

Platinum International Health Care Fund



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Performance

(compound p.a.[†], to 30 September 2022)

	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HC Fund*	5%	-30%	6%	8%	9%
MSCI AC World HC Index [^]	-1%	-1%	10%	12%	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.

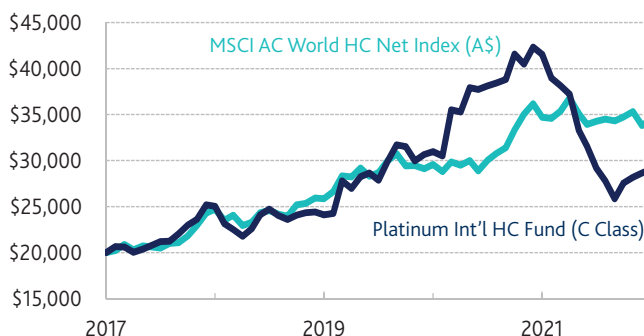
[^] Index returns are those of the MSCI All Country World Health Care Net Index in AUD. Source: Platinum Investment Management Limited, FactSet Research Systems.

Historical performance is not a reliable indicator of future performance.

See note 1, page 4. Numerical figures have been subject to rounding.

Value of \$20,000 Invested Over Five Years

30 September 2017 to 30 September 2022



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 4.

The Fund (C Class) returned 5.5% for the quarter.¹

It was an eventful quarter, particularly for the biotech sector. Early on, we saw a gradual recovery in biotech stocks, but sentiment then changed as inflation and rising interest rates once again became the dominant market narrative. Positive data for an antibody for Alzheimer's disease (AD) shifted the focus late in the quarter, putting some spark back into the biotech sector.

The share market only tells half of the story of what transpired in the biotech sector during the quarter. It was a very busy period, with acquisitions, reverse mergers, equity raises, monetisation of research and development (R&D) or manufacturing sites, a successful biotech initial public offering (IPO), and to top it off, positive phase 3 data for the BioArctic/Eisai/Biogen's lecanemab, an anti-beta-amyloid antibody for AD (as mentioned above). Many expected the drug to fail, but as is often the case in drug development, surprises do occur, which can have wide-ranging long-term effects.

As we have highlighted previously, neurology, particularly neurodegenerative diseases, will see increased drug development activity in the coming decade. No doubt there will be challenges along the way. The lecanemab antibody is by no means a cure for AD, far from it, but it will foster future investments. It is similar to what ipilimumab and nivolumab did for immuno-oncology (IO).² These antibodies have put IO firmly on the map, and today, it is a major area of oncology drug discovery and development globally.

The Fund has invested in various neurology-focused biotech companies, which generally performed well over the quarter. Highlights include Swedish biopharma company **BioArctic** (+251% over the quarter), the company that discovered lecanemab, and US biotech **Prothena**, which rallied +123%.

1 References to returns and performance contributions (excluding individual stock returns) in this Platinum International Health Care Fund report are in AUD terms, unless otherwise specified. Individual stock returns are quoted in local currency terms and sourced from FactSet Research Systems, unless otherwise specified.

2 Ipilimumab (anti-CTLA-4) and nivolumab (anti-PD-1) are both antibodies that are sold by Bristol Myers Squibb. CTLA-4 and PD-1 are immune checkpoints that play an important role in regulating the immune response towards cancers.

AC Immune (-12%), while weakening over the quarter, also benefited from the positive news re lecanemab, with its share price jumping 31% on the announcement in late September, helping it to claw back a large portion of its earlier losses during the quarter. Both Prothena and AC Immune are working on therapies for Alzheimer's disease and Parkinson's disease.

Elsewhere, **Prometheus Biosciences'** share price more than doubled during the quarter (+109%). The company held an R&D day and unveiled its next target for inflammatory bowel diseases. The company focuses on precision medicine, developing companion diagnostics alongside its therapeutics. We took the opportunity to trim our holdings on share price strength.

