Platinum International Health Care Fund

Bianca Ogden
Portfolio Manager

Performance and Changes to the Portfolio

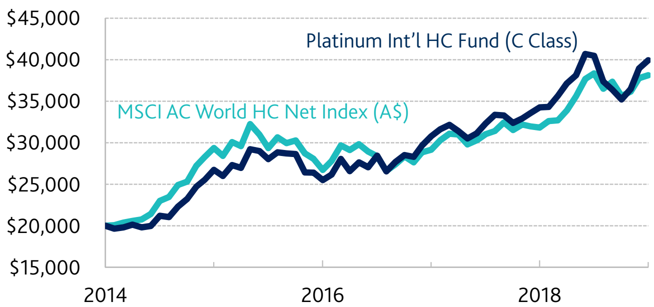
(compound pa, to 31 March 2019)

	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HC Fund*	13%	17%	16%	15%	10%
MSCI AC World HC Index^	7%	20%	13%	14%	9%

* 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.
Historical performance is not a reliable indicator of future performance.
See note 1, page 4. Numbers have been subject to rounding adjustments.

Value of $20,000 Invested Over Five Years

31 March 2014 to 31 March 2019



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.
See notes 1 & 2, page 4.

It was an eventful quarter right up to the last day. There were announcements of acquisitions, readouts of clinical trials, IPOs of Chinese biotechs, and US politics.

What a stark contrast to the last quarter of 2018 when everyone was feeling miserable. But don't be fooled! The sell-off provided a good backdrop for corporates to look for that nice purchase. Indeed, several acquisitions happened during the March quarter: Eli Lilly acquired biotech Loxo Oncology, while Bristol-Myers Squibb announced its intention to acquire big biotech Celgene. In addition, gene therapy companies also attracted much attention with acquisitions and licensing deals. On the clinical trial front, Biogen's Alzheimer's antibody aducanumab failed late stage testing. This was a widely anticipated event, but as we have seen before, Alzheimer's disease is complex and late stage trials have on more than one occasion failed to replicate the promise shown in earlier stage testing.

As highlighted in our last quarterly report, we added to a number of our biotech holdings during the sell-off in late 2018 as we saw an opportunity in the disconnect between stock valuations and the fundamentals of the companies. Many of our biotech holdings recovered well this quarter, as new data readouts continued to demonstrate the progress of their drug pipelines. In the case of our tool companies (those that supply the technologies and instruments for drug discovery and diagnostics), their sales results showed solid traction for their equipment and consumables, and stock prices responded accordingly (**Quanterix** up 41% for the quarter, **NanoString** up 61%).

One of our holdings, **Magenta Therapeutics**, had an exceptional recovery over the quarter (up 186%). This company focuses on making the process of stem cell transplants more efficient and safer for patients. Magenta is developing novel drugs for various steps of the transplant process. Cell transplantation is gaining a lot of attention due to the wave of new cell and gene therapies in development and hence there is a significant need for new technologies and therapies.

Daiichi Sankyo (up 46%) left things until the very end of the quarter, announcing a partnership with **AstraZeneca** for its late stage drug conjugated HER2-targeting antibody. It is a broad partnership with both companies working together on the development and commercialisation of the asset to treat various cancers, while sharing the profits. We always thought that these two companies would work well together, particularly as Daiichi Sankyo's head of oncology used to be a member of the team at AstraZeneca.

During the quarter, there were also a number of clinical data readouts. **Galapagos** (up 28%) released late stage data for its JAK inhibitor for rheumatoid arthritis. Galapagos has a partnership with **Gilead Sciences** (up 5%) to develop this asset and hence it is important for both companies. Now that the drug's good profile has been confirmed in late stage trials, the companies can proceed to advance regulatory filings.

Also in the area of inflammatory diseases, **Dermira** (up 88% for the quarter), a company that had a setback last year with its acne drug, released positive data during the quarter for its in-licensed IL-13 antibody in atopic dermatitis. Dermira's story again shows just how quickly the fortunes of a biotech can change and that companies with a good business development network or a solid internal pipeline can re-emerge strongly from temporary setbacks.

We trimmed some of our holdings that performed well during the quarter, while adding a number of new investments in neurology as well as in China. The scientific progress being made in the field of neurology and the pace of innovation and development at Chinese companies are both gaining speed, and hence we are gradually increasing our exposure to each.

Commentary

Gene therapy remains a hot topic with further acquisitions announced during the quarter. Roche is purchasing Spark Therapeutics, which has a haemophilia A gene therapy in clinical testing as well as other programs for rare genetic diseases. Biogen also added a gene therapy company called Nightstar Therapeutics, which has a focus on inherited retinal diseases. In April last year, Novartis acquired AveXis, a company developing a gene therapy for spinal muscular atrophy (SMA) that is expected to be approved later this year. Furthermore, there have been numerous licensing deals in this space as well.

