

Oryzon Genomics

Q124 results

Doubling down on clinical activity in 2024

Oryzon's Q124 results emphasised the company's focus on advancing and expanding its CNS and oncology pipelines, driven by its core assets, vafidemstat and iadademstat. Operating performance was in line, with the lower opex (37% y-o-y decline to €3.2m) driven by reduced R&D spending following completion of the Phase IIb PORTICO trial. Notwithstanding the mixed PORTICO results in borderline personality disorder (BPD), we expect clinical activity to pick up in the coming months, with the initiation of the iadademstat combination studies in first-line AML (Phase Ib) and SCLC (Phase Ib/II) in Q224, and the planned end of Phase II (EoP2) meeting with the FDA in BPD. We also expect interim readouts from the Phase Ib FRIDA study in advanced AML (to be presented at the European Hematology Association conference in June this year). We keep our assumptions broadly unchanged and incorporate the latest net debt figure (€3.7m at end-Q124) in our estimates. Our valuation adjusts to €12.1/share.

| Year end | Revenue (€m) | PBT* (€m) | EPS* (€) | DPS (€) | P/E (x) | Yield (%) |
|----------|--------------|-----------|----------|---------|---------|-----------|
| 12/22 | 15.7 | (6.3) | (0.07) | 0.0 | N/A | N/A |
| 12/23 | 14.2 | (6.0) | (0.06) | 0.0 | N/A | N/A |
| 12/24e | 12.9 | (4.1) | (0.03) | 0.0 | N/A | N/A |
| 12/25e | 33.7 | 15.4 | 0.29 | 0.0 | N/A | N/A |

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

2024 to be a meaningful year for CNS pipeline

Full analysis of the PORTICO data is ongoing (although more protracted than anticipated), and we now expect the FDA EoP2 meeting to take place in Q324 with an outcome by end-2024, a key catalyst for investor attention. The IND submission for the HOPE trial in Kabuki syndrome remains on track for 2024, which we see as another inflection point, given the unmet need. The EVOLUTION Phase IIb trial in schizophrenia continues to recruit patients and we expect a timeline update in the near term. Oryzon's IP position, while already strong (patent protection to 2037), should be bolstered with additional patents to be granted in the [EU](#) and South Korea.

Oncology pipeline continues to make progress

Iadademstat, Oryzon's oncology asset, is being tested in several ongoing and planned trials as a combination treatment in both haematological and solid cancers. We expect the 2024 focus to be on the Phase Ib FRIDA trial in relapsed/refractory (r/r) acute myeloid leukaemia (AML), where a third cohort (6–7 patients) is currently being recruited, as well as the planned launch of the CRADA-MSKCC trial in first-line small-cell lung cancer (SCLC), a precursor to the larger, randomised STELLAR trial.

Valuation: Adjusts to €748.8m or €12.1 per share

We have made minor adjustments to our estimates for the Q124 performance, rolled forward our model and updated the latest net debt figure; however, our underlying long-term assumptions remain unchanged. Our valuation adjusts slightly to €748.8m or €12.1/share (€732.6m or €11.8/share previously). Based on the period-end gross cash of €10.7m, and our burn rate projections, we continue to estimate that the company is funded into FY25 (excluding debt repayments), past key regulatory and clinical milestones.

Pharma and biotech

8 May 2024

Price €1.95
Market cap €122m

| | |
|--------------------------------|-----------------------|
| Net debt (€m) at 31 March 2024 | 3.7 |
| Shares in issue | 62.0m |
| Free float | 82% |
| Code | ORY |
| Primary exchange | Madrid Stock Exchange |
| Secondary exchange | N/A |

Share price performance



| | | | |
|------------------|-------|-------|--------|
| % | 1m | 3m | 12m |
| Abs | (5.7) | 4.4 | (8.8) |
| Rel (local) | (7.1) | (6.9) | (24.7) |
| 52-week high/low | | €2.29 | €1.60 |

Business description

Oryzon Genomics is a Spanish biotech focused on epigenetics. Iadademstat is being explored for acute leukaemias, small-cell lung cancer and neuroendocrine tumours. Vafidemstat, its central nervous system asset, has completed several Phase IIa trials and a Phase IIb trial in borderline personality disorder (now the lead study), and is in a Phase IIb trial in schizophrenia.

