Platinum International Health Sciences Fund

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Overview

- The Biotech sector was volatile this quarter as the market's focus on tech – and especially on AI – dragged away attention and capital
- We continue to see exciting therapeutic advances in areas like weight loss and radiotherapeutics. In immune system therapies, there is a lot of interesting work being done on the vital communication – or miscommunication – between cells. This could have significant impact in areas like oncology or Alzheimer's and neurodegenerative diseases.

Performance

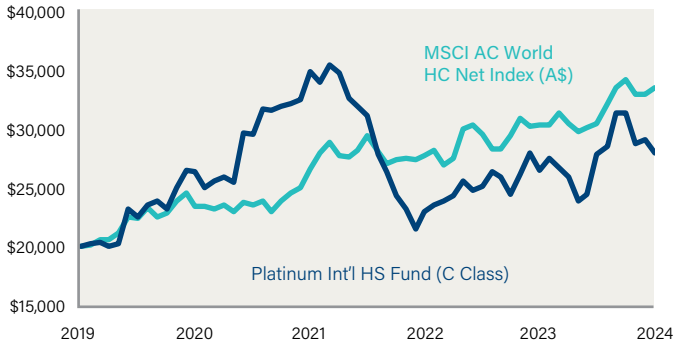
compound p.a.+, to 30 June 2024

	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HS Fund*	-10%	6%	-7%	7%	9%
MSCI AC World HC Index^	-2%	10%	8%	11%	10%

+ 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 2019 to 30 June 2024



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.

It is no secret investors have been transfixed with AI, Nvidia and the tech sector in general. The breadth of the market today is narrow and well-known growth stories are getting all the attention while many other parts of the market struggle.

Volatility on a quarter by quarter basis is high, particularly in the biotech sector and many stock moves are not reflecting the underlying fundamentals of a company. Great clinical data sees a significant rise in share price, often followed by a capital raise with shares drifting off in the months thereafter. Our holdings in **Apogee Therapeutics** (down 40% for the quarter, up 41% YTD) and **Vera Therapeutics** (down 16% for the quarter, up 135% YTD) fall into this bucket, hence we are looking to add to these stocks.

In addition, the widely-followed "XBI" Index[1] underwent a rebalancing towards larger, more liquid biotech stocks, putting temporary pressure on the smaller biotech segment and thus several of our holdings.

The life science tool sector continues to be volatile with lower capital equipment spending, a generally more cautious procurement environment and continued uncertainty about China sales. **Oxford Nanopore** (down 20% for the quarter) has been a poor performer given this more difficult environment. Given its price point and the potential in the diagnostic testing field we see Oxford Nanopore's technology as very attractive. We added to our position during the quarter.

Despite all the challenging market dynamics there has been exciting therapeutic progress. **Zealand Pharma**, the Danish biotech, announced positive data for petrelintide, the company's long-acting amylin analog. The data showed a competitive weight loss profile, but more importantly a very competitive side effect profile. Zealand subsequently raised almost US 1bn. This gives the company great flexibility in terms of clinical development but also strengthens the company when it comes to partnering negotiations. Zealand was up over 30% during the June quarter.

Merus Pharmaceuticals has also been a positive contributor to the Fund (+31%) given continued positive data for its bispecific antibody, petosemtamab[2] which is a treatment for head and neck squamous cell carcinoma.

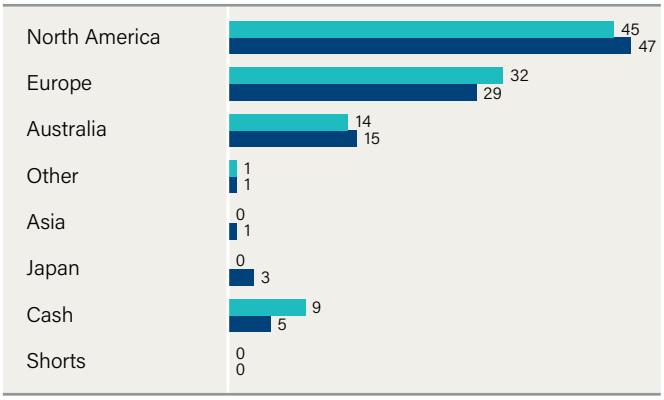
Radiotherapeutics have been a theme since the start of this Fund. As mentioned in a previous Quarterly Report, targeted radiotherapeutics saw a renaissance in recent years due to progress on the targeting agent front as well as in the supply of radionucleotides. In late March we participated in the **Clarity Pharmaceutical** equity raise as progress has been positive for lead therapeutic asset ^{67}Cu-SAR-bisPSMA, indicating good commercial potential. In late April, Clarity reported further promising early stage data in a prostate cancer patient that failed multiple other lines of treatment. Valuation subsequently doubled quickly, hence we trimmed our position a little.

Telix Pharmaceuticals has been a holding in the Fund since the IPO in 2017. Chris Behrenbruch and the Telix team have built a formidable company. However taking their global radiotherapy pipeline peers into consideration, valuation is stretched at this stage and we exited our investment.

