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EQUITY RESEARCH
Company Report

April 24, 2018

Ionis Pharmaceuticals (IONS - $48.51)

Healthcare/Biotechnology

Ticker:	**IONS**
Rating:	**Buy**
Price Target:	**$65.00**

Lower Than Expected 1Q18 Spinraza Sales were Driven by Ex-U.S. Expansion and with More Maintenance Doses

During the quarterly earnings call this morning, BIIB reported the 1Q18 Spinraza sales of $364MM, which was at the same level as 4Q17. The figure is higher than our ($355MM), but lower than the Street ($380MM) estimates.

- **Details.** The total Spinraza 1Q18 sales was flat Q/Q with $188MM from the U.S. and $176MM from ex-U.S. Two-third of ex-U.S. sales came from Germany, Italy, France and Japan. Inventory level vs. 4Q17 was also flat (~$30MM). Q/Q, the U.S. sales declined 14%, while ex-U.S. growth was 22%. The major reason for the 1Q18 U.S. sales decline is fewer new patients (280 vs. 420 in 4Q17), resulting in lower percentage of loading doses being administrated (60% vs. 75%) despite a higher number of total treated patients (1,910 vs. 1.640). 1Q18 maintenance doses were 40% (vs. 25%) with average doses per patient of 1.1 (vs. 1.6). 290 patients (vs. 280) were under the expanded access program (EAP). Ex-U.S., 1,560 patients in 1Q18 received Spinraza therapy (vs. 990 in 4Q17) with 810, 590 and 138 of Type I, II, and III SMA, respectively. Spinraza has gained reimbursements in 7 more markets in 1Q18, and in total, 17 countries have formal reimbursement, while 7 are on case-by-case basis. Going forward, management suggested that the U.S. sales could have a more stable growth in 2018 with more penetration in adult patient market as a focus. Ex-U.S. growth could potentially be a more important driver going forward. In collaboration with U Penn, BIIB also is developing gene therapy for SMA with study to start in mid-2018. BIIB also suggested that the Spinraza and gene therapy combination could be an option for SMA patients managing their disease longer term and cited a case that 7 patients participated in AVXS' (acquired by NVS) Phase I study (total 15) have taken Spinraza therapy afterward.
- **Implications.** Although the 1Q18 Spinraza sales are overall below expectation, we do not believe this as a total surprise. BIIB has indicated during their prior earnings call that near half of the U.S. revenue in 4Q17 came from patients initiated their therapy during that quarter. As such, the breakdown of the higher revenue loading doses in the U.S. would be lower in 1Q18. Since the company has previously guided that the breakdown between the loading/maintenance doses could reach a steadier state of 50% toward year-end 2018 and if BIIB is successful gaining a greater foothold in treating adult SMA patients, it would be reasonable, in our opinion, that Spinraza could enjoy a more steadily growth going forward.
- **Action.** We are reiterating our Buy rating and $65 target price to reflect our bullish view on progress in IONS's marketed and pipeline products. Our valuation is based on our DCF and probability-adjusted-NPV-driven, sum-of-the-parts analyses.

Trading Data:

Last Price (4/23/2018)	$48.51
52–Week High (10/20/2017)	$65.51
52–Week Low (4/6/2018)	$40.33
Market Cap. (MM)	$6,360
Shares Out. (MM)	126.098

Earnings Estimates: (per share)

(Dec)	1Q	2Q	3Q	4Q	FY	P/E
FY-18E	-0.23	-0.20	0.05	0.23	-0.15	NM
FY-17A	0.03	-0.09	0.00	0.02	0.08	NM
FY-16A	-0.52	-0.47	0.06	0.21	-0.72	NM
FY-15A	-0.14	0.30	-0.30	-0.59	-0.74	NM

Source: Laidlaw & Company estimates

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Anticipated milestones in 2018 and beyond