Next events

| | |
|---------------------------------|-----------|
| EoP2 meeting request (BPD) | Q324 |
| FRIDA trial interim data | June 2024 |
| HOPE trial initiation | 2024 |
| EVOLUTION trial timeline update | 2024 |

Analysts

| | |
|--------------------|---------------------|
| Soo Romanoff | +44 (0)20 3077 5700 |
| Jyoti Prakash, CFA | +44 (0)20 3077 5700 |
| Dr Arron Aatkar | +44 (0)20 3077 5700 |

healthcare@edisongroup.com
[Edison profile page](#)

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Clinical action expected to take wing in 2024

Oryzon's [Q124 results](#) summarised an active period focused on advancing and expanding the company's development programmes for central nervous system (CNS) and oncology indications. The company has a broad pipeline of programmes, underscored by its focus on Lysine-specific histone demethylase 1 (LSD1) inhibition, a validated therapeutics target in both CNS and oncology. Clinical assets include vafidemstat for CNS conditions, and iadademstat as a potential treatment for haematological and solid cancers. The company's ongoing programmes are a mix of self-funded, investigator-sponsored and collaborative studies. We expect the remainder of 2024 to be eventful for the company in terms of pipeline advancements, and note the following as the key upcoming milestones:

- EoP2 meeting with the FDA for vafidemstat as a treatment for BPD (following the results of PORTICO announced in January 2024) – Oryzon's most clinically advanced programme is evaluating vafidemstat as a treatment for BPD. PORTICO, a Phase IIb study, was not able to meet its primary endpoint (refer to our [note](#) for more details); however, two key secondary endpoints showed statistically significant improvements, indicating potential benefit, especially in light of the [unmet need](#) in the space (as there are no approved drugs specifically for BPD). Oryzon is in the process of conducting a full data analysis with plans to subsequently approach the FDA for an EoP2 meeting to discuss the data and design for a potentially registrational Phase III trial. While we were previously expecting this meeting to take place in Q224, additional time may be required, and we now estimate the meeting to take place in Q324. We expect the EoP2 results (which we anticipate by Q424 at the latest) to be one of the most significant upcoming catalysts for the company, which if positive, could potentially enhance partnering discussions.
- CRADA-MSKCC study – A key development post-period was the [FDA clearance](#) for the investigational new drug (IND) application for a Phase I/II clinical trial to evaluate iadademstat in combination with checkpoint inhibitors for first-line, extensive-stage SCLC. This trial will be conducted under the cooperative research and development agreement (CRADA) signed with the National Cancer Institute (NCI) in the US. The trial will be sponsored by the NCI, and is due to commence in Q224 (45–50 patients expected to be recruited). The data from this study will refine the design for the larger, randomised Phase Ib/II STELLAR trial (sponsored by Oryzon), which will evaluate the same drug in the same indication. We see merit in employing this strategy, given that it de-risks the company's development plan. Moreover, preliminary data from the study may allow Oryzon to directly move the STELLAR trial to Phase II, foregoing the need for the Phase Ib dose finding and tolerability study. Management asserts that STELLAR could support an accelerated approval application, and plans to submit an IND application by end-2024.
- Interim data from the FRIDA study – Another catalyst, in our opinion, will be the interim data readout from the ongoing FRIDA study, which continues to enrol patients. This Phase Ib study is assessing iadademstat in combination with gilteritinib as a potential treatment for r/r AML in patients harbouring the FLT3 mutation. The study aims to recruit c 45 patients, of which 13 (across two cohorts) have completed the study, showing desirable safety and antileukemic activity, according to management. A third cohort is currently being recruited. Based on the results, Oryzon plans to discuss next steps with the FDA. We look forward to the interim data from the study, which management has indicated will be presented at the European Hematology Association conference to be held between 13 and 16 June 2024.

In addition to the self-sponsored FRIDA study, iadademstat is also being evaluated in combination with venetoclax and azacitidine in first-line AML patients under an investigator-sponsored Phase Ib

trial, led by Oregon Health & Science University (OHSU). The company expects to commence patient enrolment in Q224. Furthermore, Oryzon is also in the process of refining the final design the Phase I/II HOPE trial in Kabuki syndrome (a rare congenital disorder), with plans for IND application submission within 2024, with the trial potentially launching by end-2024. This trial will also be self-sponsored.

Financials: No surprises in Q124

Oryzon's Q124 results were broadly in line with expectations. R&D expenses, which account for the lion's share of the operating costs, declined materially to €2.4m (vs €3.8m in Q123). This was primarily attributed to the completion of the PORTICO trial in late-2023. R&D as a percentage of opex declined to 75% (vs 78.7% in Q123). Personnel expenses remained broadly flat at €0.87m (vs €0.85m in Q123). We note that Oryzon capitalises its R&D investments, reflecting this as other income to offset the R&D expenses booked in the income statement. As a result, other income for the period declined to €2.2m (vs €3.8m in Q123), mirroring the decline in R&D expenses. Net loss was reported at €1.1m, a c 30% improvement over the Q123 figure of €1.6m. While the company has not provided a cash flow statement with the Q124 release, we roughly calculate the Q124 free cash outflow to be c €3.2m (vs c €5m in Q123). Given the in-line performance, our FY23 and FY24 estimates remain largely unchanged.

