

Platinum International Health Care Fund



Dr Bianca Ogden
Portfolio Manager

Overview

- During the quarter we took the opportunity to trim some positions that have done well (e.g. Telix and Quanterix) while adding to investments or initiating new positions that have made progress (e.g. Galapagos, and Bicycle Therapeutics).
- We have a holding in Zealand Pharma, a Danish biotech focusing on peptide therapy for metabolic diseases. Zealand is emerging as one of the key companies in obesity given the progress of its proprietary and partnered obesity pipeline.
- In our view, the investment environment for biotech and tool companies is currently affected by broader macroeconomic themes and tax loss selling. These issues are distracting from the fundamental investment case – we are close to historically low valuations in the segments we favour. We are focused on the long-term and see this as an opportunity to profit from the sell-down.

Performance

compound p.a.+, to 30 September 2023

	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HC Fund*	-2%	7%	0%	4%	9%
MSCI AC World HC Index^	0%	10%	9%	9%	9%

+ Excludes quarterly returns.

* C Class – standard fee option. Inception date: 10 November 2003.

After fees and costs, before tax, and assuming reinvestment of distributions.

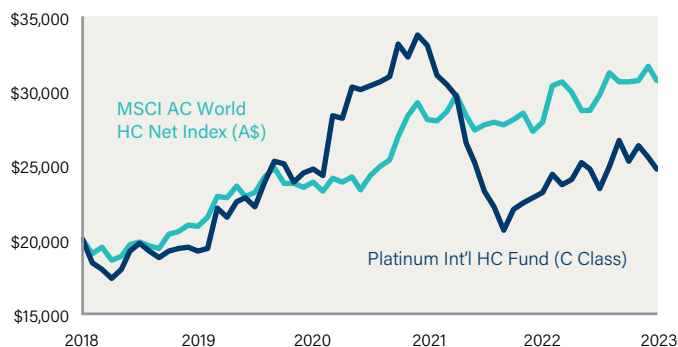
^ Index returns are those of the MSCI All Country World Health Care Net Index in AUD. Source: Platinum Investment Management Limited, FactSet Research Systems.

Historical performance is not a reliable indicator of future performance.

See note 1, page 5. Numerical figures have been subject to rounding.

Value of \$20,000 invested over five years

30 June 2018 to 30 September 2023



After fees and costs, before tax, and assuming reinvestment of distributions.

Historical performance is not a reliable indicator of future performance.

Source: Platinum Investment Management Limited, FactSet Research Systems.

See notes 1 & 2, page 5.

This quarter, three themes dominated healthcare.

- The “higher for longer interest rates” theme pressured the biotech sector. The NASDAQ Biotechnology Index was down just under 3% over the September quarter and up nearly 5% for the year to end September. While the S&P Biotechnology Select Industry index was down nearly 12% for the quarter and down nearly 8% for the year.¹
- Trends in obesity therapeutics forced a rethink on the valuations of medical device companies.
- Life science tool companies remain in a holding pattern given continued inventory adjustments at customers, and lower demand in China. The cell and gene therapy sector remains challenged.

EU pharma was mostly a bright spot but overall generalist investors continue to stay well clear of Healthcare unless it is the obesity champions Eli Lilly or Novo Nordisk which significantly contributed to the performance of the index (both up 15-20% in local currency for the quarter and between 30%

and 50% year to date). No doubt the injectable glucagon-like peptide (GLPs²) agonists are firmly on the obesity therapeutic map, however these therapies are not able to cure every ailment and oral obesity therapies are also putting runs on the board. **Structure Therapeutics** – a holding in the Fund – exemplified this trend, reporting good Phase 1 data this quarter.

During the quarter we exited and trimmed a number of investments mostly due to slower or disappointing progress (e.g. Gilead, Alector, Bayer). We continued to trim positions that have done well (e.g. **Telix** and **Quanterix**) while adding to investments or initiating new positions that have made progress (e.g. **Galapagos**, and **Bicycle Therapeutics**).

We have increased our exposure to large companies including **Johnson and Johnson** and **GSK** who are rolling out new products. **GSK** has recently received approval for momelotinib, a drug that originated here in Australia. Momelotinib can be used in the treatment of intermediate or high-risk myelofibrosis (a rare bone marrow blood cancer).

Our investment in **Exscientia** has been a clear drag on performance. The company continues to make good pipeline progress but had been caught up in the “AI hype” last quarter which turned into neglect this quarter. On many measures Exscientia is undervalued compared to its peers in the biotech sector.

