

Ionis Pharmaceuticals Inc

'25 guidance raised on licensing deal, focus on SHTG efficacy data in 3Q

1Q revs of \$132M broadly in-line, '25 rev guide raise to \$725-750M above our estimates and consensus

IONS reported 1Q25 results and hosted a call, we also caught up with management afterwards. 1Q25 revenues of \$132M between UBSe (\$141M) and Bloomberg consensus (\$129M), non-GAAP operating loss of -\$117M above UBSe (-\$145M) and cons. (-\$136M). Guidance raised on sapablursen licensing to Ono (announced 3/11: \$280M upfront, recognized in 2Q); mgmt now expects revenues \$725-750M vs > \$600M prior (UBSe/cons \$666/651M into print), non-GAAP operating loss <\$375M vs <\$495M prior (UBSe/cons \$450/473M into print). Cash guide also raised to ~\$1.9B exiting '25 (vs ~\$1.7B prior, UBSe ~\$1.6B into print). In '25, mgmt noted Angelman Ph3 initiation on track for 1H (will start in 2Q); Ph3 efficacy data in SHTG refined to 3Q from 2H—mgmt noted clarity on CORE/CORE2 trial logistics (last patient dosing, setting date for database lock) allowed greater precision on timing the readout. Tryngolza launch ongoing in FCS (\$6M in first full Q of sales), IONS readying for 2nd independent US launch (donidalorsen in HAE, PDUFA 8/21).

Focus on call around olezarsen SHTG data expectations—CORE/CORE2 readout timing refined to 3Q from 2H25

Several Qs on the call around expectations for acute pancreatitis (AP) data in SHTG—mgmt highlighted despite being on background standard of care therapy, CORE/CORE2 baseline TGs were 836/749 mg/dL (~50% were high-risk at >880 mg/dL) and 22/13% of patients had prior AP. On CORE/CORE2 data in 3Q—mgmt noted plans to present topline from both studies together (primary endpoint TG reduction at 6 months). Meta-analysis on pooled AP events from both studies at 12 months is planned and IONS will share with topline if available.

Pooled AP event data from CORE/CORE2 should improve powering (limited read from ESSENCE)—regulatory alignment on AP meta-analysis

On the ESSENCE safety study (readout in 2Q ahead of CORE/CORE2), mgmt noted on our callback they expect to see little/no AP events in ESSENCE given patient TGs in the study are <500 mg/dL (limited AP risk in this population)—limited/no read to baseline AP event rate in CORE/CORE2 where TGs are >500 mg/dL and AP risk exponentially higher. Mgmt highlighted regulatory authorities have aligned on use of pooled AP event data from CORE/CORE2 in the statistical analysis plan (enhances power), potential for SHTG indication/label to include AP though difficult to predict. On what AP event rates could look like across CORE/CORE2 compared to BALANCE in FCS (HR 0.12 for AP events at

Equities

United States
Biotechnology

12-month rating **Neutral ***

12m price target **US\$45.00**

Price (30 Apr 2025) **US\$30.71**

RIC: IONS.O BBG: IONS US

Trading data and key metrics

52-wk range	US\$51.86-25.51
Market cap.	US\$4.85b
Shares o/s	158m (COM)
Free float	95%
Avg. daily volume ('000)	1,727
Avg. daily value (m)	US\$53.2
Common s/h equity (12/25E)	US\$0.05b
P/BV (12/25E)	>100
Net debt to EBITDA (12/25E)	0.4x

EPS (UBS, diluted) (USD)

	12/25E	
	UBS	Cons.
Q1E	(1.30)	(1.12)
Q2E	(1.13)	(1.00)
Q3E	(0.74)	(0.91)
Q4E	(1.04)	(0.91)
12/25E	(4.21)	(3.86)
12/26E	(2.50)	(3.15)
12/27E	(1.35)	(1.59)