Product	Indication	Event	Timing	Importance
IONIS-APOCIII$_{Rx}$ (Volanesorsen)	Familiar chylomicronemia syndrome (FCS)	AdComm meeting	**5/10/2018**	****
		PDUFA date	**8/30/2018**	****
		Product launch	**2H18**	***
	Familiar partial lipodystrophy (FPL)	Completion of patient recuritment of Phase III study	**2018**	***
		Report of Phase III study top-line results	**2019**	****
Spinraza (Nusinersen)	Spinal muscular atrophy (infant /children)	Potential additional ROW approvals	**2018**	***
		Quarterely sales updates (recurring)	**2018**	***
IONIS-TTR$_{Rx}$ (Inotersen)	Polyneuropathy due to hereditary TTR amyloidosis (hATTR-PN)	PDUFA date	**7/6/2018**	****
		Potential ex-U.S. partnership	**2018**	***
		Potential approval	**Mid-18**	****
IONIS-TTR-L$_{Rx}$	Cardiomyopathy due to TTR amyloidosis	Possibly start Phase I study	**2H18**	***
IONIS-FXI$_{Rx}$	Atrial fibrillation of end-stage renal disease	Potential to report Phase IIb ESRD dose optimizing study	**2018/2019**	***
		Potential to start Phase III study or decision waiting for Lica product by Bayer	**2019**	***
IONIS-FXI-L$_{Rx}$	Novel anti-thrombotic agent	Potential to start Phase I study	**2018**	***
ACKEA-APOCIII-L$_{Rx}$	High risk CV patients with elevated triglyceride as major risk factor	Report Phase II dose optimization study results	**2019**	****
		NVS start Phase III CV outcome study	**2019**	****
IONIS-DMPK-2.5$_{Rx}$	Myotonic dystrophy 1	Develop the next gen. product	**2017**	***
IONIS-PKK$_{Rx}$	Hereditary angioedema	Possibly to start a LICA version drug Phase I trial	**2018**	***
IONIS-HTT$_{Rx}$	Huntington disease	Report Phase I/IIa study results at the AAN meeting	**4/21-27/2018**	***
		Potentially start Phase II/III study by Roche	**2H18**	***
ACKEA-ANGPTL3-L$_{Rx}$	Rare hyperlipidermias	Potentially report Phase II study results	**2018**	***
	Non-alcoholic fatty liver disease (NAFLD) with metabolic complications	Potentially report Phase II study results	**2018**	***
IONIS-TMPRSS6-L$_{Rx}$	β-Thalassemia	Phase I study results	**2018**	***
ACKEA-APO(a)-L$_{Rx}$	High risk CV patients with elevated Lp(a) as major risk factor	Report Phase II dose optimization study results	**2H18**	****
		NVS start Phase III CV outcome study	**2019**	****
IONIS-DGAT2$_{Rx}$	NASH	Report Phase II study results	**2018**	***
IONIS-SOD1$_{Rx}$	Amyotrophic lateral sclerosis	Report Phase I/II study results	**2018**	***
IONIS-BIIB4 - 6$_{Rx}$	Neurodegenerative disease	Report Phase I study results	**2018**	***
IONIS-GHR-L$_{Rx}$	Acromegaly	Phase II study results	**2018**	***
IONIS-AGT-L$_{Rx}$	Treatment-resistant hypertension	Phase Ib study results	**2018**	***
IONIS-FB-L$_{Rx}$	Complement-mediated diseases	Start Phase II study	**2018**	***
IONIS-HBV$_{Rx}$	HBV	Potentially report Phase II study top-line results	**2018**	****
IONIS-AR-2.5$_{Rx}$	Cancer	Start Phase II study with AZN	**2018**	***
IONIS-KRAS-2.5$_{Rx}$	Cancer	Start Phase II study with AZN	**2018**	***

***** / ***** Major catalyst event that could impact share price very significantly while *** event is more informative*

Source: Laidlaw & Company estimates and company presentation.

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Major risks

Clinical risks of study failure could have significant impacts on IONS share value. Although many ongoing studies have provided encouraging clinical outcomes following prior studies; risks remain that some current trials might not meet study endpoints in order to advance forward. As such, the value of any such clinical asset could be significantly impaired and therefore IONS shareholder value could diminish. Such a negative impact could be more pronounced if the clinical program is in very advanced development stages or with high investor expectations. Regulatory risks are part of the clinical risks as even if a drug met its endpoints for pivotal studies. The regulatory agency might not grant approval and therefore, the drug cannot be commercialized.

Commercial risk even if a therapeutic is approved, sales could be substantially below expectations. Even it is approved; the commercial sales of any drug could fall below expectations, resulting in diminishing IONS shareholder value. Factors that could impact on the commercial outlook of a drug could include execution of marketing and sales; competition from other drugs; potential change of the treatment paradigm; and unrealistic expectations or projections.

Continued consummations of partnerships could be important. Given that partnerships are a critical part of IONS product development and commercialization strategy; failure to consummate future product development or product commercialization partnerships could put share value at risk. The alternative approach could require that the company raise capital from financial markets to support its operation if the company cannot generate profits from product revenues.

