

Ionis

## 4Q: no change to cardiomyopathy trial & negative read from ALNY seems misplaced

Reiterate Rating: BUY | PO: 62.00 USD | Price: 43.56 USD

### IONS remains bullish on key pipeline programs

IONS' 4Q was a relative non-event though today's investor call came at an important juncture with the stock underperforming the broader biotech index (XBI) by ~12% since competitor ALNY announced modifications (2/15) to its Ph3 cardiomyopathy (TTR-CM; HELIOS-B trial) study analysis plan. In our view, IONS/AZN's eplontersen (TTR silencer) is well positioned to potentially secure a favorable outcome in the important all-comer population given its conservatively powered Ph3 outcomes trial that is 2x the size of its competitor and we see these data + large/stratified sub-groups as key to winning share in the 1L setting as preferred monotherapy or in combination with the current standard of care (TTR stabilizers). If there was a negative to the competitor update, it is that certain data scenarios could prompt IONS to delay unblinding of Ph3 (Cardio-TTRransform) until the final analysis in 2026 (from 1H25), but the management team was emphatic on today's call that there are no changes to its analysis plan or timing to unblind (2025). We reiterate Buy on favorable setup ahead of catalyst rich next 12 mo.

### Cardiomyopathy: trial continues as planned, timeline intact

Last week, ALNY (covered by Tazeen Ahmad) announced a 3mo push and a change in statistical plan for its Phase 3 (see our report: [initial take on IONS read-through](#)). Today, IONS management indicated blinded event rates from its own Ph3 Cardio-TTRransform continue to track in-line with internal expectations. IONS continues to anticipate a Ph3 readout sometime between 1H25 and 2026, with more precise timing driven by blinded event rates of Cardio—TTRransform and competitor's HELIOS B data.

### Angelman: management highlights mid-year update

IONS discussed its expectations for the mid-year update on ION582, an UBE3A ASO for Angelman: 1) safety and dose/population selections as the primary objectives; 2) efficacy from an open-label study should be interpreted with caution; 3) improvements in EEG and clinical outcome (eg Bayley) vs natural history would support program advancement.

### FY24E guidance: few surprises

IONS guided to >\$575m in total revenue in 2024, same as FY23 guidance, as IONS expects revenue contribution from Wainua launch in polyneuropathy to offset Y/Y decline in R&D revenue, where a number of one-time milestone payments benefitted 4Q23 topline results. On P&L outlook: '24 OpEx to increase mid-SD with longer term SG&A to increase due to expansion of commercial infrastructure to support new launches, whereas R&D is expected to stabilize near current level (cadence of trial progressions).

Estimates (Dec) (US\$)	2022A	2023A	2024E	2025E	2026E
EPS	(1.90)	(2.56)	(3.82)	(3.26)	(1.50)
EPS Change (YoY)	-804.8%	-34.7%	-49.2%	14.7%	54.0%
Consensus EPS (Bloomberg)			(3.56)	(2.71)	(0.87)
DPS	0	0	0	0	0
Valuation (Dec)					
Free Cash Flow Yield*	-1.2%	-3.1%	-6.0%	-5.2%	-1.8%

\* For full definitions of *IQmethod*<sup>SM</sup> measures, see page 5.

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21 February 2024

Equity

#### Key Changes

(US\$)	Previous	Current
2024E Rev (m)	618.2	600.8
2024E EPS	-3.23	-3.82
2025E EPS	-2.85	-3.26
2026E EPS	-0.76	-1.50

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#### Stock Data

Price	43.56 USD
Price Objective	62.00 USD
Date Established	2-Jan-2024
Investment Opinion	B-1-9
52-Week Range	32.69 USD - 54.44 USD
Mkt Val (mn) / Shares Out (mn)	6,250 USD / 143.5
Free Float	87.0%
Average Daily Value (mn)	52.60 USD
BofA Ticker / Exchange	IONS / NAS
Bloomberg / Reuters	IONS US / IONS.OQ
ROE (2024E)	-125.0%
Net Dbt to Eqty (Dec-2023A)	165.2%
ESGMeter™	High

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Acronyms: see page 3

# iQprofile<sup>SM</sup> Ionis

## iQmethod<sup>SM</sup> – Bus Performance\*

(US\$ Millions)	2022A	2023A	2024E	2025E	2026E
Return on Capital Employed	-10.3%	-15.8%	-26.6%	-24.2%	-10.9%
Return on Equity	-38.7%	-72.2%	-125.0%	-149.9%	-275.7%
Operating Margin	-70.1%	-44.8%	-98.4%	-72.3%	-19.5%
Free Cash Flow	(78)	(193)	(378)	(328)	(111)