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Highlights (US\$m)	12/22	12/23	12/24	12/25E	12/26E	12/27E	12/28E	12/29E
Revenues	587	788	705	666	1,057	1,416	1,844	2,360
EBIT (UBS)	(410)	(353)	(475)	(574)	(326)	(143)	58	373
Net earnings (UBS)	(270)	(366)	(454)	(666)	(418)	(239)	(41)	279
EPS (UBS, diluted) (US\$)	(1.90)	(2.56)	(3.03)	(4.21)	(2.50)	(1.35)	(0.22)	1.42
DPS (net) (US\$)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Net (debt) / cash	632	928	942	208	(298)	(597)	(716)	(539)
Profitability/valuation	12/22	12/23	12/24	12/25E	12/26E	12/27E	12/28E	12/29E
EBIT (UBS) margin %	(69.8)	(44.8)	(67.4)	(86.2)	(30.8)	(10.1)	3.1	15.8
ROIC (EBIT) %	164.7	62.2	65.0	96.3	72.2	54.5	(87.2)	224.3
EV/EBITDA (UBS core) x	NM	NM	NM	NM	NM	NM	57.7	12.2
P/E (UBS, diluted) x	(20.3)	(16.2)	(14.2)	(7.3)	(12.3)	(22.7)	NM	21.7
Equity FCF (UBS) yield %	(5.4)	(6.4)	(8.7)	(15.1)	(10.4)	(6.2)	(2.5)	3.7
Dividend yield (net) %	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Source: Company accounts, LSEG Eikon, UBS estimates. Metrics marked as (UBS) have had analyst adjustments applied. Valuations: based on an average share price that year, (E): based on a share price of US\$ 30.71 on 30-Apr-2025

This report has been prepared by UBS Securities LLC. * Exception to core rating bands; See page . **ANALYST CERTIFICATION AND REQUIRED DISCLOSURES, INCLUDING INFORMATION ON THE QUANTITATIVE RESEARCH REVIEW PUBLISHED BY UBS, BEGIN ON PAGE 7.** UBS does and seeks to do business with companies covered in its research reports. As a result, investors should be aware that the firm may have a conflict of interest that could affect the objectivity of this report. Investors should consider this report as only a single factor in making their investment decision.

12mos), mgmt reminded us BALANCE in FCS had much higher baseline TGs (~2600 mg/dL) and ~70% of patients had prior AP—though mgmt also noted the SHTG studies CORE/CORE2 are ~10/6x the size and 22/13% of patients had AP history.

We see IONS as well-capitalized especially in context of recent guidance raise (~\$2.3B of cash exiting FY24, now expect +\$200M from prior guide to ~\$1.9B exiting FY25), think pipeline attractive long-term—Angelman (Ph3 starting in 2Q) and Tau (with BILB, Ph2 data '26) could drive upside to our base case. SHTG Ph3 data in 3Q is a key near-term focus & success on AP reduction would be upside, though we think investors may take some time to buy into the commercial story (though strong AP data may change this). TTR silencer Wainua in ATTR-PN (marketed w/ AZN) remains a focus for shares; though with data not coming until 2H26 we think ATTR-CM expansion a longer-term story—expectations for eventual readout generally positive (largest & longest ATTR-CM trial), though we think ALNY's silencer Amvuttra has meaningful first-mover advantage (approved 3/20/2025).

Valuation:

Our valuation is based on an EV/Sales multiple and is informed by our DCF sensitivity.

