



Platinum[®] World Portfolios PLC Quarterly Investment Manager's Report

Platinum World Portfolios - Health Sciences Fund

31 December 2023

 **Platinum[®]**
WORLD PORTFOLIOS PLC



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Performance Returns

to 31 December 2023

SUB-FUND	PORTFOLIO VALUE (US\$ MIL)	QUARTER	1 YEAR	2 YEARS COMPOUND P.A.	3 YEARS COMPOUND P.A.	5 YEARS COMPOUND P.A.	SINCE INCEPTION COMPOUND P.A.	INCEPTION DATE
PWP - Health Sciences Fund								
Class D (USD)	29.9	15.4%	18.0%	-	-	-	18.1%	28 Oct 2022
Class FB (USD)	2.6	15.5%	18.5%	-	-	-	19.0%	07 Dec 2022

Fund returns are net of accrued fees and expenses, are pre-tax, and assume the accumulation of net income and capital gains. Where a particular share class is not denominated in USD, the net asset value per share in USD, being the Fund's base currency, is converted into the denomination currency of that share class using the prevailing spot rate.

Historical performance is not a reliable indicator of future performance. Returns could be reduced, or losses incurred due to currency fluctuations. See note 1, page 8.

Source: Platinum Investment Management Limited for Fund returns; FactSet Research Systems for MSCI Index returns.

Platinum World Portfolios - Health Sciences Fund



Dr Bianca Ogden
Portfolio Manager

Overview

- This quarter there was significant acquisition activity in the Health Sciences space as big pharma companies seek to refresh their portfolio of tools, technologies and commercial therapeutics. Some of our Fund holdings – including **Orchard Therapeutics** and **Icosavax** – were acquired during the quarter and this benefited investors.
- Radiopharmaceuticals is an area we have been watching and working on for many years. In broad terms, they're agents – an antibody, a small molecule or other synthetic carrier – that 'deliver' a radioactive isotope to assist in the treatment of a disease – especially cancers. **RayzeBio** is a standout in this space. The company was likely to benefit from the accelerated approval of a core product and was building a quality pipeline of differentiated oncology-related assets. Just as importantly, RayzeBio's efficient R&D engine positions them to build a radiotherapeutic pipeline for the future. The company has now been acquired and this was positive for Fund performance.

Performance

compound p.a.⁺, to 31 December 2023

	QUARTER	6 MTHS	SINCE INCEPTION
PWP Health Sciences Fund Class D USD	15%	12%	18%

Fund returns are net of accrued fees and costs. Inception date is 28 Oct 2022. The Fund uses an absolute return hurdle for performance comparison purposes and for the purposes of calculating performance fees payable to the investment manager. Source: Platinum Investment Management Limited.
Historical performance is not a reliable indicator of future performance. Returns could be reduced, or losses incurred due to currency fluctuations.
 See notes 1 & 2, pages 8 & 9.

As at the date of this document there is insufficient data for the Value of US\$100,000 Invested chart.

Weight-loss drugs and heavyweight acquisitions

It was a dramatic year in Healthcare, particularly for the biotech sector. The sector started promisingly, wobbled in the middle of the year but staged a stellar recovery as the rising interest rate cycle *appeared* to be nearing an end. It was also a year that brought new varieties of diabetes and weight loss drugs – GLP-1s – to the notice of the general public and saw increased market worries about the performance of medical device companies. In 2023 the number of new drug approvals by the US FDA was the second highest in the past 30 years (55 new molecular entities or biologics license applications).¹

This quarter there were several significant biotech acquisitions and some of our holdings were acquired:

- **Orchard Therapeutics** (a portfolio holding) was bought by Kyowa Kirin²
- Our holding, **Icosavax**, was bought by AstraZeneca
- We invested in **RayzeBio** in September. We had been engaging with the company for some time and saw a strong team putting together a great radiopharmaceutical pipeline. Valuation was very reasonable and, as always in biotech, if the data and execution holds up acquirers will take note. This happened earlier than we thought with Bristol Myer Squibb acquiring the company in late December.

These acquisitions were highly rewarding for Fund investors this quarter with the premia on takeover ranging from 100% to 180%.

