

# Platinum International Health Care Fund



**Bianca Ogden**  
Portfolio Manager

## Disposition of Assets

REGION	31 MAR 2018	31 DEC 2017	31 MAR 2017
Europe	39%	38%	39%
North America	37%	36%	35%
Australia	11%	7%	5%
Japan	4%	5%	5%
Asia and Other	<1%	<1%	1%
Cash	9%	14%	15%
Shorts	<1%	0%	0%

Source: Platinum Investment Management Limited. See note 3, page 4.

## Top 10 Holdings

STOCK	COUNTRY	INDUSTRY	WEIGHT
AstraZeneca PLC	UK	Health Equip & Services	3.9%
Roche Holding AG	Switzerland	Pharmaceuticals	3.3%
Sanofi SA	France	Pharmaceuticals	3.1%
Gilead Sciences Inc	USA	Biotechnology	3.0%
Johnson & Johnson	USA	Pharmaceuticals	2.8%
MorphoSys AG	Germany	Biotechnology	2.6%
Imugene Limited	Australia	Biotechnology	2.4%
Daiichi Sankyo	Japan	Pharmaceuticals	2.2%
Qiagen NV	Germany	Health Equip & Services	2.2%
BTG PLC	UK	Pharmaceuticals	2.1%

As at 31 March 2018.

Source: Platinum Investment Management Limited. See note 4, page 4.

For further details of the Fund's invested positions, including country and industry breakdowns and currency exposure, updated monthly, please visit <https://www.platinum.com.au/investing-with-us/investment-updates>.

## Performance and Changes to the Portfolio (compound pa, to 31 March 2018)

	QUARTER	1YR	3YRS	5YRS	SINCE INCEPTION
Platinum Int'l HC Fund*	6%	11%	12%	18%	10%
MSCI AC World HC Index	1%	9%	3%	18%	8%

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

Net of accrued fees and costs. Refer to note 1, page 4.

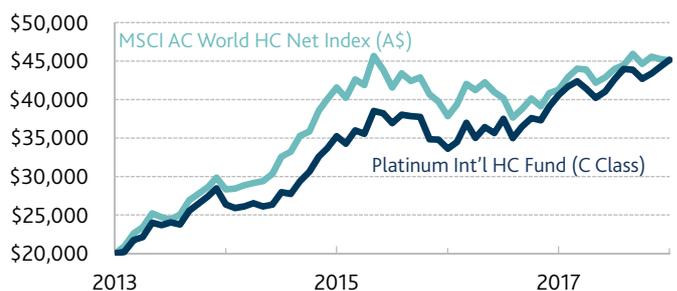
Source: Platinum Investment Management Limited, RIMES Technologies. Historical performance is not a reliable indicator of future performance.

We are in an era of unprecedented innovation within a changing healthcare landscape. In times like this uncertainty tends to prevail, causing a dichotomy in the market, which right now is particularly pronounced in the US. On one hand, venture capital and healthcare specialists are very happy to support a myriad of new companies, while on the other, generalist investors remain on the sidelines, preferring the tool and medtech sectors over drug developers or simply remaining committed to "the stocks that have worked".

Indeed, our pharma holdings have been disappointing and are approaching valuation levels close to those seen at the height of the patent expirations. Some of our portfolio companies have started to use their cash piles while others are busy launching new drugs. There is no sign of complacency, scientists are very busy, and we continue to see value, particularly as the medtech safe haven will at some stage cease to be a safe bet.

## Value of \$20,000 Invested Over Five Years

31 March 2013 to 31 March 2018



Net of accrued fees and costs. Refer to note 2, page 4.

Source: Platinum Investment Management Limited, RIMES Technologies. Historical performance is not a reliable indicator of future performance.

These innovation phases offer many new opportunities and we are seeing solid licensing activity as well as more frequent equity investments rather than straight out buyouts, resembling the post-human genome sequencing era. This is the best time to start refreshing the portfolio and gain access to the next wave of innovators.

Over the past 12 months we have been gradually redistributing money towards new opportunities ranging from diagnostics, gene editing and rare neurological diseases to women's health as well as oncology and implants. This, together with the progress made at our Australian biotech holdings, has contributed to the positive performance. Over the past year we have added a number of Australian biotechs as the valuation disconnect with their European and US peers was unjustified.

We are agnostic to where companies are based, but rather follow the science as well as keep a close eye on staff changes within companies.

For the year and the quarter Daiichi Sankyo has been a solid performer for us. This Japanese company recruited a number of scientists from AstraZeneca who have quickly solidified Daiichi Sankyo's differentiated antibody expertise. The market was preoccupied with the company's patent expirations and failed to see the internal changes which, for us, turned out to be a great opportunity.

The current market obsession of "staying with the winners" also offers short-selling opportunities. This quarter we successfully shorted AbbVie, a company that was seen as "the stock to own". It reminded us of where Celgene was at not long ago (a company we stayed away from). Both companies were market darlings despite stretched valuations and serious patent expirations within the next five years. The pipeline that each had accumulated via acquisitions and licensing was regarded as the best in the industry. But as often is the case, drug development is not linear. In the current environment we continue to look out for such opportunities stemmed from mispricing.

## Commentary

Genetic engineering lies at the heart of what a molecular biologist does. It is all about manipulating genes and studying the effects thereof. Since 2012, molecular biologists' toolbox has received a new exciting gene editing tool. There were other existing gene editing systems available, but none has been as cheap and easy to use, as well as reliable, as the CRISPR-Cas system, hence the significant amount of excitement it has generated and the many papers published about it each week.

