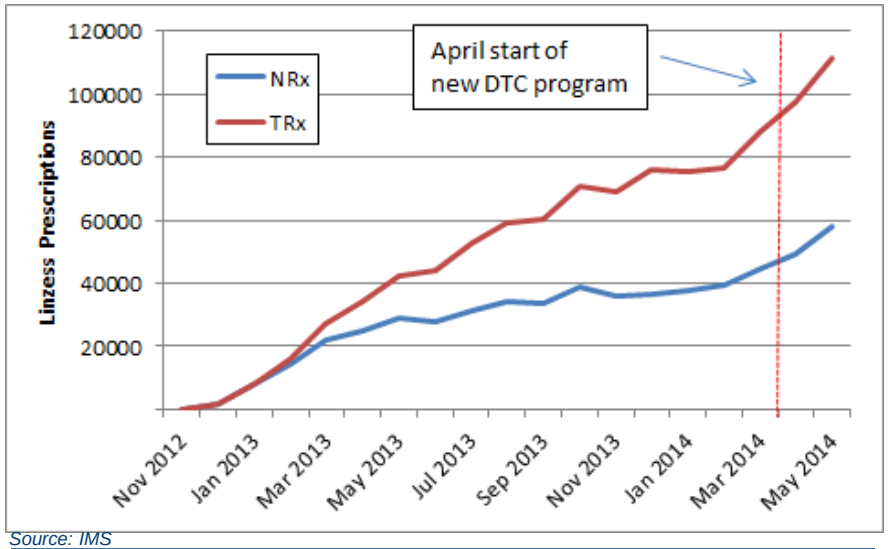
Linzess Has Expanded the Market



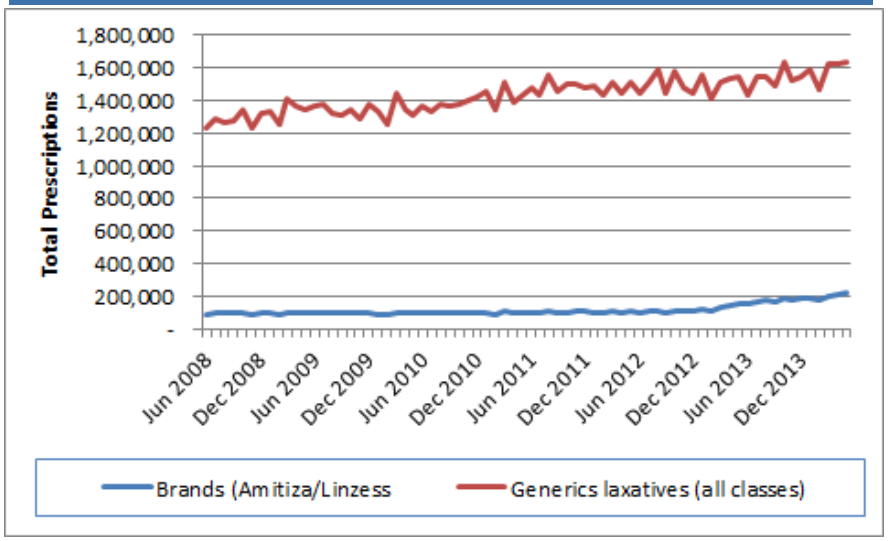
Source: IMS

Linzess Appear to Be Responding to DTC



Source: IMS

Linzess Likely Taking Share from OTC



Source: IMS

LS Commentary

- By most metrics, Linzess has had a successful launch and the drug is on track to achieve blockbuster status. On the positive side, Linzess is on track to becoming the dominant branded anti-constipation medicine and the drug has helped grow the overall market for branded drugs in the category. Based on our GI physician checks, television advertising was key to increasing patient awareness and driving Zelnorm usage, and we believe DTC TV advertising could be key to driving material acceleration of Linzess' launch trajectory.

Tenapanor US Market Assumptions

- **How it works:** Tenapanor works on the upper GI tract; it's unclear if the drug affects pain, but the drug was developed in IBS under the hypothesis that pain improvement would follow improvements in motility.

