Platinum International Health Care Fund

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Portfolio Manager

Performance

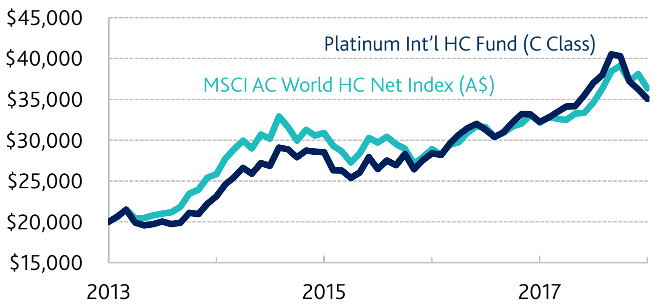
(compound pa, to 31 December 2018)

	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HC Fund*	-13%	9%	7%	12%	9%
MSCI AC World HC Index^	-7%	13%	6%	13%	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 December 2013 to 31 December 2018



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 has been a tough quarter for the health care sector, with the broad sell-off across biotech stocks being particularly intense. We had been cautious about valuations in biotech for some time, and hence had been raising our cash position. We also increased our short positions early in the quarter, but, in hindsight, we had not been aggressive enough.

Our pharma holdings have performed well, while our exposure to the smaller biotechs detracted significantly from performance. Investing in biotech requires patience and long-term thinking. Innovative themes come and go with the majority having to go through cycles of hype and doubts, euphoria and disillusionment, before maturation. Keeping these facts in mind, we remain firmly focused on the long-term performance of the companies in our portfolio, while these recent sell-offs have in fact provided us with some great opportunities to buy.

We selectively added to a number of positions during the quarter, particularly those biotechs that have seen a drastic decline in valuation due to changing market dynamics. It is now not unusual to find small biotechs trading at prices that are close to or even below their cash balance while the fundamentals of their core businesses remain solid.

This quarter we also trimmed several of our steady positions, such as Johnson & Johnson and AstraZeneca, as their valuations have become less appealing, particularly when compared to the other opportunities on offer.

For the year, our European biotech investments have done well (Swedish Orphan Biovitrum +73%, Oxford BioMedica +60%, MorphoSys +16%), along with a number of our tool companies, including NanoString Technologies (+97%).

Commentary

Setting aside the performance, 2018 has been a remarkable year for the industry. There were almost as many drug approvals in the US as there were in 1996, the record year for drug approvals. The first drug based on RNA interference is now approved, while gene therapy and gene editing are no longer conceptual proposals. Given the very generous funding environment in recent years, innovation has been well supported, as have been new biotech listings, with the number of US-listed biotech companies having doubled over this funding cycle.

However, this generosity was always going to subside at some stage, and in the last quarter of 2018 market dynamics changed. Raising money has become more difficult and the focus has shifted to real data, as opposed to mere pipeline dreams.

The macroeconomic environment has definitely played a part, with the impact of US monetary tightening beginning to be felt by markets. As for the biotech sector specifically, nothing in science follows a straight line, and a quarter is a very short time horizon in an industry where a simple dose escalation study in humans takes six months – not days – to complete.

The other important aspect to remember is that themes come and go, with early excitement followed by fading interest, boredom and, in the end, continued success at a much more mature level. Two recent examples, immuno-oncology (IO) and the so-called PARP inhibitors, illustrate how these cycles can unfold in the market and what it takes to ride out the ups-and-downs which at times can feel schizophrenic and uncomfortable.

Immuno-oncology is undoubtedly a major step forward in oncology, and in 2013 the financial market started to get very excited. More than five years on, investors have soured on the theme, which is ironic as the 2018 Noble Prize for Medicine was awarded to scientists who had made major contributions to immuno-oncology. It is safe to say we have reached "peak IO" for the moment. A recent medical meeting in Munich showcasing the latest data on new IO treatments illustrated clearly that immuno-oncology is a lot more complex than what simple schematics suggest. One analyst summed it up well with an old adage: "it's like throwing spaghetti at a wall to see what will stick". For a scientist, this is not at all surprising. Science is all about testing and re-testing a hypothesis, learning from failures and assembling the puzzle pieces along the way. That is what is happening in IO.

Top 10 Holdings

COMPANY	COUNTRY	INDUSTRY	WEIGHT
SpeeDx	Australia	Healthcare Providers	4.1%
Roche Holding AG	Switzerland	Pharmaceuticals	3.9%
Sanofi SA	France	Pharmaceuticals	3.4%
Gilead Sciences Inc	USA	Biotechnology	2.3%
Quanterix Corp	USA	Pharmaceuticals	2.3%
UCB SA	Belgium	Pharmaceuticals	2.3%
Swedish Orphan Biovitrum	Sweden	Pharmaceuticals	2.1%
NanoString Technologies	USA	Health Equip & Serv	2.0%
Takeda Pharmaceutical	Japan	Pharmaceuticals	2.0%
Moderna Inc	USA	Pharmaceuticals	2.0%

As at 31 December 2018. See note 6, page 4.
Source: Platinum Investment Management Limited.

One of the angles through which we seek to profit from this theme is to invest in tool companies (e.g. NanoString). These companies provide the technologies and instruments that allow the interrogation of the tumour microenvironment and support the mutation profiling of the tumour itself. For now, immuno-oncology is going through a maturation phase, with drug developers busy testing hypotheses while investors have stepped to the sidelines. For a long-term investor, there are very interesting opportunities now emerging.