Ionis Pharmaceuticals Inc (IONS.O)

Income Statement (US\$m)	12/22	12/23	12/24	12/25E	%ch	12/26E	%ch	12/27E	12/28E	12/29E
Revenues	587	788	705	666	-5.5	1,057	58.7	1,416	1,844	2,360
Gross profit	573	779	694	660	-4.9	1,017	54.0	1,338	1,688	2,139
EBITDA (UBS)	(393)	(340)	(463)	(561)	-21.2	(307)	45.2	(119)	87	408
Depreciation & amortisation	(17)	(13)	(12)	(13)	-10.4	(18)	-38.7	(23)	(29)	(35)
EBIT (UBS)	(410)	(353)	(475)	(574)	-20.9	(326)	43.3	(143)	58	373
Associates & investment income	(7)	(2)	0	0	-	0	-	0	0	0
Other non-operating income	142	(34)	(72)	(78)	-7.9	(78)	0.0	(81)	(84)	(79)
Net interest	17	55	87	(14)	-	(15)	-3.7	(15)	(15)	(15)
Exceptionals (incl goodwill)	0	0	0	0	-	0	-	0	0	0
Pre-tax profit	(258)	(334)	(460)	(666)	-44.8	(418)	37.3	(239)	(41)	279
Tax	(12)	(32)	6	0	-	0	-	0	0	0
Profit after tax	(270)	(366)	(454)	(666)	-46.8	(418)	37.3	(239)	(41)	279
Preference dividends	0	0	0	0	-	0	-	0	0	0
Minorities	0	0	0	0	-	0	-	0	0	0
Extraordinary items	0	0	0	0	-	0	-	0	0	0
Net earnings (local GAAP)	(270)	(366)	(454)	(666)	-46.8	(418)	37.3	(239)	(41)	279
Net earnings (UBS)	(270)	(366)	(454)	(666)	-46.8	(418)	37.3	(239)	(41)	279
Tax rate (%)	0.0	0.0	0.0	0.0	-	0.0	-	0.0	0.0	0.0
Per Share (US\$)	12/22	12/23	12/24	12/25E	%ch	12/26E	%ch	12/27E	12/28E	12/29E
EPS (UBS, diluted)	(1.90)	(2.56)	(3.03)	(4.21)	-39.0	(2.50)	40.6	(1.35)	(0.22)	1.42
EPS (local GAAP, diluted)	(1.90)	(2.56)	(3.03)	(4.21)	-39.0	(2.50)	40.6	(1.35)	(0.22)	1.42
EPS (UBS, basic)	(1.90)	(2.56)	(3.03)	(4.21)	-39.0	(2.50)	40.6	(1.35)	(0.22)	1.42
DPS (net) (US\$)	0.00	0.00	0.00	0.00	-	0.00	-	0.00	0.00	0.00
Cash EPS (UBS, diluted) ¹	(1.78)	(2.47)	(2.95)	(4.12)	-39.9	(2.39)	42.0	(1.22)	(0.06)	1.59
Book value per share	4.03	2.68	3.73	0.29	-92.2	(1.37)	-	(1.75)	(0.96)	1.42
Average shares (diluted)	142	143	150	158	5.6	167	5.6	177	187	197
Balance Sheet (US\$m)	12/22	12/23	12/24	12/25E	%ch	12/26E	%ch	12/27E	12/28E	12/29E
Cash and equivalents	1,987	2,331	2,298	1,564	-31.9	1,057	-32.4	759	640	817
Other current assets	216	311	323	305	-5.5	484	58.7	648	844	1,080
Total current assets	2,203	2,642	2,620	1,869	-28.7	1,541	-17.5	1,407	1,483	1,897