All that the CRISPR-Cas system requires are a so-called guide RNA that binds to the area of interest in the genome and a

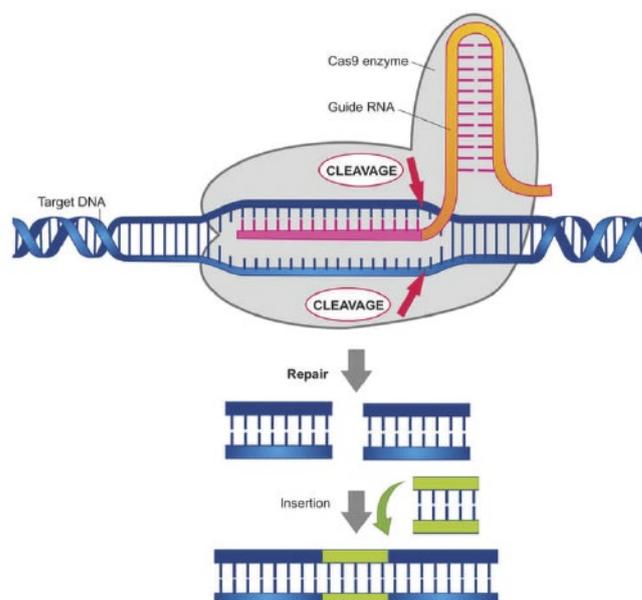
particular enzyme that "cuts" a DNA sequence like a biological pair of scissors. Using the cell's own repair system, a new gene can then be inserted, if desired.

The CRISPR-Cas system has its origin in the adaptive immune system of bacteria. It is a very elegant system, highlighting just how sophisticated these prokaryotes are. Bacteria are prone to infection and hence they had to develop a system that memorises and battles infections. Essentially what the bacteria have done is to build an "invader database" that forms the backbone of their adaptive immunity.

Upon infection by, say, a virus, bacteria integrate short fragments of the invader's nucleic acid (so-called "Spacers") into a repetitive locus (called "Repeats") within its own genome. This "Spacer-Repeat" sequence forms the "Clustered Regularly Interspaced Short Palindromic Repeat" (or "CRISPR") locus. These loci tend to be flanked by sequences encoding a CRISPR-associated enzyme (short-named "Cas") which functions as biological scissors. Upon re-infection, the bacteria can now activate their "memory", and a so-called "guide RNA" is made of the CRISPR sequence which is complementary to parts of the invading virus' genome. This guide RNA then "guides" the Cas enzyme to its target where it will then cut accordingly.

This bacteria-inspired system has been adapted as a gene editing tool. Designing the right guide RNA is a key step, along with designing the perfect biological scissors.

## How the CRISPR-Cas Gene Editing System Works



Source: <https://labiotech.eu/crispr-cas9-review-gene-editing-tool/>

Compared to CRISPR-Cas, which is a natural system adapted for molecular biological use, other gene editing systems (ZFNs<sup>1</sup> and TALENs<sup>2</sup>) are more synthetic and more cumbersome to design and execute. However, the non-CRISPR systems are by no means less interesting and are ahead of CRISPR-Cas in clinical development. Ultimately, patients will rarely care how a disease is treated as long as the treatment works with minimal side effects.

Delivery of these gene editing systems is a challenge that will gradually be resolved. Delivery can occur ex-vivo, which means cells (e.g. T-cells or hematopoietic stem cells) are obtained from the patient, edited in the lab, and then reinfused back into the patient's body. Alternatively, the editing machinery can be packaged up in a viral vector and delivered systemically (i.e. a manipulated virus that carries the edited gene is injected or delivered intravenously into the patient's body tissue where it is taken up by individual cells). This year will see both approaches in the clinic, which is a remarkable achievement.

## Outlook

The toolbox of drug developers continues to evolve beyond the humble small molecule and towards complex antibodies, antibody fragments, oligonucleotides, modified T-cells, and now gene editing systems. The Fund has investments in the area of gene editing as well as viral vector manufacturing and T-cell manipulation, all areas that are evolving rapidly.

Given the complexity of these technological developments, no company can "do it all" these days and hence deal-making will continue to be a hallmark of the industry. While the large companies are interesting, greater excitement lies with the well-funded smaller innovators.

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1 Zinc finger nucleases

2 Transcription activator-like effector nucleases

## Notes

1. Fund returns are calculated using the net asset value per unit (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. Returns are net of accrued fees and costs, are pre-tax, and assume the reinvestment of distributions. 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.

Index returns are in Australian dollars and assume the reinvestment of dividends from constituent companies, but do not reflect fees and 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 indices were used prior to 31 December 1998 as the net MSCI indices did not exist then. Fund returns have been provided by Platinum Investment Management Limited; MSCI index returns have been sourced from RIMES Technologies.

Platinum does not invest by reference to the weightings of any index or benchmark, and index returns are provided as a reference only. 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.

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 fund over the specified five year period relative to the relevant net MSCI index in Australian dollars.

Fund returns are calculated using the net asset value per unit (which does not include the buy/sell spread) of C Class of the fund and represent the combined income and capital returns of C Class over the specified period. Returns are net of accrued fees and costs, are pre-tax, and assume the reinvestment of distributions. 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.

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3. The geographic disposition of assets (i.e. the positions listed other than "cash" and "shorts") represents the fund's exposure to physical holdings and long derivatives (of stocks and indices) as a percentage of the fund's net asset value.

4. The table shows the fund's top 10 long stock positions (through physical holdings and long derivatives) as a percentage of the fund's net asset value.
5. Sector breakdown represents the fund's net exposure to physical holdings and both long and short derivatives (of stocks and indices) as a percentage of the fund's net asset value.
6. The table shows the fund's major currency exposure as a percentage of the fund's net asset value, taking into account currency hedging.

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