- **Market Size**: We assume an overall IBS-CC/CIC patient prevalence in the U.S. of ~40M; we est. ~35% (14.2M) of these patients seek medical care. Unmet needs with existing therapy include:
  - Current therapies still have issues: (1) OTC laxatives, such as Miralax, have suboptimal tolerability/efficacy profile; (2) Linzess's issues include: (a) side effects – mainly diarrhea which occurs in 15-20% of patients; (b) lack of dose response – inability to titrate the dose. To date, our KOL checks have revealed fairly divergent views on Linzess' efficacy and safety profile: while KOLs generally agree that Linzess is effective, some believe it is "too effective," resulting in cases of diarrhea.

- **Penetration:** Given a late order of entry, behind IRWD's (MP) Linzess and SGYP's plecanatide, we forecast tenapanor capturing a peak share of 5% (vs. 10% peak share for Linzess). KOL specialists have told us a product with tenapanor's potential benefits, which may include better tolerability and ease of administration (can be taken anytime, of full or empty stomach), are attractive features which would expand the market for branded therapy and capture meaningful market share. However – we note that until tenapanor Ph. 2b proof-of-concept study reads out, the above product profile remains theoretical

- **Duration of therapy**: Similar to Linzess, we forecast ~4 prescriptions per patient per year, on average, which equates to ~120 days of therapy (DOT), but over time we forecast tenapanor's DOT increasing to ~140

- **Pricing & price increases**: We assume tenapanor pricing of $7.50/tablet, or $225/net price per script. This is on par with ACT/IRWD's Linzess pricing.

- **Risks**: Given that tenapanor is still pre-proof of concept and the profile has yet to be validated, we assume 35% probability of success (cumulative commercial & clinical risk) in IBS.

Tenapanor US Revenue Model -- IBS

IBS-C	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Total IBS-C/CIC Prevalent pts (MM)	40	40	40	40	40	40	40	40	40	40	40	40	40
% seeking medical care	0.355	0.355	0.355	0.355	0.355	0.355	0.355	0.355	0.355	0.355	0.355	0.355	0.355
IBS/CIC pts receiving medical care	14.2	14.2	14.2	14.2	14.2	14.2	14.2	14.2	14.2	14.2	14.2	14.2	14.2
% patient share	1%	2%	3%	4%	5%	5%	5%	5%	5%	5%	5%	5%	5%
Ardelyx pts	0.1	0.3	0.4	0.5	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Avg Rx/patient/year	4	4.2	4.4	4.6	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7
Net price per/Rx	225	236	248	260	273	287	302	317	332	349	367	385	404
Tenapanor IBS US Sales	115	254	418	612	821	862	906	951	998	1048	1101	1156	1214
% POS	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
Tenapanor IBS sales (risk adj)	**40**	**89**	**146**	**214**	**287**	**302**	**317**	**333**	**349**	**367**	**385**	**405**	**425**
% royalty	8%	10%	10%	13%	13%	13%	13%	13%	15%	15%	15%	15%	15%
IBS royalties (risk adj)	**3**	**9**	**15**	**27**	**36**	**38**	**40**	**42**	**52**	**55**	**58**	**61**	**64**

Source: Leerink estimates, IMS

Mechanics of ARDX-AZN (MP) Partnership

- In 2012, ARDX & AZN entered into a worldwide development & commercialization collaboration for tenapanor. Under the agreement:
  - AZN owns exclusive rights to tenapanor in exchange for milestone payments and royalties on net sales. ARDX may receive up to ~$225m in development milestones. The royalty is tiered, starting in the high single digits and escalating to the high teens. ARDX has the option of buying back 1-3% of royalties if the Phase 2 data (in 2015) are impressive
  - Tenapanor is being developed for three indications, but ARDX cannot clawback rights to specific indications if AZN opts to not move forward with a particular indication.
- How the collaboration leverages AZN's commercial strengths:
  - Renal & GI – AZN has demonstrated its extensive experience to develop and commercialize drugs in the Renal & GI market: (1) AZN's Renal franchise: Atacand1 (~$600m); Plendil (~$260m); Seloken/Toprol-XL (~$750m) are all treatments for hypertension; (2) AZN's total GI franchise generated over ~$4B in revenues in 2013; (3) AZN is also investigating roxadustat for anemia in CKD/ESRD patients and has historically had a presence in GI through the sale of proton pump inhibitors, namely Nexium (heartburn)
  - If AZN gets bought by PFE (MP) – PFE appears to view CV/Diabetes as important categories but GI is a wildcard given the company's limited exposure to the category

Intellectual Property

- **Robust patent portfolio around tenapanor**. At present, Ardelyx has an issued patent (U.S. Patent No. 8,541,448) on tenapanor covering the composition of matter. The issued US patent is currently predicted to expire in 2029, and two additional pending US patent applications cover methods of using tenapanor. ARDX has patent applications in most major markets which would also expire in 2029.