Net tangible fixed assets	74	71	94	131	38.7	168	28.3	207	249	294
Net intangible fixed assets	0	0	0	0	-	0	-	0	0	0
Investments / other assets	257	277	289	388	34.2	416	7.2	450	493	531
Total assets	2,534	2,990	3,004	2,387	-20.5	2,124	-11.0	2,063	2,225	2,722
Trade payables & other ST liabilities	312	404	309	235	-23.9	253	7.6	275	304	329
Short term debt	0	44	0	0	-	0	-	0	0	0
Total current liabilities	312	448	309	235	-23.9	253	7.6	275	304	329
Long term debt	1,355	1,359	1,355	1,355	0.0	1,355	0.0	1,355	1,355	1,355
Other long term liabilities	295	797	751	751	0.0	751	0.0	751	751	751
Preferred shares	0	0	0	0	-	0	-	0	0	0
Total liabilities (incl pref shares)	1,961	2,603	2,415	2,341	-3.1	2,359	0.8	2,381	2,410	2,435
Common s/h equity	573	387	588	46	-92.2	(235)	-	(318)	(185)	287
Minority interests	0	0	0	0	-	0	-	0	0	0
Total liabilities & equity	2,534	2,990	3,004	2,387	-20.5	2,124	-11.0	2,063	2,225	2,722
Cash Flow (US\$m)	12/22	12/23	12/24	12/25E	%ch	12/26E	%ch	12/27E	12/28E	12/29E
Net income (before pref divs)	(270)	(366)	(454)	(666)	-46.8	(418)	37.3	(239)	(41)	279
Depreciation & amortisation	17	13	12	13	10.4	18	38.7	23	29	35
Net change in working capital	8	(77)	(209)	(155)	25.9	(189)	-21.6	(176)	(210)	(249)
Other operating	(29)	81	150	124	-17.6	137	10.7	155	175	192
Operating cash flow	(274)	(349)	(501)	(684)	-36.6	(451)	34.1	(236)	(48)	257
Tangible capital expenditure	(16)	(24)	(45)	(50)	-9.6	(55)	-11.5	(62)	(71)	(79)
Intangible capital expenditure	(4)	(4)	(5)	0	-	0	-	0	0	0
Net (acquisitions) & disposals	0	0	0	0	-	0	-	0	0	0
Other investing	(243)	(186)	(84)	1,000	-	460	-54.0	100	200	0
Investing cash flow	(263)	(214)	(134)	950	-	405	-57.4	38	129	(79)
Equity dividends paid	0	0	0	0	-	0	-	0	0	0
Share issues / (buybacks)	6	49	523	0	-	0	-	0	0	0
Other financing	(11)	595	(45)	0	-	0	-	0	0	0
Change in debt & pref shares	(51)	0	0	0	-	0	-	0	0	0
Financing cash flow	(55)	644	478	0	-	0	-	0	0	0
Cash flow inc/(dec) in cash	(592)	81	(157)	266	-	(47)	-	(198)	81	177
FX / non cash items	464	263	123	(1,000)	-	(460)	54.0	(100)	(200)	0
Balance sheet inc/(dec) in cash	(128)	344	(34)	(734)	NM	(507)	31.0	(298)	(119)	177