While gene therapy has only in recent years made it into the financial press, in the science world it is not a new concept, with first clinical trials dating back to 1989. What has

Top 10 Holdings

COMPANY	COUNTRY	INDUSTRY	WEIGHT
SpeeDx	Australia	Health Care Providers	3.5%
Sanofi SA	France	Pharmaceuticals	3.0%
Roche Holding AG	Switzerland	Pharmaceuticals	2.8%
Quanterix Corp	USA	Pharmaceuticals	2.8%
Moderna Inc	USA	Pharmaceuticals	2.2%
Takeda Pharmaceutical	Japan	Pharmaceuticals	2.1%
Zai Lab Ltd	China	Biotechnology	2.1%
Gilead Sciences Inc	USA	Biotechnology	2.1%
Telix Pharmaceuticals	Australia	Biotechnology	2.1%
NanoString Technologies	USA	Health Equip & Serv.	2.1%

As at 31 March 2019. See note 6, 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.

Disposition of Assets

REGION	31 MAR 2019	31 DEC 2018	31 MAR 2018
North America	37%	33%	37%
Europe	24%	26%	39%
Australia	13%	14%	11%
Asia	5%	3%	<1%
Japan	4%	3%	4%
Cash	17%	21%	9%
Shorts	-8%	-7%	<1%

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

Net Sector Exposures

SECTOR	31 MAR 2019	31 DEC 2018	31 MAR 2018
Health Care	74%	71%	90%
Consumer Staples	1%	1%	0%
Financials	0%	0%	1%
TOTAL NET EXPOSURE	75%	72%	91%

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

Net Currency Exposures

CURRENCY	31 MAR 2019	31 DEC 2018	31 MAR 2018
US dollar (USD)	51%	48%	39%
Japanese yen (JPY)	16%	15%	5%
Euro (EUR)	10%	19%	24%
British pound (GBP)	8%	10%	11%
Swiss franc (CHF)	7%	6%	6%
Swedish krona (SEK)	2%	2%	2%
Norwegian krone (NOK)	2%	0%	0%
Hong Kong dollar (HKD)	2%	<1%	0%
Australian dollar (AUD)	2%	<1%	12%
Danish krone (DKK)	1%	1%	1%
Canadian dollar (CAD)	<1%	<1%	1%
Korean won (KRW)	-1%	-2%	0%

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

matured and improved is our understanding of the molecular basis of many diseases as well as the gene delivery technologies that allow more precise and reliable delivery of genes. In addition, large-scale manufacturing of gene delivery shuttles ("vectors" in science jargon) has come a long way, as have gene therapy clinical trials. In essence, gene therapy is simply a new drug modality that is now becoming a commercial reality. With that comes the demand for lower-cost manufacturing and automation.

Genetic information cannot simply be given in a pill form or by injection. The gene would very quickly get degraded and would never make it to its destination. It therefore needs to be packaged and delivered in very specific ways. Here, either lipids or special gene shuttles called vectors can come into play. Lipids are often used in gene editing, while vectors are used widely for gene therapy.

Vectors are genetically engineered viruses. Essentially, the viral genome has been modified so that it contains the desired gene as well as control elements, but does not carry the genetic information that causes viral infection (in science jargon, this is called a non-virulent virus). So, basically, the virus has all the pieces necessary to infect the target tissue and deliver the gene of interest without causing an infection in the traditional sense.

Companies and researchers are currently working on developing ways to make these viral vectors consistently and in large amounts. It reminds us of the time when monoclonal antibodies (large-molecules made in human cells) started to become a new drug modality. A lot of investment is happening and new expertise is required. Viral vector manufacturing requires significant expertise in vectorology, virology as well as downstream processing know-how, which was what attracted us to **Oxford BioMedica**, a holding in the Fund which we first introduced in our December 2015 report[1] and again in our September 2017 report.[2] At the time of that second report, Novartis' T-cell therapy *Kymriah* was gaining approval. Oxford BioMedica is the company that supplies Novartis with viral vectors for its T-cell therapy. In addition, Oxford BioMedica also has alliances with other gene therapy companies which over time should become lucrative.

Large tool companies are also paying attention to this space, given the demand for new tools as well as service offerings. This quarter, Thermo Fisher acquired Brammer Bio, another viral vector specialist which will fit in nicely with Thermo Fisher's biologics manufacturing capabilities, while Danaher will be acquiring GE BioPharma, adding to its portfolio a biomanufacturing division that has significant expertise in cell therapy, an area that overlaps with gene therapy.