## iQmethod<sup>SM</sup> – Quality of Earnings\*

(US\$ Millions)	2022A	2023A	2024E	2025E	2026E
Cash Realization Ratio	NM	NM	NM	NM	NM
Asset Replacement Ratio	0.3x	0.3x	0.2x	0.3x	0.4x
Tax Rate	NM	NM	15.0%	17.0%	18.0%
Net Debt-to-Equity Ratio	67.3%	165.2%	101.1%	NM	NM
Interest Cover	-41.1x	-5.1x	NA	NA	NA

## Income Statement Data (Dec)

(US\$ Millions)	2022A	2023A	2024E	2025E	2026E
Sales	587	788	601	714	1,046
% Change	-27.5%	34.3%	-23.8%	18.8%	46.5%
Gross Profit	573	779	589	699	1,021
% Change	-28.3%	36.0%	-24.4%	18.7%	46.0%
EBITDA	(343)	(285)	(522)	(447)	(136)
% Change	NM	17.0%	-83.6%	14.4%	69.6%
Net Interest & Other Income	153	19	(60)	(60)	(67)
<b>Net Income (Adjusted)</b>	<b>(270)</b>	<b>(366)</b>	<b>(554)</b>	<b>(478)</b>	<b>(223)</b>
<b>% Change</b>	<b>-821.3%</b>	<b>-35.5%</b>	<b>-51.3%</b>	<b>13.7%</b>	<b>53.4%</b>

## Free Cash Flow Data (Dec)

(US\$ Millions)	2022A	2023A	2024E	2025E	2026E
Net Income from Cont Operations (GAAP)	(270)	(366)	(554)	(478)	(223)
Depreciation & Amortization	68	69	69	69	68
Change in Working Capital	32	12	8	(5)	(26)
Deferred Taxation Charge	0	0	0	0	0
Other Adjustments, Net	110	116	116	106	96
Capital Expenditure	(18)	(23)	(17)	(19)	(27)
<b>Free Cash Flow</b>	<b>-78</b>	<b>-193</b>	<b>-378</b>	<b>-328</b>	<b>-111</b>
<b>% Change</b>	<b>NM</b>	<b>-147.7%</b>	<b>-95.9%</b>	<b>13.3%</b>	<b>66.1%</b>
Share / Issue Repurchase	12	12	550	12	12
Cost of Dividends Paid	0	0	0	0	0
Change in Debt	(50)	(100)	0	0	0

## Balance Sheet Data (Dec)

(US\$ Millions)	2022A	2023A	2024E	2025E	2026E
Cash & Equivalents	716	398	533	181	45
Trade Receivables	23	32	24	29	42
Other Current Assets	1,416	1,379	1,369	1,358	1,373
Property, Plant & Equipment	184	195	200	206	221
Other Non-Current Assets	89	89	89	89	89
<b>Total Assets</b>	<b>2,428</b>	<b>2,093</b>	<b>2,215</b>	<b>1,863</b>	<b>1,769</b>
Short-Term Debt	0	0	0	0	0
Other Current Liabilities	253	256	266	275	297
Long-Term Debt	1,138	1,038	1,038	1,038	1,038
Other Non-Current Liabilities	412	412	412	412	412
<b>Total Liabilities</b>	<b>1,802</b>	<b>1,705</b>	<b>1,716</b>	<b>1,724</b>	<b>1,746</b>
<b>Total Equity</b>	<b>626</b>	<b>387</b>	<b>499</b>	<b>138</b>	<b>23</b>
<b>Total Equity &amp; Liabilities</b>	<b>2,428</b>	<b>2,093</b>	<b>2,215</b>	<b>1,863</b>	<b>1,769</b>

\* For full definitions of iQmethod<sup>SM</sup> measures, see page 5.

## Company Sector

Biotechnology

## Company Description

Ionis Pharmaceuticals is a biotechnology company focused on discovery and development of RNA-targeted therapeutics. The company's drug platform is called antisense technology which aims to modify/reduce the production of disease-causing proteins by binding/destroying RNA so that the amount of disease-causing protein is dramatically decreased. IONS has three commercial drugs approved in major markets, four drugs in Ph3 of development and over 30 medicines in early to mid-stage development.

## Investment Rationale

We rate IONS Buy on favorable stock setup ahead of catalyst-rich path in 2024-1H25. There will be multiple mid-/late-stage clinical readouts that can increase likelihood of success for four assets with \$300m-1bn nominal peak revenue estimates (Wainua, donidalorsen, olezarsen, ION582). Approval of Wainua in polyneuropathy with a clean label indicates ION's improved antisense (ASO) platform can mitigate legacy safety issues, effectively validating the safety profile of IONS' broader pipeline.