In addition, **Roivant** (a holding in the Fund) sold Televant to Roche (which we also hold). Televant was the Roivant subsidiary dedicated to the development of a treatment for Inflammatory Bowel Disease and Ulcerative Colitis. The transaction is worth over \$US 7billion.³

Roche also acquired Carmot Therapeutics this quarter to gain access to the biotech's obesity pipeline. Carmot had been on our radar for some time and we were looking to participate in the IPO. While many have lost interest in Roche's R&D capability we believe recent deal activity has been sound and Roche is gradually restocking its drug development pipeline.

Obesity therapies continue to garner attention. Denmark's **Zealand Pharma** (up 22% this quarter), is a peptide specialist that we hold. It has a serious development pipeline in the metabolic and inflammatory disease space and is garnering significant industry attention. On the flip side, another holding, **Structure Therapeutics**, was down 19% for the quarter after delivering mixed data for its oral GLP-1 receptor agonist in diabetics. However, in our view the data in obese patients showed great promise hence we added to our position.

In the life science tool⁴ space the hope for recovery at bioprocessing companies was squashed quickly during the year with companies missing earnings forecasts and seeing their China business fall away. So far M&A in the sector has been muted, however we expect that to change in 2024.

One Fund holding, **908 Devices**, has been a solid performer (up 68% this quarter) as short selling is subsiding. The company is all about miniaturising mass spectrometry into handheld and desktop devices. These devices can be deployed in the field to detect substances such as counterfeit drugs or linked to cell manufacturing to allow real-time data analysis. We believe the company is in an outstanding position to benefit from the recovery in bioprocessing.

AI makes its mark in medicine

The increasing use of AI in drug discovery is generating demand for partnerships. Our holding, **Exscientia**, expanded its alliance with Sanofi and was up around 40% for the quarter. **Absci**, a generative AI biotech that focuses on biologics, formed new partnerships with AstraZeneca and Almirall and was up 218% for the quarter.

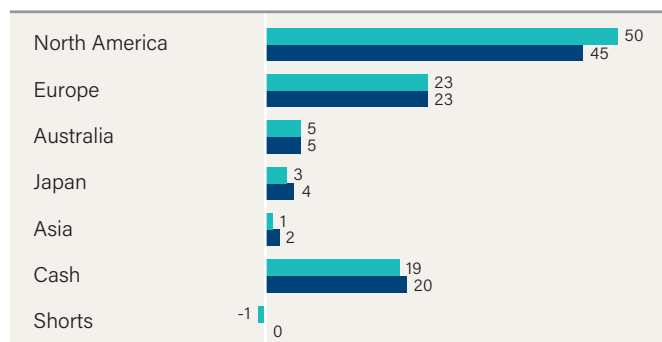
¹ Source: US Food and Drug Administration

² Orchard Therapeutics develops hematopoietic stem cell gene therapy for genetic and rare diseases; Icosavax develops VLP (Viral like particle) vaccines for respiratory disease; RayzeBio focuses on radiotherapy.

³ Source: Roivant Press Release, 23/10/23

⁴ Life science tool companies develop technologies, instruments and tests for use in medical research, diagnosis and treatment. These companies also provide tools and equipment used in biomanufacturing.

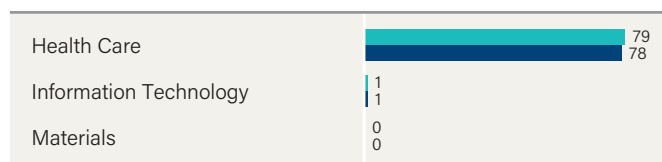
Disposition of Assets %



■ 31 DEC 2023 ■ 30 SEP 2023

See note 4, page 9. Numerical figures have been subject to rounding.
Source: Platinum Investment Management Limited.