Source: Company accounts, UBS estimates. (UBS) metrics use reported figures which have been adjusted by UBS analysts.¹ Cash EPS (UBS, diluted) is calculated using UBS net income adding back depreciation and amortization.

Ionis Pharmaceuticals Inc (IONS.O)

Valuation (x)	12/22	12/23	12/24	12/25E	12/26E	12/27E	12/28E	12/29E
P/E (local GAAP, diluted)	NM	NM	NM	NM	NM	NM	NM	21.7
P/E (UBS, diluted)	(20.3)	(16.2)	(14.2)	(7.3)	(12.3)	(22.7)	NM	21.7
P/CEPS	NM	NM	NM	NM	NM	NM	NM	19.3
Equity FCF (UBS) yield %	(5.4)	(6.4)	(8.7)	(15.1)	(10.4)	(6.2)	(2.5)	3.7
Dividend yield (net) %	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
P/BV	9.6	15.4	11.6	NM	NM	NM	NM	21.7
EV/revenues (core)	7.3	5.9	7.3	5.3	3.3	3.4	2.7	2.1
EV/EBITDA (UBS core)	NM	NM	NM	NM	NM	NM	57.7	12.2
EV/EBIT (core)	NM	NM	NM	NM	NM	NM	86.6	13.3
EV/OpFCF (core)	NM	NM	NM	NM	NM	NM	>100	15.2
EV/op. invested capital	NM	NM	NM	NM	NM	NM	NM	29.9
Enterprise value (US\$m)	12/22	12/23	12/24	12/25E	12/26E	12/27E	12/28E	12/29E
Market cap.	5,483	5,896	6,371	4,849	4,849	4,849	4,849	4,849
Net debt (cash)	(939)	(939)	(939)	(939)	(939)	448	656	656
Buy out of minorities	0	0	0	0	0	0	0	0
Pension provisions/other	0	0	0	0	0	0	0	0
Total enterprise value	4,545	4,958	5,432	3,911	3,911	5,297	5,506	5,506
Non core assets	(257)	(277)	(289)	(388)	(416)	(450)	(493)	(531)
Core enterprise value	4,288	4,680	5,143	3,523	3,495	4,847	5,013	4,974
Growth (%)	12/22	12/23	12/24	12/25E	12/26E	12/27E	12/28E	12/29E
Revenue	(27.5)	34.2	(10.5)	(5.5)	58.7	33.9	30.2	28.0
EBITDA (UBS)	NM	13.5	(36.1)	(21.2)	45.2	61.2	-	NM
EBIT (UBS)	NM	13.9	(34.6)	(20.9)	43.3	56.2	-	NM
EPS (UBS, diluted)	NM	(34.5)	(18.4)	(39.0)	40.6	45.9	83.8	-
Net DPS	-	-	-	-	-	-	-	-
Margins & Profitability (%)	12/22	12/23	12/24	12/25E	12/26E	12/27E	12/28E	12/29E
Gross profit margin	NM	NM	NM	NM	NM	NM	NM	NM
EBITDA margin	NM	NM	NM	NM	NM	NM	4.7	17.3
EBIT (UBS) margin	(69.8)	(44.8)	(67.4)	(86.2)	(30.8)	(10.1)	3.1	15.8
Net earnings (UBS) margin	NM	NM	NM	NM	NM	NM	NM	11.8
ROIC (EBIT)	NM	62.2	65.0	NM	72.2	54.5	NM	NM
ROIC post tax	NM	62.2	65.0	NM	72.2	54.5	NM	NM
ROE (UBS)	(40.1)	(76.2)	(93.1)	(210.1)	442.6	86.3	16.3	>500
Capital structure & Coverage (x)	12/22	12/23	12/24	12/25E	12/26E	12/27E	12/28E	12/29E
Net debt / EBITDA	1.6	2.7	2.0	0.4	(1.0)	(5.0)	8.2	1.3
Net debt / total equity %	(110.4)	(240.1)	(160.2)	NM	(127.0)	(187.5)	NM	188.0
Net debt / (net debt + total equity) %	NM	NM	NM	NM	NM	NM	NM	65.3
Net debt/EV %	(16.8)	(15.7)	(17.2)	(14.7)	1.2	8.4	11.9	11.4
Capex / depreciation %	109.7	NM	NM	NM	NM	NM	NM	NM
Capex / revenue %	2.7	3.0	6.4	7.4	5.2	4.4	3.9	3.4
EBIT / net interest	-	-	-	-	-	-	3.8	24.8
Dividend cover (UBS)	-	-	-	-	-	-	-	-
Div. payout ratio (UBS) %	-	-	-	-	-	-	-	-
Revenues by division (US\$m)	12/22	12/23	12/24	12/25E	12/26E	12/27E	12/28E	12/29E
Others	587	788	705	666	1,057	1,416	1,844	2,360
Total	587	788	705	666	1,057	1,416	1,844	2,360
EBIT (UBS) by division (US\$m)	12/22	12/23	12/24	12/25E	12/26E	12/27E	12/28E	12/29E
Others	(410)	(353)	(475)	(574)	(326)	(143)	58	373
Total	(410)	(353)	(475)	(574)	(326)	(143)	58	373

Source: Company accounts, UBS estimates. (UBS) metrics use reported figures which have been adjusted by UBS analysts.