## Stock Data

Average Daily Volume 1,207,500

## Quarterly Earnings Estimates

	2023	2024
Q1	NAA	NA
Q2	NAA	NA
Q3	NAA	NA
Q4	NAA	NA

## Acronyms

IONS: Ionis

ALNY: Alnylam (covered by Tazeen Ahmad)

AZN: AstraZeneca (covered by Sachin Jain, Graham Parry)

XBI: S&P Biotech ETF

TTR: transthyretin

CM: cardiomyopathy

UBE3A: drug target

ASO: antisense

EEG: electroencephalogram

SD: single digit

## Price objective basis & risk

### Ionis (IONS)

Our \$62 price objective (PO) is based on a risk-adjusted DCF analysis, in which we assume: (1) risk-adjustment to pipeline programs based on abundance and strength of supportive clinical data, with <30% POS generally assigned to early-stage programs vs. >50% POS for mid-to-late stage assets, (2) the biggest value drivers in our DCF valuation are Wainua, Olezarsen, and Spinraza, (3) we assign marginal value to more speculative, early-stage program, (4) we assume 9.5% discount rate and 0% terminal growth rate.

Downside risks to our PO: 1) key product sales underperform relative to our forecast, 2) failure of key clinical trials, 3) competitor clinical data outperform vs. our expectation.

Upside risks to our PO: 1) delay to regulatory approval of competitors' drug products, 2) failure of competitors' clinical trials, 3) better than expected clinical data readouts

## Analyst Certification

I, Jason M. Gerberry, hereby certify that the views expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the specific recommendations or view expressed in this research report.

### US - Specialty Pharma & Biotechnology Coverage Cluster

Investment rating	Company	BofA Ticker	Bloomberg symbol	Analyst
<b>BUY</b>				
	Arcellx, Inc.	ACLX	ACLX US	Jason M. Gerberry
	Arrowhead Pharmaceuticals	ARWR	ARWR US	Jason M. Gerberry
	bluebird bio	BLUE	BLUE US	Jason M. Gerberry
	Exelixis	EXEL	EXEL US	Jason M. Gerberry
	Immunovant, Inc.	IMVT	IMVT US	Jason M. Gerberry
	Intra-Cellular Therapies	ITCI	ITCI US	Jason M. Gerberry
	Ionis	IONS	IONS US	Jason M. Gerberry
	Jazz Pharmaceuticals	JAZZ	JAZZ US	Jason M. Gerberry
	Lyra Therapeutics	LYRA	LYRA US	Jason M. Gerberry
	Oculis Holding AG	OCS	OCS US	Jason M. Gerberry
	Relay Therapeutics	RLAY	RLAY US	Jason M. Gerberry
	Tarsus Pharmaceuticals	TARS	TARS US	Jason M. Gerberry
	Teva Pharmaceuticals	TEVA	TEVA US	Jason M. Gerberry
	Vaxcyte Inc	PCVX	PCVX US	Jason M. Gerberry
	Xenon Pharmaceuticals	XENE	XENE US	Jason M. Gerberry
<b>NEUTRAL</b>				
	Alkermes	ALKS	ALKS US	Jason M. Gerberry
	Amphastar Pharmaceuticals	AMPH	AMPH US	Jason M. Gerberry
	Axsome Therapeutics	AXSM	AXSM US	Jason M. Gerberry
	Galapagos	GLPG	GLPG US	Jason M. Gerberry
	ProKidney Corp	PROK	PROK US	Jason M. Gerberry
	Roivant	ROIV	ROIV US	Chi M. Fong
<b>UNDERPERFORM</b>				
	Bausch Health Cos Inc	BHC	BHC US	Jason M. Gerberry
	FibroGen Inc.	FGEN	FGEN US	Jason M. Gerberry
	Harmony Biosciences	HRMY	HRMY US	Jason M. Gerberry
	Organon	OGN	OGN US	Jason M. Gerberry
	Viartis Inc.	VTRS	VTRS US	Jason M. Gerberry

## iQmethod<sup>SM</sup> Measures Definitions

### Business Performance

Return On Capital Employed

Return On Equity

Operating Margin

Earnings Growth

Free Cash Flow

### Quality of Earnings

Cash Realization Ratio

Asset Replacement Ratio

Tax Rate

Net Debt-To-Equity Ratio

Interest Cover

### Valuation Toolkit

Price / Earnings Ratio

Price / Book Value

Dividend Yield

Free Cash Flow Yield

Enterprise Value / Sales

EV / EBITDA

### Numerator

$\text{NOPAT} = (\text{EBIT} + \text{Interest Income}) \times (1 - \text{Tax Rate}) + \text{Goodwill Amortization}$