Future capital raises could potentially dilute value of current shareholders. If it is not profitable, the company may need to raise capital from financial markets to support its operations; even if the company already has partners to provide milestone and other types of payments and/or product revenue. As such, the company might not always be able to raise capital from financial markets at favorable terms. Share dilution under this scenario could reduce the value of the investment to current shareholders of the company

Although antisense drugs have been approved, this modality might not be broadly accepted and therefore limit its commercial potential. Although two antisense drugs are already approved and commercialized in the U.S. and other part of the world; this treatment modality remains with limited exposure to the medical world. As such, it is possible that going forward, antisense or other RNA-based medication could have limited use due to market acceptance. Such a scenario could reduce the market potential of antisense drugs and have negative impact on IONS shareholder value.

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Figure 1: Income Statement

Ionis Pharmaceuticals – Income Statement

($'MM)	2014	2015	2016	2017	1Q18E	2Q18E	3Q18E	4Q18E	2018E	2019E	2020E
Revenue											
IONIS-TTR$_{Rx}$ (Inotersen) revenue			0.0	0.0	-	-	16.3	32.6	48.9	233.5	348.8
IONIS-APOCIII$_{Rx}$ & L$_{Rx}$ (Volanesorsen) revenue			0.0	0.0			3.3	7.3	10.6	49.1	78.1
Spinraza (Nusinersen) revenue			0.0	112.5	38.4	45.4	52.6	53.4	189.8	256.4	290.6
Pipeline products - Prob. Adj					-	-	-	-	0.0	14.6	68.5
R&D revenue under collaborative agreements	202.5	281.4	325.9	385.6	85.0	91.0	109.0	114.0	399.0	401.8	385.7
Licensing and royalty revenue	11.6	2.3	20.7	9.5	2.0	1.0	1.5	1.8	6.3	6.3	6.3
Total revenue	214.2	283.7	346.6	507.7	125.4	137.4	182.6	209.2	654.6	961.6	1,178.1
Costs of goods							2.3	4.8	7.1	33.9	51.2
Research and development	241.8	322.3	344.3	374.6	101.3	102.4	106.5	108.6	418.7	435.5	452.9
General and administrative	20.1	37.2	48.6	108.5	47.1	54.1	60.6	66.1	227.9	248.5	268.3
Total Operating Expenses	261.9	359.5	392.9	483.1	148.4	156.5	169.4	179.5	653.8	717.9	772.5
Operating Incomes (losses)	(47.7)	(75.8)	(46.3)	24.5	(23.0)	(19.1)	13.2	29.7	0.8	243.8	405.6
Equity in net loss of Regulus Therapeutics Inc.											
Investment income	2.7	4.3	5.5	8.2	2.5	2.5	2.5	2.5	10.0	11.0	12.1
Interest expense	(22.2)	(36.7)	(38.8)	(44.8)	(10.9)	(11.0)	(11.7)	(11.3)	(44.9)	(49.4)	(49.4)
Gain on investments, net	1.8	0.1	(0.0)	0.0	0.0	0.0	0.0	0.0	0.0	(27.0)	(27.0)
Gain on investment in Regulus Therapeutics Inc.	19.4	20.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Loss on extinguishment of financing liability for leased facility				(7.7)							
Loss on early retirement of debt	(8.3)		(4.0)	0.0							
Other expenses				(3.5)	(2.0)	(2.0)	(2.0)	(2.0)	(8.0)	(8.4)	(8.8)
Total Other Income, net	(6.7)	(12.1)	(37.3)	(47.8)	(10.4)	(10.5)	(11.2)	(10.8)	(34.9)	(65.4)	(64.3)
Income before tax	(54.4)	(87.9)	(83.6)	(23.2)	(33.4)	(29.6)	2.0	18.9	(42.1)	178.4	341.3
Tax	15.4	(0.4)	(2.9)	6.0	0.0	0.0	0.7	7.0	7.7	(66.0)	(126.3)
Net Income (Loss) GAAP	(39.0)	(88.3)	(86.6)	(17.3)	(33.4)	(29.6)	2.7	25.9	(34.4)	112.4	215.0
Net loss attributable to noncontrolling interest in Akcea				11.3	4.0	4.0	4.0	4.0	16.0	16.8	17.6
Net Income (Loss) Applicable to Common Shareholders	(39.0)	(88.3)	(86.6)	(5.9)	(29.4)	(25.6)	6.7	29.9	(18.4)	129.2	232.7
Net Earnings (Losses) Per Share—Basic and Diluted	($0.33)	($0.74)	($0.72)	$0.08	($0.23)	($0.20)	$0.05	$0.23	($0.15)	$1.02	$1.80
Shares outstanding—basic	117.7	119.7	120.9	124.0	124.8	124.9	125.1	125.3	125.0	127.0	129.0
Shares outstanding--diluted	118.8	119.7	120.9	126.1	126.9	126.9	127.1	127.3	127.0	129.0	131.0
Margin Analysis (% of Sales/Revenue)											
Costs of goods			0%	0%					0%	0%	0%
R&D	113%	114%	99%	74%	81%	74%	58%	52%	64%	45%	38%
MG&A	9%	13%	14%	21%	38%	39%	33%	32%	35%	26%	23%
Operating Income (loss)	-22%	-27%	-13%	5%	-18%	-14%	7%	14%	0%	25%	34%
Net Income	-18%	-31%	-25%	-1%	-23%	-19%	4%	14%	-3%	13%	20%
Financial Indicator Growth Analysis (YoY%)											
R&D revenue under collaborative agreements	40%	39%	16%	18%	-16%	12%	25%	-1%	3%	-2%	-4%
Licensing and royalty revenue	277%	-80%	784%	-54%	-44%	80%	71%	-60%	-34%	0%	0%
Total Revenue	45%	32%	22%	46%	14%	32%	51%	21%	29%	47%	23%
R&D	31%	33%	7%	9%	23%	23%	33%	-15%	12%	4%	4%
SG&A	35%	85%	31%	123%	244%	143%	126%	45%	110%	9%	8%
Marketing and sales									5%	6%	5%
Operating Loss	-8%	59%	-39%	-153%	-265%	1043%	-5%	-1854%	-97%	31534%	66%
Total Other Income, net	-55%	82%	207%	28%	623%	13%	-37%	7%	-27%	87%	-2%
Pretax Income	-18%	62%	-5%	-72%	-1064%	169%	-150%	-260%	81%	-523%	91%
Net Income	-36%	126%	-2%	-93%	-948%	128%	-789%	989%	210%	-802%	80%
EPS	-40%	123%	-3%	-111%	-935%	123%	2356%	968%	-284%	-791%	77%