At end-Q124, Oryzon had net debt of €3.7m. This includes €10.7m in cash and cash equivalents, €10.4m in short-term debt (bonds – €4.3m; credit institutions – €6.1m) and €4.1m in long-term bank debt. We remind that in November 2023, Oryzon had raised €45m in convertible debt (4,500 bonds worth €10,000 each; 48-month maturity), of which €10m has been drawn down to date (two €4m tranches disbursed in November and December 2023 and an additional €2m tranche in February 2024). Of the 1,000 bonds issued, 736 have been converted to equity as of 23 January 2024, against an issue of 3.05m shares of common stock. We note that there have been no further debt-to-equity conversions since January 2024, and hence, the number of shares outstanding remains unchanged at 62.0m.

Based on our projected cash burn rates (free cash outflow of €3.6m per quarter in FY24), we estimate the gross cash balance (excluding upcoming debt repayments) will support operations into FY25. We reiterate the upcoming bank debt maturing in FY24 (€5.6m), and estimate that the company will draw down a further €10m from the €45m financing facility during 2024 (c €2m drawn in February 2024). We also expect the remaining €25m of the facility to be utilised in FY25. We currently reflect these capital infusions as illustrative debt in our model.

Valuation

We presented our updated assumptions and valuation drivers in a [previous note](#), and these remain unchanged following the Q124 results. We have made only minor tweaks to our estimates to reflect the Q124 trend and have incorporated the latest net debt figure. This, along with rolling forward our model, results in our valuation adjusting slightly to €748.8m or €12.1 per share, from €732.6m or €11.8/share previously. A breakdown of our risk-adjusted net present value (NPV) valuation is shown in Exhibit 1.

Exhibit 1: Valuation of Oryzon

| Product | Indication | Launch | Peak sales (US\$m) | Value (€m) | Probability | rNPV (€m) | NPV/share (€/share) |
|----------------------------|----------------------------------|--------|--------------------|----------------|-------------|--------------|---------------------|
| ladademstat | 2L AML | 2029 | 555 | 527.7 | 30% | 150.8 | 2.4 |
| | 1L SCLC | 2030 | 720 | 617.9 | 20% | 116.7 | 1.9 |
| Vafidemstat | BPD | 2028 | 1,625 | 803.7 | 20% | 234.6 | 3.8 |
| | Schizophrenia, negative symptoms | 2029 | 702 | 566.3 | 15% | 117.5 | 1.9 |
| | Aggression related to AD | 2029 | 911 | 666.5 | 15% | 132.9 | 2.1 |
| Net debt at end-March 2024 | | | | (3.7) | 100% | (3.7) | (0.1) |
| Valuation | | | | 3,178.5 | | 748.8 | 12.1 |

Source: Edison Investment Research

We assume licensing deals in FY25 and FY26, associated with cash inflows that should support break-even in FY26. If Oryzon does not finalise a partnership deal, and self-commercialises all programmes, we estimate the need to raise a further €45m in funds across FY26 and FY27 (modelled as illustrative debt) before becoming self-sustainable in FY28. Assuming all funding requirements across FY24–27 (c €80m) are realised through equity raises, Oryzon would have to issue 41m shares (assuming the current trading price of €1.952/share). Our per share valuation would be diluted to €8.0/share, from €12.1/share currently (shares outstanding would increase from 62m to 103.0m).