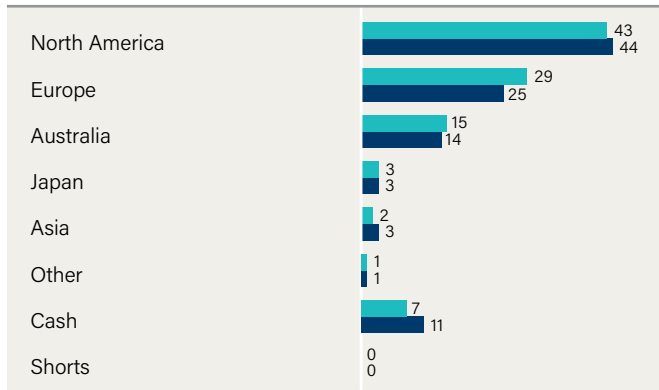
Icosavax drifted lower this quarter despite its vaccine technology showing competitive durability. We added to our position.

We have a holding in Zealand Pharma, a Danish biotech focussing on peptide therapy for metabolic diseases. Zealand is emerging as one of the key companies in obesity given the progress of its proprietary and partnered obesity pipeline.

Immunovant reported long-awaited data for its next generation anti-FcRn antibody in healthy volunteers. This emerging class of antibodies has the potential to be used in a wide array of autoimmune diseases. We invested in Immunovant when it was trading below cash. Based on our due diligence of the FcRn space and also the development approach at Immunovant, we saw the company as significantly undervalued versus peers. This quarter, Immunovant showed that its antibody achieved solid IgG reduction when given weekly as a subcutaneous injection to healthy volunteers. More importantly no decrease in albumin (vs baseline) and no increase in LDL-C (vs baseline) were observed. This was the best-case scenario for us and we believe that even after significant share price appreciation a valuation disconnect remains vs other anti-FcRn companies.

² Glucagon-like peptide-1 receptor (GLP-1) are a class of drugs that mimic the naturally occurring GLP-1 hormone. Upon food intake GLP-1 hormones stimulate insulin production hence “GLP-1 agonists” are used for diabetes. In addition to insulin secretion these hormones also reduce gastric emptying and reduce appetite.

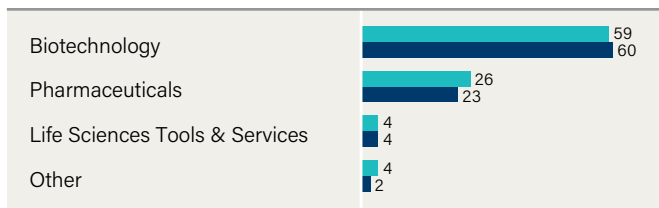
Disposition of Assets %



■ 30 SEP 2023 ■ 30 JUN 2023

See note 3, page 5. Numerical figures have been subject to rounding.
Source: Platinum Investment Management Limited.

Net Sector Exposures %



■ 30 SEP 2023 ■ 30 JUN 2023

See note 4, page 5. Numerical figures have been subject to rounding.
Source: Platinum Investment Management Limited.

Top 10 Holdings

COMPANY	COUNTRY	INDUSTRY	WEIGHT
SpeeDx Pty Ltd	Australia	Biotechnology	7.1%
Takeda Pharmaceutical Co	Japan	Pharmaceuticals	3.2%
Sanofi SA	US	Pharmaceuticals	3.1%
Zealand Pharma A/S	Denmark	Biotechnology	2.9%
UCB SA	Belgium	Pharmaceuticals	2.8%
Exscientia Plc	UK	Biotechnology	2.8%
Immunovant Inc	US	Biotechnology	2.7%
Telix Pharmaceuticals Ltd	Australia	Biotechnology	2.7%
Quanterix Corp	US	Life Sciences Tools	2.6%
Ideaya Biosciences Inc	US	Biotechnology	2.5%

As at 30 September 2023. See note 5, page 5.
Source: Platinum Investment Management Limited.

Commentary

This year's Noble Prize for Medicine will be awarded to Professors Katalin Karikó and Drew Weissman, the two scientists that worked out that by modifying a building block of the mRNA the molecule is able to fly under the radar of the body's immune response. This was a fundamental discovery that paved the way for mRNA to be used as a vaccine and as a therapeutic.