Net Income

Operating Profit

Expected 5 Year CAGR From Latest Actual

Cash Flow From Operations – Total Capex

### Numerator

Cash Flow From Operations

Capex

Tax Charge

Net Debt = Total Debt – Cash & Equivalents

EBIT

### Numerator

Current Share Price

Current Share Price

Annualised Declared Cash Dividend

Cash Flow From Operations – Total Capex

$\text{EV} = \text{Current Share Price} \times \text{Current Shares} + \text{Minority Equity} + \text{Net Debt} +$

Other LT Liabilities

Enterprise Value

### Denominator

$\text{Total Assets} - \text{Current Liabilities} + \text{ST Debt} + \text{Accumulated Goodwill}$

Amortization

Shareholders' Equity

Sales

N/A

N/A

### Denominator

Net Income

Depreciation

Pre-Tax Income

Total Equity

Interest Expense

### Denominator

Diluted Earnings Per Share (Basis As Specified)

Shareholders' Equity / Current Basic Shares

Current Share Price

$\text{Market Cap} = \text{Current Share Price} \times \text{Current Basic Shares}$

Sales

Basic EBIT + Depreciation + Amortization

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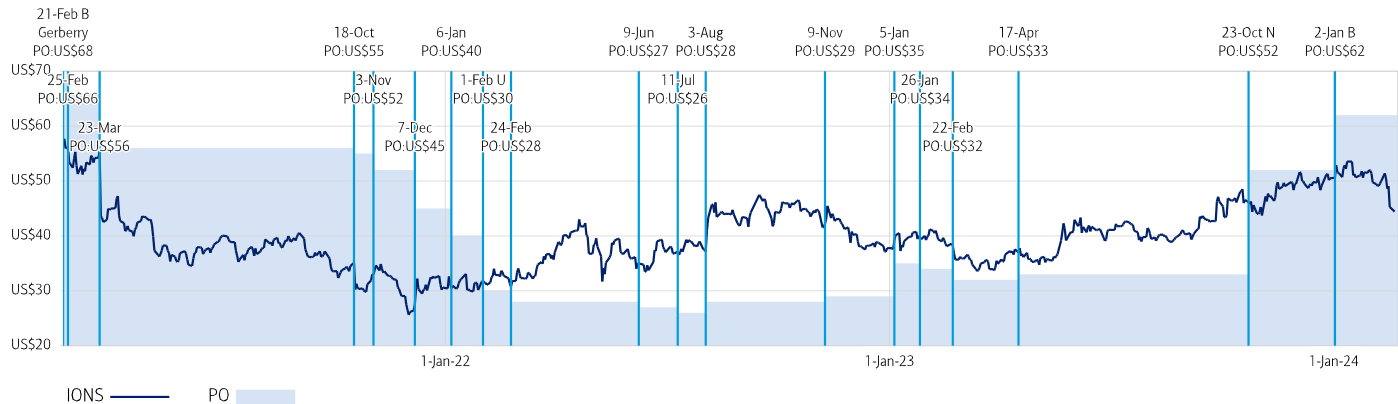
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## Important Disclosures

### Ionis (IONS) Price Chart



B: Buy, N: Neutral, U: Underperform, PO: Price Objective, NA: No longer valid, NR: No Rating

The Investment Opinion System is contained at the end of the report under the heading "Fundamental Equity Opinion Key". Dark grey shading indicates the security is restricted with the opinion suspended. Medium grey shading indicates the security is under review with the opinion withdrawn. Light grey shading indicates the security is not covered. Chart is current as of a date no more than one trading day prior to the date of the report.

### Equity Investment Rating Distribution: Health Care Group (as of 31 Dec 2023)

Coverage Universe	Count	Percent	Inv. Banking Relationships <sup>R1</sup>	Count	Percent
Buy	234	60.94%	Buy	115	49.15%
Hold	80	20.83%	Hold	36	45.00%
Sell	70	18.23%	Sell	29	41.43%

### Equity Investment Rating Distribution: Global Group (as of 31 Dec 2023)

Coverage Universe	Count	Percent	Inv. Banking Relationships <sup>R1</sup>	Count	Percent
Buy	1895	53.62%	Buy	1083	57.15%
Hold	832	23.54%	Hold	454	54.57%
Sell	807	22.84%	Sell	383	47.46%

<sup>R1</sup> Issuers that were investment banking clients of BofA Securities or one of its affiliates within the past 12 months. For purposes of this Investment Rating Distribution, the coverage universe includes only stocks. A stock rated Neutral is included as a Hold, and a stock rated Underperform is included as a Sell.

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