Cell therapy is a broad subject. It encompasses therapies that simply use a particular cell population obtained from a patient, as well as therapies that require the patient's cells to undergo genetic modifications before being re-administered. The latter is obviously more complex as it involves a genetic engineering step that happens in an accredited lab. Overall, isolating the right cell population, characterising it, expanding it and then purifying it to produce a proper "drug" is a highly complex process and requires solid supply chain management. Many biotechs in this space are investing in all of the above by themselves, but at times these investments have attracted partners or even become the basis for acquisition.

As biotechs continue to innovate, we will also see "off-the-shelf" versions of cell therapies using donor master cells instead of the patient's own cells. This type of therapy has its own challenges (which we may discuss in a future issue). However, the key take-away message is that cell therapy as well as gene therapy are both areas of intensive activity where progress is being made to overcome challenges step-by-step, offering many opportunities for long-term investors.

Outlook

These are exciting times in biotech. For a long time, developments in small-molecule chemical drugs dominated the industry. Then came monoclonal antibodies which were initially seen as too complex, too expensive and too cumbersome to manufacture. Fast forward to today, simple monoclonal antibodies can be made on demand by several service providers and we now have generic versions of monoclonal antibodies (or biosimilars) commercially available. New drug modalities are emerging fast. Yes, they can be more complex, but they are tackling the molecular complexities of diseases more effectively. As always, as an investor, we look at the long-term potential of this sector and try to envisage what the industry may look like in the years to come. Oncology has made great strides. Neurology remains intriguing and more funding is being allocated to study diseases of the brain. While this quarter saw Biogen's Alzheimer's antibody fail its late stage trials, there are other companies looking deeply into the immune system and its role in Alzheimer's disease.

The flip side to all of this innovation is the demand for different pricing models. The debate is happening and will continue, but it is clear that pricing pressure has never stopped this sector from innovating. So we are excited, but as always, valuation remains important.

1 https://www.platinum.com.au/PlatinumSite/media/Investing-with-Us/Investment%20Updates%20PDF/pihfqtr_1215.pdf

2 https://www.platinum.com.au/PlatinumSite/media/Reports/pihfqtr_0917.pdf

Notes

1. Fund returns are calculated using the net asset value (NAV) unit price (which does not include the buy/sell spread) of the stated unit class of the Fund and represent the combined income and capital returns of the stated unit class over the specified period. Fund returns are net of fees and costs, are pre-tax, and assume the reinvestment of distributions. Returns for P Class are net of any accrued investment performance fee.

   The MSCI Index returns are in Australian Dollars and are inclusive of net official dividends, but do not reflect fees or expenses. For the purpose of calculating the "since inception" returns of the MSCI Index, the inception date of C Class of the Fund is used. Where applicable, the gross MSCI Index was used prior to 31 December 1998 as the net MSCI Index did not exist then. Fund returns are provided by Platinum Investment Management Limited; MSCI index returns are sourced from FactSet.

   Platinum does not invest by reference to the weightings of the Index. A Fund's underlying assets are chosen through Platinum's bottom-up investment process and, as a result, the Fund's holdings may vary considerably to the make-up of the Index that is used as its reference benchmark. Index returns are provided as a reference only.

   The investment returns shown are historical and no warranty can be 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.

   The stated portfolio values of C Class and P Class of the Platinum International Fund (PIF) do not include funds invested in PIF by the Platinum International Fund (Quoted Managed Hedge Fund), a feeder fund that invests primarily in PIF. The stated portfolio values of C Class and P Class of the Platinum Asia Fund (PAF) do not include funds invested in PAF by the Platinum Asia Fund (Quoted Managed Hedge Fund), a feeder fund that invests primarily in PAF.
2. The investment returns depicted in this graph are cumulative on A$20,000 invested in C Class (standard fee option) of the specified Fund over the specified period relative to the specified net MSCI Index in Australian Dollars.
3. The geographic disposition of assets (i.e. the positions listed other than "cash" and "shorts") represents, as a percentage of the Fund's net asset value, the Fund's exposures to the relevant countries/regions through direct securities holdings and long derivatives of stocks and indices.
4. The table shows, as a percentage of the Fund's net asset value, the Fund's exposures to the relevant sectors through direct securities holdings as well as both long and short derivatives of stocks and indices. In the case of the Platinum Unhedged Fund, the Fund does not undertake any short-selling. Its net exposures are therefore the same as its long exposures.
5. The table shows the effective net currency exposures of the Fund's portfolio as a percentage of the Fund's net asset value, taking into account the Fund's currency exposures through securities holdings, cash, forwards, and derivatives. The table may not exhaustively list all of the Fund's currency exposures and may omit some minor exposures.
6. The table shows the Fund's top 10 long equity positions as a percentage of the Fund's net asset value, taking into account direct securities holdings and long stock derivatives. The designation "China" in the "Country" column means that the company's business is predominantly based in mainland China, regardless of whether the company's securities are listed on exchanges within mainland China or on exchanges outside of mainland China.

Disclaimers

MSCI Inc Disclaimer