- **NaP2b patent portfolio is being handled by Ardelyx, but SNY has an option to pick up prosecution duties.**
  - Currently 1-2 compounds are in more advanced stages and may be pursued in IND studies, but additional medicinal chemistry work is needed beforehand.
  - Includes 5 pending US patent applications covering compositions of matter or methods of using NaP2b inhibitor compounds. If issued, pending patent applications are predicted to expire in 2031, as well as pending patent applications in Europe and Japan.
  - Once a lead compound is chosen, Ardelyx will seek to broaden its IP scope.

ARDX Revenue and P&L

ARDX Annual P&L Summary (Adj. Basis)																				
ARDX Annual Product Summary																				
(figures in $m, except per share data)																				
	2012A	**2013**	**1Q14**	**2Q14E**	**3Q14E**	**4Q14E**	**2014E**	**2015E**	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026**	**19-26E**
Tenapanor ESRD	-	-	-	-	-	-	-	-	-	-	4	8	17	29	36	37	37	38	46	28%
Tenapanor CKD	-	-	-	-	-	-	-	-	-	-	-	10	27	51	70	90	92	94	115	42%
Tenapanor IBS	-	-	-	-	-	-	-	-	-	-	**2**	**5**	**7**	**10**	**12**	**11**	**10**	**9**	**10**	12%
Total tenapanor royalties	-	-	-	-	-	-	-	-	-	-	**6**	**23**	**50**	**90**	**118**	**137**	**139**	**141**	**171**	**34%**
Licensing revenue	3	8	3	1	1	1	6	5	-	-	-	-	-	-	-	-	-	-	-	na
Collaborative development revenue	2	21	5	4.0	4.5	4	18	35	35	35	35	-	-	-	-	-	-	-	-	na
AZN milestones	-	-					-	10	25	25	50	-	-	-	-	-	-	-	-	na
Total Revenue (MM)	**5**	**29**	**8.6**	**5.0**	**5.5**	**5.0**	**24**	**50**	**60**	**60**	**91**	**23**	**50**	**90**	**118**	**137**	**139**	**141**	**171**	34%
% y/y growth	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*nm*	*51%*	*-75%*	*123%*	*80%*	*31%*	*16%*	*1%*	*1%*	*22%*	
COGS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	na
% of sales	0	0%	*na*	*na*	*na*	*na*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	
Gross Income	5.4	28.9	8.6	5.0	5.5	5.0	24.0	50.0	60	60	91	23	50	90	118	137	139	141	171	34%
% of net sales	100%	100%					100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
Discovery research	6.3	7.7	2.4	2.4	2.4	2.2	9.4	9.5	9.5	8.0	8.0	8.0	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	5.3	4.0	4.5	4.2	18.0	35	35	35	35	-	-	-	-	-	-	-	-	na
Total R&D	10.2	28.1	7.6	6.4	6.9	6.5	27.4	44.5	44.5	43.0	43.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	0%
% of sales	188%	nm	na	na	na	na	114%	89%	74%	*72%*	*47%*	*35%*	*16%*	*9%*	*7%*	*6%*	*6%*	*6%*	*5%*	
G&A	4.0	3.7	1.4	1.3	1.3	1.2	5.2	7.0	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	0%
% of sales	75%	13%	na	na	na	na	22%	14%	12%	*12%*	*8%*	*33%*	*15%*	*8%*	*6%*	*5%*	*5%*	*5%*	*4%*	
Selling & Marketing	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	na
Total operating expenses	14.2	31.8	9.0	7.7	8.2	7.7	32.6	51.5	52.0	50.5	50.5	15.5	15.5	15.5	15.5	15.5	15.5	15.5	15.5	0%
Operating (loss)/gain	**(8.8)**	**(2.9)**	(0.5)	(2.7)	(2.7)	(2.7)	**(8.6)**	**(1.5)**	**8.0**	**9.5**	**40.4**	**7.1**	**34.8**	**74.9**	**102.9**	**121.9**	**123.5**	**125.3**	**155.8**	56%
% of sales	-163%	nm	na	na	na	na	-36%	-3%	13%	16%	44%	31%	69%	83%	87%	89%	89%	89%	91%	
Net financial expense	**(1.0)**	**(3.6)**	(2.6)	-	-	-	(2.6)	1.0	1.3	1.5	2.1	2.3	2.6	3.4	4.3	5.3	6.4	7.4	8.7	21%
Pre-tax Income	**(9.8)**	**(6.4)**	**(3.1)**	**(2.7)**	**(2.7)**	**(2.7)**	**(11.2)**	**(0.5)**	**9.3**	**11.0**	**42.5**	**9.3**	**37.4**	**78.3**	**107.3**	**127.2**	**129.9**	**132.7**	**164.5**	51%
