

Ionis Pharmaceuticals (IONS - \$45.85)

Healthcare/Biotechnology

New Biogen Collaboration is a Current Biotech Mega Deal

Biogen and IONS announced this morning the consummation of a new 10-year collaboration deal in neurological (includes neuropsychological) indications. The deal is expected to close in 2Q18.

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

- Details.** The terms of the deal include \$1 billion upfront payment, broken down between a \$500MM tech access fee and a \$500MM equity investment (at \$54.34/share, ~ 25% premium with BIIB becoming IONS' second largest shareholder). For each advanced program, IONS is entitled for up to \$270MM in milestone and tiered royalties, starting from mid-teens to 20%. IONS and BIIB will jointly identify the molecular targets. IONS is responsible for the identification of antisense drug candidates, and BIIB will be responsible for paying the expense and development of clinical studies, manufacturing, and commercialization. IONS has not revealed the total number of indications but indicated that disease areas could include dementia, neuromuscular diseases, movement disorders, ophthalmology, diseases of the inner ear, and neuropsychiatry. Besides Spinraza, IONS/BIIB already have 7 neurological programs in development with 4 [ALS and Alzheimer's Disease(AD)] in Phase I/II and 4 in preclinical. All 7 existing neurological drugs are delivered intrathecally but future programs may have greater flexibility. IONS-SOD1_{Rx} (PII) and IONS-C9_{Rx} (enter P1/II in mid-18) are the two ALS programs. The AD program is IONS-MAPT_{Rx} (PII). More than 20 additional research-stage programs, including Parkinson's disease and Angelman syndrome, are also underway. IONS also expect to advance several wholly owned programs in the next year and half.

Trading Data:

Last Price (4/19/2018)	\$45.85
52-Week High (10/20/2017)	\$65.51
52-Week Low (4/6/2018)	\$40.33
Market Cap. (MM)	\$5,992
Shares Out. (MM)	126.10

- Implications.** BIIB has publicly mentioned that the IONS' neurological disease collaboration is an important part of their overall drug development; the new collaboration further strengthens BIIB's commitment to advance their antisense-based future neurological franchise. The success of Spinraza and the compelling data with the possible success of IONS-HTT_{Rx} in Huntington's disease (opted in by Roche) further supports the notion that intrathecally delivered antisense is a validated format addressing the root causes of many neurological diseases and provides disease-modifying benefits. We believe IONS is exploring different chemistries and conjugates to further enhance efficacy of neurological-focused antisense drugs – an attempt that already started based on BIIB's recently announced collaboration for developing better next gen. SMA drugs.
- 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.

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

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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 recruitment 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	***
		Quarterly 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-HIT _{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 hyperlipidemias	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.

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 if 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.

Figure 1: Income Statement

Ionis Pharmaceuticals – Income Statement											
(\$'MM)	2014	2015	2016	2017	2018				2018E	2019E	2020E
					1Q18E	2Q18E	3Q18E	4Q18E			
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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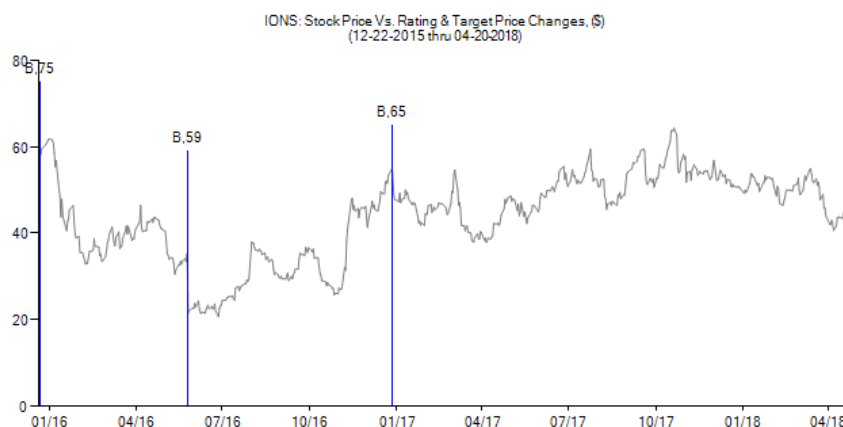
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Rating and Price Target Change History



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%
Buy (B)	Expected to outperform the sector average over 12 months.	65.38%	26.92%	3.85%
Hold (H)	Expected returns to be in line with the sector average over 12 months.	0.00%	0.00%	0.00%
Sell (S)	Returns expected to significantly underperform the sector average over 12 months.	0.00%	0.00%	0.00%

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

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