Myovant (+44%) was another strong contributor to performance over the quarter. The company continues to expand the label for Myfembree®, this time for the management of pain associated with endometriosis. Myovant is a commercial biotech company that has gradually expanded the use of relugolix, a gonadotropin-releasing hormone antagonist. In early October, Sumitomo Pharma, the majority shareholder of Myovant, offered to buy Myovant in full, however, Myovant rejected the offer.

US life sciences tools company **Quanterix** (-32%) had a volatile quarter. Quanterix focuses on biomarker detection in neurology. It is currently working with US pharmaceutical company Eli Lilly on Alzheimer's markers. Its chairman and CEO Kevin Hrusovsky retired, and Masoud Toloue was appointed as CEO, while Martin Madaus assumed the Chairman's role.³ At the same time, the company reduced sales guidance and essentially cleaned house, causing a significant sell-off in the company. We saw this as a buying opportunity, as the management transition was a natural progression and the skillsets of both Toloue and Madaus will help pave the way for the next chapter in Quanterix's journey. The significant restructuring, albeit painful, is important as the company moves from research tool provider to also providing diagnostic tests. For Quanterix to trade below its cash balance was, in our opinion, unjustified. Given its focus on Alzheimer's disease, Quanterix also saw its share price rise sharply (+56%) after the positive antibody news. The stock provided a small positive contribution to the Fund's return in Australian dollar terms.

Sanofi (-19%) was a key detractor from performance. Just when Sanofi started to find its mojo, the known Zantac litigation reared its head again and investors abandoned ship. In 2019, it emerged that nitrosamine impurities were found in

³ Masoud Toloue joined Quanterix in July 2021 after having been part of PerkinElmer's diagnostic division. Martin Madaus is a life sciences veteran who was the CEO of Millipore for many years.

Disposition of Assets

REGION	30 SEP 2022	30 JUN 2022	30 SEP 2021
North America	40%	41%	43%
Europe	25%	26%	19%
Australia	12%	13%	10%
Japan	4%	4%	4%
Asia	3%	4%	8%
Other	1%	1%	1%
Cash	15%	11%	15%
Shorts	-5%	-3%	-1%

See note 3, page 4. Numerical figures have been subject to rounding. Source: Platinum Investment Management Limited.

Net Sector Exposures

SECTOR	30 SEP 2022	30 JUN 2022	30 SEP 2021
Biotechnology	50%	54%	55%
Pharmaceuticals	24%	25%	21%
Life Sciences Tools & Services	6%	5%	6%
Other	1%	2%	2%
TOTAL NET EXPOSURE	80%	86%	84%

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

Top 10 Holdings

COMPANY	COUNTRY	INDUSTRY	WEIGHT
SpeedX Pty Ltd	Australia	Biotechnology	6.7%
Takeda Pharmaceutical	Japan	Pharmaceuticals	3.7%
Bayer AG	Germany	Pharmaceuticals	3.2%
Sanofi SA	France	Pharmaceuticals	3.0%
Exscientia Plc	UK	Biotechnology	2.7%
Ideaya Biosciences Inc	US	Biotechnology	2.7%
Quanterix Corp	US	Life Sciences Tools	2.7%
Telix Pharmaceuticals Ltd	Australia	Biotechnology	2.4%
Gilead Sciences Inc	US	Biotechnology	2.3%
UCB SA	Belgium	Pharmaceuticals	2.2%

As at 30 September 2022. See note 5, page 4. 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 <https://www.platinum.com.au/our-products/pihcf>.

Zantac products at an elevated level. NMDA can be found in many things at low levels, and the ongoing debate for many years has been about its carcinogenic potential, specifically around what levels and what length of exposure are required to cause cancer. Sanofi withdrew Zantac from the market in 2019, and since then, the lawsuits have mounted, with court cases to start next year. In drug development, these lawsuits are not uncommon, nor are settlements. While many quickly point the finger at bad pharma companies, it's important to note that science evolves over time, and with any therapeutic it is all about the benefit-risk profile. Zantac has been around for over 35 years. It has been sold by many companies, with Sanofi only selling the product since 2016. This is a complex litigation with many companies involved. Our analysis of the fundamentals of Sanofi continue to show a solid vaccine business and a pharma business that is gradually being transformed, while at the same time, it is also a consumer business that offers options. We continue to stay invested.