% Pre-tax Margin	nm	nm	*nm*	*nm*	*nm*	*nm*	nm	nm	nm	18.4%	46.8%	41.4%	74.4%	86.6%	90.6%	92.6%	93.4%	94.3%	96.0%	
Taxes (benefit)	-	0.1	-	-	-	-	-	-	-	-	4.3	1.4	7.5	19.6	32.2	44.5	45.5	46.5	57.6	70%
% 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%*	*35.0%*	*35.0%*	*35.0%*	
Net Income/(loss) (MM)	**(10)**	**(7)**	**(3.1)**	**(2.7)**	**(2.7)**	**(2.7)**	**(11)**	**(1)**	**9**	**11**	**38**	**8**	**30**	**59**	**75**	**83**	**84**	**86**	**107**	45%
% of net sales	NM	NM	*N/M*	*N/M*	*N/M*	*N/M*	NM	nm	15.6%	18.4%	42.1%	35.2%	59.6%	65.0%	63.4%	60.2%	60.7%	61.3%	62.4%	
Basic & Diluted EPS	**($1.26)**	**($0.65)**	**($0.23)**	**($0.20)**	**($0.15)**	**($0.15)**	**($0.72)**	**($0.03)**	**$0.51**	**$0.53**	**$1.81**	**$0.37**	**$1.36**	**$2.62**	**$3.29**	**$3.55**	**$3.55**	**$3.56**	**$4.32**	**42%**
Y/Y	*NM*	*NM*					*NM*	*NM*	*NM*	*5%*	*240%*	*-80%*	*270%*	*92%*	*25%*	*8%*	*0%*	*0%*	*22%*	
Weighted Avg Basic & Diluted Shares (MM)	7.8	10.2	13.3	13.3	17.9	17.9	15.6	18.0	18.3	20.7	21.1	21.5	22.0	22.4	22.8	23.3	23.8	24.2	24.7	2%
% growth	NM	31%					54%	15%	2%	13%	2%	2%	2%	2%	2%	2%	2%	2%	2%	

Source: Company reports and Leerink Research estimates

ARDX (abbreviated) Balance Sheet & Cash Flow Statement

ARDX Cash Flows	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E
Net Income/Loss	(9.8)	(6.6)	(11)	(1)	9	11	38	8	30	59	75	83	84	86	107
Use of NOLs	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Deferred revenue (milestone/upfront adjustments)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stock based comp	0.5	0.4	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Depreciation/amortization	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Stock issued to vendor	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Warrants issued in connection with related party note conv	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Chg fair value convert preferred stk warrant	1.0	3.5	-	-	-	-	-	-	-	-	-	-	-	-	-
Other	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Change in operating assets and liabilities	29.6	3.9	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Accounts receivable	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Inventory	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Accounts payable	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Other	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cash from operations	**22.0**	**1.8**	**(7)**	**4**	**13**	**15**	**42**	**12**	**34**	**63**	**79**	**87**	**89**	**90**	**111**
PP&E (capex)	(0.1)	(0.3)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	1.2
Other (financing)	0.27	(0.00)	-	-	-	-	-	-	-	-	-	-	-	-	-
FCF	22	2	(7)	3	13	15	42	12	34	63	79	87	88	90	110
FCF/share	2.81	0.21	(0.47)	0.19	0.72	0.72	2.00	0.55	1.54	2.80	3.46	3.72	3.72	3.72	4.44
Y/Y															
Common stock sale, options	-	-	48	-	-	-	-	-	-	-	-	-	-	-	-
Debt sale	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Repayment of notes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Other financing	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cash from financing	-	-	48	-	-	-	-	-	-	-	-	-	-	-	-
Cash flow to equity holders															
Debt	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cash (MM)	33	34	75	78	91	106	148	160	194	257	336	422	511	601	711