Today we see this as a ground-breaking step but when Karikó was looking for grants to do her experiments she was rejected. Similarly, in 2005 when Karikó and Weissman were looking to publish their work, rejections were the norm with *Nature* journal rejecting it as "an incremental contribution." In the end it did get published (*Immunity* 2005 Aug;23(2):165-75) but it failed to generate excitement.

To say theirs was a challenging road is an understatement. To get from a hypothesis to a commercial product, a lot of pieces, money and luck have to coalesce. It is a bumpy journey and currently many investors are shunning the biotech sector altogether. However, biotechs are the ones that will give us new and better medicines in the future. A bumpy road is part of it and just giving up because the wind changes is not an option.

Take Biontech, a company that is working on non-COVID uses for mRNA. In 2016 we got interested in mRNA as a therapeutic after reading a *Nature* paper from Biontech highlighting the use of mRNA as immune therapy in cancer. The same year Genentech and Biontech entered an alliance to develop cancer vaccines. We invested in Biontech's pre-IPO (Moderna at IPO stage) as their plan to develop multiple modalities to treat cancer appealed to us. So did the team running the company – including Katalin Karikó.

The pandemic changed our investment case temporarily and we did exit our investments due to valuation. Today Biontech is back in the portfolio. COVID sales are not our main thesis, we are intrigued by the pipeline, particularly the alliance with private biotech firm, OncoC4, providing access to a next generation CTLA-4 antibody (ONC-392).

CTLA-4 (cytotoxic T-lymphocyte -associated protein 4) is a known immune checkpoint, with two anti-CTLA-4 antibodies approved. Anti-CTLA-4 is not a crowded space and approved drugs have limitations.

OncoC4 has an antibody with a twist, it allows CTLA-4 recycling while other inhibitors disrupt this process hence causing adverse immunotherapy-related effects.³ We have met with OncoC4 to understand more about their approach and the clinical data on ONC-392.

So far, clinical data is indeed intriguing, showing activity in non-small cell lung cancer patients who progressed following PD-1/PD-L1 therapy. The drug has just started Phase 3 and if the data holds up in this larger trial, Biotech could have a drug on the market in 2025. One can imagine that a safer CTLA-4 antibody could find use in earlier lines of treatment and may open opportunities in adjuvant treatment.⁴ In short, there is the potential for an emerging non-COVID franchise for Biotech that could see the company match up with our pre-COVID investment case – albeit with a much better cash balance of around \$17 billion on hand.

Outlook

The investment environment for biotech and tool companies is yet again dancing to the tune of broader macroeconomic themes. This theme – plus tax loss selling – is distracting from the fundamentals of the investment case.

In our view we are again close to historically low valuations in the segments we favour and it is crucial we focus on the long-term and use this opportunity to take advantage of the sell-down. The financial updates from life science tools companies in the coming weeks will be closely watched for any indication about end market recovery, while medical device companies will have to continue to explain how they see their business fare in times of obesity therapeutics.

In the coming weeks, Novo Nordisk will also present the cardiovascular outcome data where Novo Nordisk's GLP-1 agonist (2.4mg semaglutide) was tested against placebo. The trial was successful but details will help understand the ramifications for the wider healthcare system.

As is the custom in biotech and pharma, we continue to expect further consolidation in the sector.

Note:

From 3/10/2023, the Platinum International Health Care Fund was renamed the Platinum International Health Sciences Fund to better reflect the characteristics of the Fund's investments.

³ See Zhang, Y., Du, X., Liu, M. et al. Cell Res 29, 609–627 (2019).

⁴ Adjuvant treatments follow primary treatments (such as surgery) and are designed to reduce the chance of cancer recurring.

Notes

Unless otherwise specified, all references to "Platinum" in this report are references to Platinum Investment Management Limited (ABN 25 063 565 006, AFSL 221935).

Some numerical figures in this publication have been subject to rounding adjustments. References to individual stock or index performance are in local currency terms, unless otherwise specified.

1. Fund returns are calculated by Platinum using the net asset value unit price (i.e. excluding the buy/sell spread) of the stated unit class and represent the combined income and capital returns over the specified period. Fund returns are net of fees and costs, pre-tax, and assume the reinvestment of distributions. The MSCI index returns are in AUD, 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. 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 investment returns depicted in the graph are cumulative on A\$20,000 invested in C Class (standard fee option) of the Fund over the specified period relative to the specified MSCI index in AUD.
3. 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 derivative transactions.
4. 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".
5. 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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