Commentary

The biotech industry is currently experiencing challenging times. It's not the first time, and it won't be the last. Companies with limited pipeline optionality or 'in-demand' technology will struggle to raise money or attract partnership interest. In addition, the Inflation Reduction Act of 2022⁴ will most likely particularly impact small molecule drug development, given that the Act contains a provision for price negotiations to occur after nine years post approval. Companies will likely rethink their development approach to focus on their most lucrative indication first. As a consequence, some believe that we will see a further shift towards biologics (medicines that are grown and then purified from large-scale cell cultures of bacteria or yeast, or plant or animal cells).⁵

Keeping these trends in mind, **Merus** is a company that we find interesting. Merus is a Dutch biotech founded in 2003 that focuses on making antibodies that combine two or more different antigen-binding sites, so-called bi-, tri-, or multi-specific antibodies, that target cancer.

This is a growing therapeutic modality that traces its origins back to the 1960s. A lot of work has been done to convert these complex molecules into a therapeutic class. The evolution of genomic, molecular, and protein-engineering tools has played an important role in making manufacturing easier and, most importantly, cheaper. Merus is one company

that has a unique and competitive 'platform' in this space, namely its MeMo[®] mouse (a genetically engineered mouse that makes 'single-light chain' antibodies), along with a screening process and heterodimerisation technology. Having a platform is great, but it is only as good as the clinical data that the pipeline produces. To get the best antibody for further development, a diverse set of antibodies is the best starting point to initiate screening for perfect binding to their target as well as the side-effect profile. Merus is able to quickly produce potential pipeline candidates. Over the years, Merus has developed a pipeline of bi-specific antibodies and has also entered into a number of partnerships with Incyte and Eli Lilly, both acquiring shares in Merus. Today, Merus has four molecules in clinical development with zenocatumab (Zeno), a bi-specific in the late stages of development for pancreatic cancer with Neuregulin-1 (NRG1) fusions. The plan is to get a cancer agonist approval and hence allow usage in advanced NRG1 fusion positive cancers. It is expected that this company will have an approved product within 18 months. Merus is under no illusion that it may need a partner for commercialisation. Zeno's market opportunity is limited as NRG-1 fusions are rare. However, Zeno represents proof that this platform can produce viable products, and hence the pipeline is expected to become more valuable. We have seen companies being acquired for these types of targeted oncology drugs and also for the platform once the lead drug receives approval.

Outlook

We are gradually moving through a changing macroeconomic environment. During the quarter, we saw life sciences tool companies weaken as they noted longer timelines for purchase decisions. Quarterly results for medical device companies are eagerly awaited by investors to assess the impact of the economic downturn on elective surgery procedure development. Similarly, many are watching closely at how the clinical research organisations are faring, given the less-than-stellar financing environment for biotechs. Medical conferences will return in this upcoming quarter, while many companies will hold R&D days to showcase their assets and report on their progress. We are keeping a close eye on the detailed presentations of various Alzheimer's disease programs to be released in late November. Undoubtedly, this is a challenging market, but we have also seen a lot of positive progress being rewarded.

Out of misery comes innovation. As the author Max Frisch said, "*Krise ist ein productiver Zustand. Man muss nur den eschmack der Katastrophe nehmen*".⁶

6 Translated: "A crisis is a productive state. You simply have to eliminate the aura of it being a catastrophe."

Source: <https://www.zitate.eu/autor/max-frisch-zitate/189201>

4 The Inflation Reduction Act includes large investments in fighting climate change, making health care and prescription drugs more affordable, and taxing wealthy corporations. <https://www.whitehouse.gov/briefing-room/statements-releases/2022/08/15/by-the-numbers-the-inflation-reduction-act/>

5 https://www.who.int/health-topics/biologics#tab=tab_1

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. With effect from 31 May 2020, country classifications for securities were updated to reflect Bloomberg's "country of risk" designations and the changes were backdated to prior periods. "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.

Disclaimers

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