Forecast returns

Forecast price appreciation	46.5%
Forecast dividend yield	0.0%
Forecast stock return	46.5%
Market return assumption	8.6%
Forecast excess return	37.9%

Company Description

IONS discovers and develops RNA-targeted therapeutics. The company has created an efficient and broadly applicable drug discovery platform leveraging management expertise in antisense oligonucleotide (ASO) therapeutics that the company believes has fundamentally changed medicine and transformed the lives of people with devastating diseases. The large, diverse, and advancing pipeline of the company has over 45 drug candidates designed to address a broad spectrum of therapeutic areas, such as neurodegenerative diseases, cardiometabolic diseases and others.

Valuation Method and Risk Statement

Valuation method: Our price target is derived using a discounted peak sales multiple. We review peak-year sales multiple of a set of comparable companies that we believe represent the risk profile of IONS. We specifically review companies with clinical stage RNAi-based therapeutics assets as well as companies with a focus on neuroscience. In addition, our price target is also supported by our 10-year discounted cash flow (DCF) analysis.

Risks: We believe the risks for IONS shareholders include 1) Spinraza royalties and R&D collaboration revenues from existing partnerships could decline, 2) stable revenues from Tegsedi may not be maintained, 3) potential for competitive pressures in recruiting patients in clinical trials, and 4) clinical trial failure of the ongoing CARDIO-TTTransform trial. Separately, we note the stock may also be subject to broader market risks typical of the SMID cap biotech segment that include changes in FDA guidelines, payer pressure, and key management changes.

Quantitative Research Review

UBS Global Research publishes a quantitative assessment of its analysts' responses to certain questions about the likelihood of an occurrence of a number of short term factors in a product known as the 'Quantitative Research Review'. The views for this month can be found below. Views contained in this assessment on a particular stock reflect only the views on those short term factors which are a different timeframe to the 12-month timeframe reflected in any equity rating set out in this note. For previous responses please make reference to (i) previous UBS Global Research reports; and (ii) where no applicable research report was published that month, the Quantitative Research Review which can be found at <https://neo.ubs.com/quantitative>, or contact your UBS sales representative for access to the report or the Quantitative Research Team on ubs-quant-answers@ubs.com. A consolidated report which contains all responses is also available and again you should contact your UBS sales representative for details and pricing or the Quantitative Research Team on the email above.

Ionis Pharmaceuticals Inc

Question	Response
1. Is the industry structure facing the firm likely to improve or deteriorate over the next six months? Rate on a scale of 1-5 (1 = getting worse, 3 = no change, 5 = getting better, N/A = no view)	3
2. Is the regulatory/government environment facing the firm likely to improve or deteriorate over the next six months? Rate on a scale of 1-5 (1 = getting tougher, 3 = no change, 5 = getting better, N/A = no view)	3
3. Over the last 3-6 months in broad terms have things been improving/no change/getting worse for this stock? Rate on a scale of 1-5 (1 = getting a lot worse, 3 = not much change, 5 = getting a lot better, N/A = no view)	4
4. Relative to the current CONSENSUS EPS forecast, is the next company EPS update likely to lead to: (1 = negative surprise vs consensus, 3 = in-line with consensus, 5 = positive surprise vs consensus expectations, N/A = no view)	3
5. What's driving the difference?	
6. Relative to YOUR current earnings forecast, is there relatively greater risk at the next earnings result of: (1 = downside skew risk to earnings, 3 = equal upside or downside risk to earnings, 5 = upside skew risk to earnings, N/A = no view)	3
7. What's driving the difference?	
8. Is there an upcoming catalyst for the company over the next three months?	No Catalyst
9. Is there an actual or approximate date for the catalyst?	
10. Is the catalyst date an actual or approximate date?	
11. What is the catalyst?	