Source: Company reports and Leerink Research estimates

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.

Distribution of Ratings/Investment Banking Services (IB) as of 06/30/14				
			IB Serv./Past 12 Mos.	
Rating	Count	Percent	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.

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Leerink Partners LLC Equity Research

Director of Equity Research	**John L. Sullivan, CFA**	(617) 918-4875	john.sullivan@leerink.com
Associate Director of Research	**Alice C. Avanian, CFA**	(617) 918-4544	alice.avanian@leerink.com
Healthcare Strategy	**John L. Sullivan, CFA**	(617) 918-4875	john.sullivan@leerink.com
	Alice C. Avanian, CFA	(617) 918-4544	alice.avanian@leerink.com
Biotechnology	**Howard Liang, Ph.D.**	(617) 918-4857	howard.liang@leerink.com
	Joseph P. Schwartz	(617) 918-4575	joseph.schwartz@leerink.com
	Marko Kozul, M.D.	(415) 905-7221	marko.kozul@leerink.com
	Michael Schmidt, Ph.D.	(617) 918-4588	michael.schmidt@leerink.com
	Gena Wang, Ph.D., CFA	(212) 277-6073	gena.wang@leerink.com
	Jonathan Chang, Ph.D.	(617) 918-4015	jonathan.chang@leerink.com
	Paul Matteis	(617) 918-4585	paul.matteis@leerink.com
	Richard Goss	(617) 918-4059	richard.goss@leerink.com
Life Science Tools	**Dan Leonard**	(212) 277-6116	dan.leonard@leerink.com
and Diagnostics	Justin Bowers, CFA	(212) 277-6066	justin.bowers@leerink.com
Pharmaceuticals/Major	**Seamus Fernandez**	(617) 918-4011	seamus.fernandez@leerink.com
	Ario Arabi	(617) 918-4568	ario.arabi@leerink.com
	Aneesh Kapur	(617) 918-4576	aneesh.kapur@leerink.com
Specialty Pharmaceuticals	**Jason M. Gerberry, JD**	(617) 918-4549	jason.gerberry@leerink.com
Medical Devices, Cardiology	**Danielle Antalffy**	(212) 277-6044	danielle.antalffy@leerink.com
	Puneet Souda	(212) 277-6091	puneet.souda@leerink.com
& Orthopedics	**Richard Newitter**	(212) 277-6088	richard.newitter@leerink.com
	Ravi Misra	(212) 277-6049	ravi.misra@leerink.com
Healthcare Services	**Ana Gupte, Ph.D.**	(212) 277-6040	ana.gupte@leerink.com
Healthcare Technology	**David Larsen, CFA**	(617) 918-4502	david.larsen@leerink.com
& Distribution	Christopher Abbott	(617) 918-4010	chris.abbott@leerink.com
Sr. Editor/Supervisory Analyst	**Mary Ellen Eagan, CFA**	(617) 918-4837	maryellen.eagan@leerink.com
Supervisory Analysts	Robert Egan		bob.egan@leerink.com
	Amy N. Sonne		amy.sonne@leerink.com
Editorial	Cristina Diaz-Dickson	(617) 918-4548	cristina.diaz-dickson@leerink.com
Research Assistant	Carmen Augustine	(212) 277-6012	carmen.augustine@leerink.com

New York
299 Park Avenue, 21st floor
New York, NY 10171
(888) 778-1653

Boston
One Federal Street, 37th Floor
Boston, MA 02110
(800) 808-7525

San Francisco
201 Spear Street, 16th Floor
San Francisco, CA 94105
(800) 778-1164