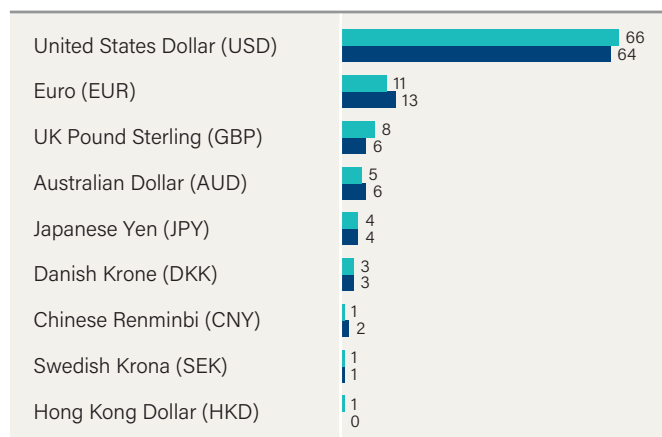
Net Sector Exposures %



■ 31 DEC 2023 ■ 30 SEP 2023

See note 5, page 9. Numerical figures have been subject to rounding.
Source: Platinum Investment Management Limited.

Net Currency Exposures %



■ 31 DEC 2023 ■ 30 SEP 2023

See note 6, page 9. Numerical figures have been subject to rounding.
Source: Platinum Investment Management Limited.

Top 10 Holdings

COMPANY	COUNTRY	INDUSTRY	WEIGHT
RayzeBio Inc	US	Health Care	4.1%
Icosavax Inc	US	Health Care	3.5%
Exscientia Plc	UK	Health Care	3.0%
Zealand Pharma A/S	Denmark	Health Care	2.6%
Ideaya Biosciences Inc	US	Health Care	2.6%
Galapagos NV	Belgium	Health Care	2.6%
Takeda Pharmaceutical	Japan	Health Care	2.5%
Sanofi SA	US	Health Care	2.5%
Immunovant Inc	US	Health Care	2.4%
Roivant Sciences Ltd	US	Health Care	2.2%

As at 31 December 2023. See note 7, page 9.

Source: Platinum Investment Management Limited.

For further details of the Fund's invested positions, including country and industry breakdowns and currency exposures, updated monthly, please visit www.platinumworldportfolios.ie/The-Funds/PWP-Health-Sciences-Fund

Detractors from performance this quarter included our pharma holdings **Sanofi**, **Takeda** and **Bayer** (down around 25%). All three are investing more in R&D due to pipeline setbacks. Our Australian holdings, **Pharmaxis** and **Telix**, fell due to capital raisings or poorer than expected sales growth.

During the quarter we trimmed many of our holdings due to their exceptional price performance, while adding to our holdings in neurodegenerative biotechs like Wave Life Sciences.

Aura Biosciences has been added to the Fund. This biotech is developing viral-like drug conjugates for oncology – ocular cancers are a focus for Aura and the company has recently started its phase 3 trials.

Commentary

In recent years we have noticed a renaissance in the therapeutic radiopharmaceutical space.

Radiopharmaceuticals are made up of three components, a cell-targeting component also known as a “binder”, which can be an antibody, a small molecule or other synthetic carrier molecules. The binder is connected via a linker to a radioactive isotope, which can either be an alpha or beta emitting isotope. Beta emitters are less potent, travel further but are readily available, hence more popular.

Until recently, the general approach to binders has been to repurpose an available antibody or small molecule, conjugate it to a beta emitter and start clinical development.

New biotech start-ups have now emerged that are building proper precision radiopharmaceuticals instead of repurposing available modalities as isotope carrier molecules.

Some of these new biotechs are investing in the supply of alpha emitters. Alpha emitting isotopes are in short supply but as a therapeutic payload they are very effective, inducing double stranded DNA breaks efficiently while limiting surrounding damage. This indicated real innovation – and new investment opportunities.

Pharmacokinetic properties

Having the right binder-therapeutic modality-isotope combination is crucial as it determines the pharmacokinetics of the molecule – how fast it penetrates the tumour, how long will it hang around and where else will it accumulate in the body. We saw real change happening and we engaged with various private companies to further our understanding.

These next generation of radiopharma biotechs were different, the focus was on new targets and on identifying new binder molecules that have the best pharmacokinetic properties when linked to radiation. In addition, the leadership teams at these various companies knew about the complexity of the field and had solid drug development and biotech experience.

San Diego based biotech, RayzeBio, founded in 2020, impressed us the most given its R&D approach and the fact it had a valuable late stage pipeline asset. This late stage assets has similarities with an approved drug (Novartis Lutathera) but used the more powerful alpha emitter. Clinical data looks promising. This was a sound strategy with potential for accelerated approval.