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Source: Bloomberg LP; Company reports; Laidlaw & Company estimates.

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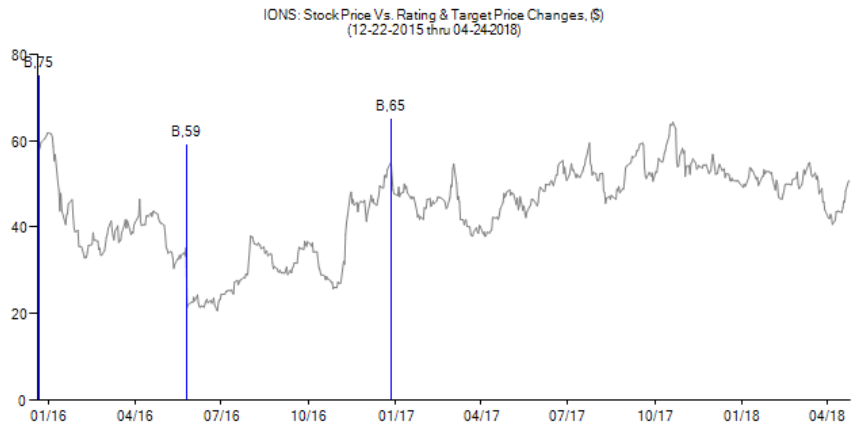
Rating and Price Target Change History



3 Year Rating Change History

Date	Rating	Closing Price ($)
12/22/...	Buy (B)	57.85

3 Year Price Change History

Date	Target Price ($)	Closing Price, ($)
12/22/...	75.00	57.85
05/26/...	59.00	21.36
12/27/...	65.00	55.12

Source: Laidlaw & Company **Created by: Blue-Compass.net** *Note: Company changed its ticker symbol to IONS from ISIS on 12/22/2015.*

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			Investment Banking	Brokerage
Strong Buy (SB)	Expected to significantly outperform the sector over 12 months.	0.00%	0.00%	0.00%
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Sell (S)	Returns expected to significantly underperform the sector average over 12 months.	0.00%	0.00%	0.00%

ADDITIONAL COMPANIES MENTIONED

Biogen (BIIB – Not Rated)
Roche (ROG – Not Rated)

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