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12-Month Rating	Definition	Coverage ¹	IB Services ²
Buy	FSR is > 6% above the MRA.	52%	24%
Neutral	FSR is between -6% and 6% of the MRA.	40%	20%
Sell	FSR is > 6% below the MRA.	8%	22%
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Buy	Stock price expected to rise within three months from the time the rating was assigned because of a specific catalyst or event.	<1%	<1%
Sell	Stock price expected to fall within three months from the time the rating was assigned because of a specific catalyst or event.	<1%	<1%

Source: UBS. Rating allocations are as of 31 March 2025.

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2:Percentage of companies within the 12-month rating category for which investment banking (IB) services were provided within the past 12 months.

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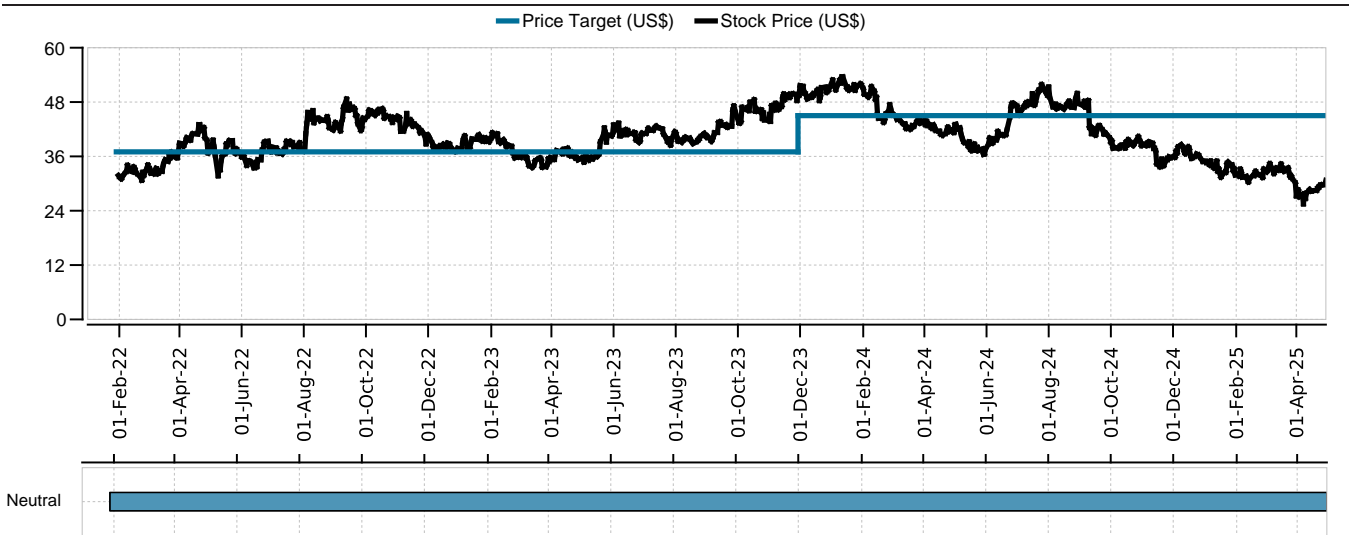
Company Name	Reuters	12-month rating	Price	Price date
Ionis Pharmaceuticals Inc ^{16,28,20}	IONS.O	Neutral (CBE)	US\$30.71	30 Apr 2025

Source: UBS Global Research; LSEG Eikon. All prices as of local market close. Ratings in this table are the most current published ratings prior to this report. They may be more recent than the stock pricing date.

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Ionis Pharmaceuticals Inc (US\$)



Date	Stock Price (US\$)	Price Target (US\$)	Rating
2022-01-28	31.68	37.00	Neutral
2023-11-28	48.34	45.00	Neutral

Source: UBS Global Research; LSEG Eikon as of 30-Apr-2025. All prices as of local market close. Ratings as of date shown.

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