RayzeBio's R&D platform also produced RYZ801, a GPC3⁵ peptide binder that to us was very interesting given early data from other modalities such as ADCs⁶ or cell therapy.

The team around RayzeBio's CEO Ken Song has been thoughtful and innovative while also having no illusions that this space can be very costly to operate in. We invested in RayzeBio in the belief that if this company continued to execute someone would step in to acquire it. This happened earlier than we thought with Bristol Myer Squibb acquiring the company in late December.

Targeted therapeutic radiopharmaceutical companies like RayzeBio are of great interest to big pharma companies. The barriers to entry are very high, the supply chain is complex and hence generic competition is less likely. That can underpin better long-term revenue and profit growth for the acquiring pharma company.

Outlook

Biotech and pharma companies alike continue to reprioritise pipeline assets and hence are reining in spending. Consolidation will continue and pharma company business development teams will be as important as the CEO and CFO as they drive the ability of pharma companies to acquire high quality research (and new product) at the right price through acquisition.

Private biotech firms looking to list in 2024 should start to get some traction as funds freed up due to recent M&A activity will be recycled into new investments.

Given the interest rate environment is now more predictable, we also expect to see M&A pick up in the life science tool and diagnostic space. Obesity and Alzheimer's disease will remain a focus for many companies.

⁵ Glypican-3 is an oncofetal protein that is overexpressed in up to 75% of hepatocellular tumors.

⁶ Antibody Drug Conjugates.

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1. Fund returns are calculated by Platinum using the Fund's net asset value per share (i.e. excluding the anti-dilution levy) attributable to the specified share class. Where a share class is not denominated in USD, the net asset value per share in USD, being the Fund's base currency, is converted into the denomination currency of that share class using the prevailing spot rate. Fund returns are net of fees and expenses, pre-tax, and assume the accumulation of the net income and capital gains, each as attributable to the specified share class. The MSCI index returns are in USD, are inclusive of net official dividends, but do not reflect fees or expenses. MSCI index returns are sourced from FactSet Research Systems. Platinum does not invest by reference to the weightings of the specified MSCI index. As a result, the Fund's holdings may vary considerably to the make-up of the specified MSCI index. MSCI index returns are provided as a reference only. The investment returns shown are historical and no warranty is given for future performance. Historical performance is not a reliable indicator of future performance. Returns could be reduced, or losses incurred due to currency fluctuations. Due to the volatility in the Fund's underlying assets and other risk factors associated with investing, investment returns can be negative, particularly in the short term.

2. The portfolio inception dates for each active share class of the relevant Fund are as follows:

- Platinum World Portfolios - Health Sciences Fund
- Class D USD (Accumulating) (ISIN: E0000SJFC91): 28 Oct 2022

For the purpose of calculating the "since inception" returns of the MSCI index, the inception date of Class D of the Fund is used (as Class D was the first share class activated).

3. The investment returns depicted in this graph are cumulative on US\$100,000 invested in Class D of the specified Fund over the specified period relative to the specified net MSCI Index in US Dollars.
4. The geographic disposition of assets (i.e. other than "cash" and "shorts") shows the Fund's exposures to the relevant countries/regions through its long securities positions and long securities/index derivative positions, as a percentage of its portfolio market value. Country classifications for securities reflect Bloomberg's "country of risk" designations. "Shorts" show the Fund's exposure to its short securities positions and short securities/index derivative positions, as a percentage of its portfolio market value. "Cash" in this table includes cash at bank, cash payables and receivables and cash exposures through long derivative transactions.
5. The table shows the Fund's net exposures to the relevant sectors through its long and short securities positions and long and short securities/index derivative positions, as a percentage of its portfolio market value. Index positions (whether through ETFs or derivatives) are only included under the relevant sector if they are sector specific, otherwise they are included under "Other".
6. The table shows the Fund's net exposures to the relevant currencies through its long and short securities positions, cash at bank, cash payables and receivables, currency forwards and long and short securities/index derivative positions, as a percentage of its portfolio market value. Currency classifications for securities reflect the relevant local currencies of the relevant Bloomberg country classifications. The table may not exhaustively list all of the Fund's currency exposures and may omit some minor exposures.
7. The table shows the Fund's top ten positions as a percentage of its portfolio market value taking into account its long securities positions and long securities derivative positions.

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