Exhibit 2: Financial summary

| Accounts: Spanish GAAP. Year end 31 December (€000s) | 2021 | 2022 | 2023 | 2024e | 2025e |
|--|----------|----------|----------|----------|----------|
| INCOME STATEMENT | | | | | |
| Total revenues | 10,615 | 15,698 | 14,192 | 12,933 | 33,650 |
| Cost of sales | (746) | (464) | (244) | (317) | (333) |
| Gross profit | 9,869 | 15,234 | 13,948 | 12,617 | 33,317 |
| Gross margin % | 93% | 97% | 98% | 98% | 99% |
| SG&A (expenses) | (3,782) | (3,163) | (3,390) | (3,424) | (3,458) |
| R&D costs | (9,746) | (13,681) | (12,177) | (12,318) | (13,000) |
| Other income/(expense) | (3,203) | (3,714) | (2,777) | 70 | 0 |
| Exceptionals and adjustments | (4) | 0 | 0 | 0 | 0 |
| Reported EBITDA | (6,866) | (5,323) | (4,396) | (3,055) | 16,859 |
| Depreciation and amortisation | (144) | (167) | (153) | (129) | (111) |
| Reported EBIT | (7,011) | (5,490) | (4,549) | (3,185) | 16,748 |
| Finance income/(expense) | (169) | (1,067) | (1,555) | (912) | (1,352) |
| Other income/(expense) | 0 | 0 | 0 | 0 | 0 |
| Reported PBT | (7,180) | (6,557) | (6,104) | (4,097) | 15,396 |
| Income tax expense (includes exceptionals) | 2,493 | 2,325 | 2,751 | 2,538 | 2,645 |
| Reported net income | (4,687) | (4,231) | (3,353) | (1,559) | 18,040 |
| Basic average number of shares, m | 53.1 | 53.3 | 57.6 | 61.6 | 62.0 |
| Basic EPS (€) | (0.09) | (0.08) | (0.06) | (0.03) | 0.29 |
| Adjusted EBITDA | (6,862) | (5,323) | (4,396) | (3,055) | 16,859 |
| Adjusted EBIT | (7,007) | (5,490) | (4,549) | (3,185) | 16,748 |
| Adjusted PBT | (6,896) | (6,320) | (6,004) | (4,097) | 15,396 |
| Adjusted EPS (€) | (0.08) | (0.07) | (0.06) | (0.03) | 0.29 |
| Adjusted diluted EPS (€) | (0.08) | (0.07) | (0.06) | (0.03) | 0.29 |
| BALANCE SHEET | | | | | |
| Property, plant and equipment | 682 | 611 | 481 | 379 | 298 |
| Intangible assets | 60,254 | 75,843 | 89,895 | 102,802 | 116,421 |
| Investments | 29 | 31 | 26 | 26 | 26 |
| Deferred tax assets | 1,812 | 2,050 | 2,222 | 2,222 | 2,222 |
| Total non-current assets | 62,778 | 78,535 | 92,624 | 105,428 | 118,967 |
| Cash and equivalents | 28,725 | 21,317 | 12,257 | 4,098 | 30,504 |
| Trade and other receivables | 3,645 | 3,709 | 1,909 | 2,809 | 2,359 |
| Inventories | 104 | 10 | 6 | 6 | 6 |
| Other current assets | 132 | 129 | 104 | 104 | 104 |
| Total current assets | 32,606 | 25,165 | 14,276 | 7,017 | 32,973 |
| Deferred tax liabilities | 1,812 | 2,050 | 2,222 | 2,222 | 2,222 |
| Long term debt | 13,354 | 10,346 | 6,335 | 3,172 | 3,148 |
| Other non-current liabilities | 285 | 0 | 155 | 155 | 155 |
| Total non-current liabilities | 15,451 | 12,396 | 8,711 | 5,549 | 5,525 |
| Trade and other payables | 3,518 | 5,742 | 4,210 | 4,976 | 4,593 |
| Short term debt | 4,306 | 12,920 | 12,194 | 19,914 | 41,776 |
| Other current liabilities | 847 | 70 | 11 | 11 | 11 |
| Total current liabilities | 8,672 | 18,732 | 16,414 | 24,901 | 46,379 |
| Equity attributable to company | 71,262 | 72,572 | 81,775 | 81,996 | 100,036 |
| CASH FLOW STATEMENT | | | | | |
| Profit before tax | (7,180) | (6,557) | (6,104) | (4,097) | 15,396 |
| Cash from operations (CFO) | (3,626) | (1,848) | (575) | (1,563) | 18,218 |
| Capex | (175) | (76) | 0 | 0 | 0 |
| Acquisition of intangible assets | (11,586) | (14,195) | (14,503) | (12,933) | (13,650) |
| Other investing activities | 37 | (1) | (1) | 0 | 0 |
| Cash used in investing activities (CFIA) | (11,724) | (14,271) | (14,504) | (12,933) | (13,650) |
| Net proceeds from issue of shares | 0 | (932) | (1,880) | 0 | 0 |
| Movements in debt | 4,123 | 9,642 | 7,901 | 6,338 | 21,838 |
| Other financing activities | 0 | 0 | 0 | 0 | 0 |
| Cash from financing activities (CFF) | 4,123 | 8,710 | 6,021 | 6,338 | 21,838 |
| Increase/(decrease) in cash and equivalents | (10,880) | (7,408) | (9,060) | (8,159) | 26,406 |
| Currency translation differences and other | 348 | 1 | (3) | 0 | 0 |
| Cash and equivalents at start of period | 39,605 | 28,725 | 21,317 | 12,257 | 4,098 |
| Cash and equivalents at end of period | 28,725 | 21,317 | 12,257 | 4,098 | 30,504 |
| Net (debt)/cash | 11,065 | (1,948) | (6,272) | (18,988) | (14,420) |
| Free cash flow (CFO + net capex + Intangible assets) | (15,388) | (16,118) | (15,078) | (14,496) | 4,568 |

Source: company reports, Edison Investment Research

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