Disposition of Assets

REGION	31 DEC 2018	30 SEP 2018	31 DEC 2017
North America	33%	35%	36%
Europe	26%	29%	38%
Australia	14%	12%	7%
Japan	3%	3%	5%
Asia	3%	2%	<1%
Cash	21%	19%	14%
Shorts	-7%	-1%	0%

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

Net Sector Exposures

SECTOR	31 DEC 2018	30 SEP 2018	31 DEC 2017
Health Care	71%	79%	85%
Consumer Staples	1%	0%	0%
Financials	0%	1%	1%
TOTAL NET EXPOSURE	72%	80%	86%

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

Net Currency Exposures

CURRENCY	31 DEC 2018	30 SEP 2018	31 DEC 2017
US dollar (USD)	48%	41%	41%
Euro (EUR)	19%	18%	26%
Japanese yen (JPY)	15%	4%	4%
British pound (GBP)	10%	9%	11%
Swiss franc (CHF)	6%	5%	5%
Swedish krona (SEK)	2%	3%	2%
Danish krone (DKK)	1%	1%	1%
Australian dollar (AUD)	<1%	19%	9%
Canadian dollar (CAD)	<1%	1%	1%
Korean won (KRW)	-2%	0%	0%

See note 5, page 4. Numbers have been subject to rounding adjustments.
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.

Another theme that has gone from hot to cold to lukewarm is the development of PARP inhibitors. These are drugs that inhibit an enzyme called **p**oly **A**DP **r**ibose **p**olymerase (PARP). PARP plays an important role in repairing DNA damage. A number of cancers arise from gene mutations that render the DNA repair mechanism of a cell unreliable. As a consequence of the mutation, when DNA damage occurs in a cell, the damage is not repaired properly, and the cell can turn cancerous. One way to deal with this is to leave the DNA damage unrepaired and let the damaged cell die (before or after it turns cancerous). To do that, we need to prevent the faulty DNA repair mechanism from trying to do its job, and, according to the PARP inhibitor theory, this can be done by stopping PARP from doing its job of initiating the DNA repair process. So the hypothesis of an inhibitor of PARP makes a lot of sense. Several biotech firms set out to find these inhibitors. Two of these companies were acquired early on with AstraZeneca buying Kudos in 2005 and Sanofi acquiring BiPar in 2009. The BiPar drug looked promising initially, but failed late stage trials, which we now know was due to the drug not being PARP specific enough.

Meanwhile at AstraZeneca the Kudos PARP inhibitor saw itself on the shelf until Pascal Soriot (who joined AstraZeneca as CEO in October 2012) had a closer look. He saw the potential of targeting DNA damage, and he saw a fast path for AstraZeneca's PARP inhibitor drug. Analysts were sceptical of targeting DNA damage as a means to treat cancer, and at the time immuno-oncology was all the rage. We liked AstraZeneca's approach and also saw value in not focusing solely on the immuno-oncology theme. Two years later, AstraZeneca's PARP inhibitor was approved for advanced ovarian cancer and interest in PARP inhibitors was re-ignited.

Besides AstraZeneca, two other biotech firms were also developing PARP inhibitors, Tesaro and Clovis. Excitement for the two companies reached a peak last year with Tesaro's valuation almost reaching US$8 billion while Clovis' valuation exceeded US$5 billion. Both companies received approval for their PARP inhibitors and, for a while, both were seen as clear acquisition targets. However, no acquisition materialised while AstraZeneca, together with Merck (the two companies entered a PARP alliance in 2017), made commercial life difficult for Tesaro and Clovis. Early this quarter, both biotechs reached "trough PARP" with Tesaro valued at less than US$1.3 billion and Clovis's valuation falling to US$550 million.

The Fund first added **Tesaro** to its portfolio earlier this year as its valuation became very attractive, PARP inhibitors were still full of potential, and the company had promising collaborations with oncology companies, one being Johnson & Johnson and the other Roche. Tesaro's PARP inhibitor did struggle commercially (causing some further sell-off in its shares), but we felt that the drug had a role to play and a larger company would in due course recognise its potential. We continued to add to our position, and this quarter GlaxoSmithKline announced its intention to acquire Tesaro for over US$5 billion.

These examples illustrate many attributes of the biotech sector, experiences common to many biotech companies and themes. But, most of all, they demonstrate how patience and going against the crowd can pay off.

Outlook

Consolidation in the sector is inevitable. The number of listed biotechs has expanded significantly in recent years, as has the number of oncology biotechs working on the same gene targets. It is not unusual to have five or even ten companies (for some targets there can be more than 30 companies) pursuing the same oncology target. However, commercially only a handful or fewer will be successful and profitable. This dynamic makes us highly selective when investing in oncology companies.

Venture funding continues to be stellar, particularly as Chinese investors have increased their interest in early stage biotechs. On the flip side, we are seeing a closer interaction between US and Chinese biotechs, which should put Western pharma companies on alert as obtaining Chinese rights for licensing opportunities may become more difficult in future if these rights have already been given to Chinese biotechs.

Medtech companies have been a hiding place amid recent market falls. However, beating high growth expectations will not be as easy as it has been in recent years. We remain selective on medtech.

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.

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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.

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