1 SPDR S&P Biotech ETF

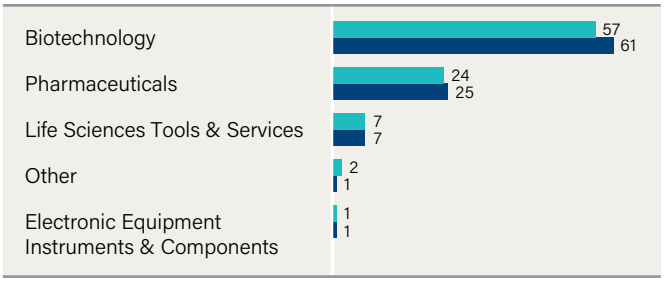
2 Bispecific Target: EGFRxLGR5

Disposition of Assets %



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

Net Sector Exposures %



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	Health Care	5.8%
Zealand Pharma A/S	Denmark	Health Care	5.2%
Exscientia Plc	UK	Health Care	3.7%
Roche Holding AG	US	Health Care	3.4%
Sanofi SA	US	Health Care	3.1%
Oxford Nanopore Technologies	UK	Health Care	2.7%
Roivant Sciences Ltd	US	Health Care	2.5%
Bicycle Therapeutics PLC	UK	Health Care	2.5%
Apogee Therapeutics Inc	US	Health Care	2.5%
Percheron Therapeutics Ltd	Australia	Health Care	2.3%

As at 30 June 2024. See note 5, page 5.
Source: Platinum Investment Management Limited.

Commentary – A failure to communicate in the immune system

The immune system plays a role in almost any disease. We know that cancers and pathogens develop skills to evade the immune system, but we also know that the immune system can be out of control and cause autoimmune and inflammatory diseases.

The immune system is a complex network of many different cells that have an elaborate way of 'talking' to each other to deal with challenges – or to simply maintain the status quo. Our understanding of how this communication works has improved immensely as has our understanding of how the communication fails. Fixing the miscommunication is what many biotech and pharma companies focus on these days, whether in oncology or in Alzheimer's and neurodegenerative diseases. Immunology is an overarching theme across the industry.

Immune oncology is about forcing the immune cells to attack the tumor by eliminating the signals the tumor sends out to divert those immune cells. By developing drugs that amplify an immune response or, alternatively, by reprogramming immune cells altogether via cell therapy.

Cell therapy is powerful but comes with logistical challenges as generally the cells from the patient are harvested, manipulated in the lab and then reinfused into the patient. Side effects can also be challenging. However as is always the case in this industry, no challenge is too difficult and in recent years we have seen a lot of money invested to make immune cell therapy a commercial opportunity.

When it comes to cell therapy, investor attitudes can fluctuate. In 2017/18 T-cell therapy was a hot topic with Gilead buying Kite for almost $12b, while Celgene (now owned by Bristol Myer Squibb) acquired Juno Therapeutics for $9b.

Subsequently, enthusiasm for autologous T-cell therapy leveled off as commercially things were slow and focus shifted to different immune cells as well as off the shelf options. Today off the shelf has lost its shine while the next frontier cell therapy for autoimmune and inflammatory diseases has captured significant investments. This is indeed a very interesting area but in its infancy – so buyer beware.

In August 2021 Professor Schett and his team from the Friedrich-Alexander-University in Erlangen, Germany, published a case study of a patient with severe refractory systemic lupus erythematosus (SLE) who achieved clinical remission when undergoing autologous CD19 T cell therapy.[3] The team then followed up with another publication describing additional patients reaching remission in 2022.[4] The plot was thickening. Many management execs and board members reconsidered their cell therapy strategy and investors got excited. Biotechs focusing on cell therapy for oncology pivoted and today the challenge is to recruit patients and expand clinical datasets.

We have been watching the field carefully but struggle to identify differentiation between the different CD19 therapy approaches (this is the lead target in the space currently). There is a lot to be learned in term of what drives remissions, what biomarkers are indicative of success and how it will work commercially. Also more work to be done on how you can scale this more complex therapeutic modality given the patient numbers for autoimmune and inflammatory diseases are a magnitude higher than in oncology.

Recent clinical data caused a reset of valuations as it had become clear that expectations of 100% cure rates and 0% tolerability were misplaced and unrealistic. While many short term investors may have run for the hills, physicians (and long-term investors like Platinum) remain very interested and as Professor Schett has said recently… "anything which is more than 50% long term drug-free remission is a big success, because we don't get drug-free remission with our current therapy".[5]

Outlook

We believe the bioprocessing industry is in flux and that's creating mixed messages about growth rates in this sector.

Overall, biotech funding this quarter was more subdued versus the first quarter and the biotech IPO window remains narrow. Most newly listed companies are trading below the offering price, so private companies are rethinking their next steps. On the flip side, this is forcing private companies to stay private for longer. This could make their pipelines mature and ultimately allow for a better IPO market in the future, or, as a sell sider recently suggested to me, "more public-market ready".

Obesity and its comorbidities will continue to be a focus for the industry and the field will evolve from the current GLP1 molecules towards a more diversified set of therapies.

3 NEJM correspondence: Schett, NEJM 2021; 385:567-569

4 Mackensen, A., Müller, F., Mougiakakos, D. *et al*. Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus. *Nat Med* **28**, 2124–2132 (2022). doi.org/10.1038/s41591-022-02017-5

5 J.P. Morgan: Biotech Fireside Series with KYTX's Scientific Advisor Dr. Georg Schett (17th June 2014).

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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