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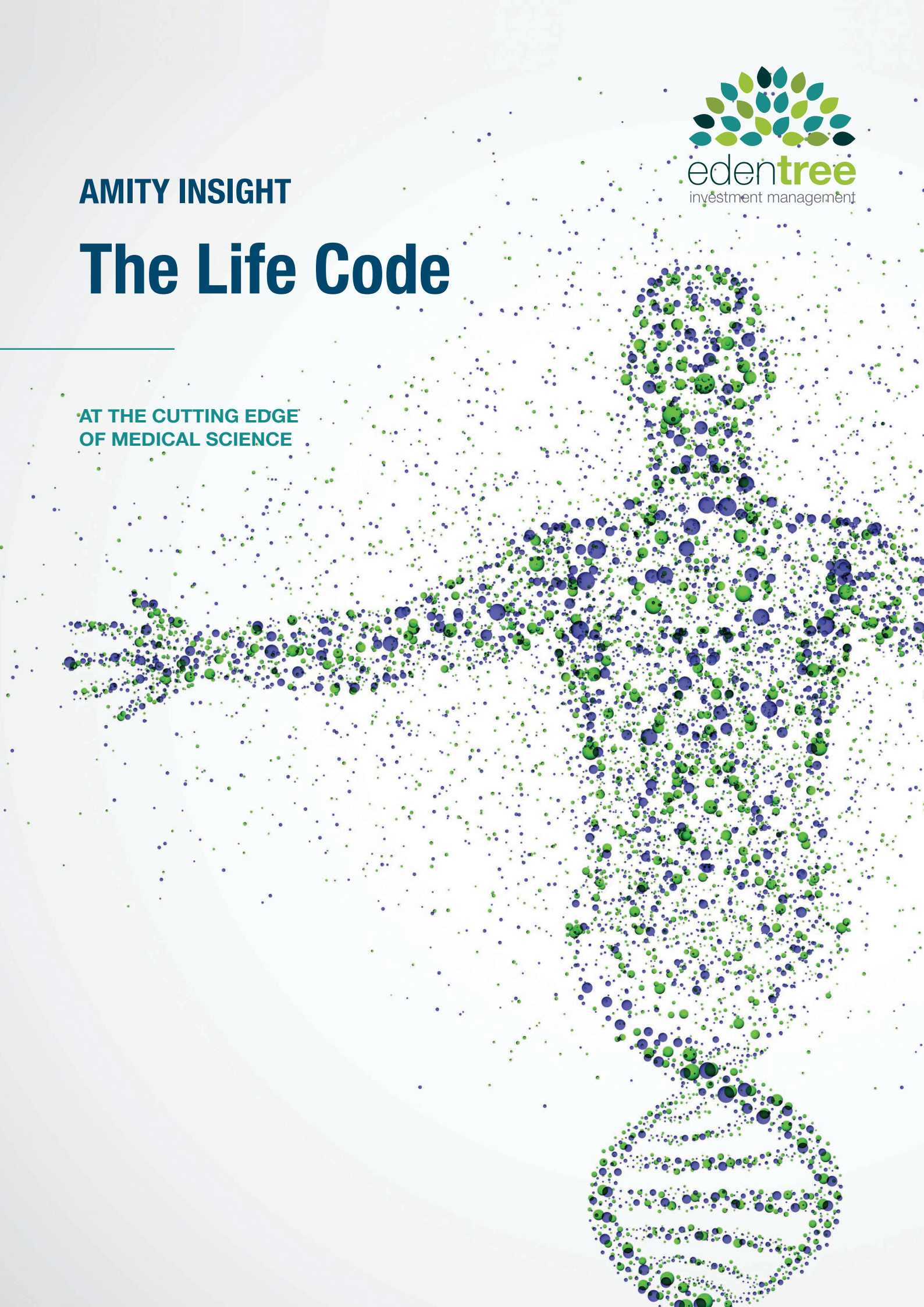
AMITY INSIGHT

The Life Code

AT THE CUTTING EDGE OF MEDICAL SCIENCE



Introduction

> **It is far more important to know what person the disease has than what disease the person has.**
>
> Hippocrates (460-370BC)

By Lydia Greasley MSci

Investment Analyst, EdenTree Investment Management Ltd.

Health & wellbeing

- Affordable healthcare
- Access to medicine
- Pharmaceuticals R&D
- Biotechnology
- Clinical care
- Nutrition & wellbeing

Our role as thought leaders in the responsible investment space is to identify emerging investment opportunities and any attendant ethical issues. The areas covered within this Amity Insight are at the cutting edge of developments in medical science where many of the ethical dilemmas are still to emerge, and to be regulated by policy makers. Consequently, to some degree we too are very early in the process of forming opinions.

Hippocrates, often thought of as the father of medicine, prophetically stated that 'science is the father of knowledge' and science, technology and medicine are constantly evolving, solving old questions and posing new. Despite this progression in understanding, medicines are still prescribed using inelegant, impersonal, trial and error approaches. There are still large gaps in medicine and in knowledge for successfully treating genetic diseases and other conditions such as cancer and Parkinson's.

A growing area of research, fuelled by scientific and technological advancement, offers great promise in de-coding difficult to treat diseases and in understanding why some individuals respond where others do not. The answers lie in our life code – DNA (deoxyribonucleic acid).

The application of DNA related knowledge is creating a range of investment opportunities throughout the value chain in diagnostics, genetic editing, research and treatment.

The cutting edge nature of *The Life Code* does not align perfectly with UN Sustainable Development Goal #3 – Good Health & Wellbeing – which is focused on conventional approaches to tackling medical inequality via bold commitments to combat AIDS, tuberculosis, malaria, and other communicable diseases. However, Health & Wellbeing in the widest sense is one of Amity's key sustainable themes focused on improving efficacy of treatments, reducing drug waste and powering discovery of new drugs for unmet medical conditions. *The Life Code* represents an exciting new area of investment exploration and discovery.

Nevertheless, our fairly recent mastery over the building blocks of life pose many unsolved ethical dilemmas. How do we protect this important data? What are the implications of genetic editing that may cause us to contemplate what it really means to be human, and how far should the Life Code itself be manipulated for profit? We do not have all the answers to these dilemmas, but we do hope you enjoy the voyage of discovery, and as ever, welcome your feedback and comments.

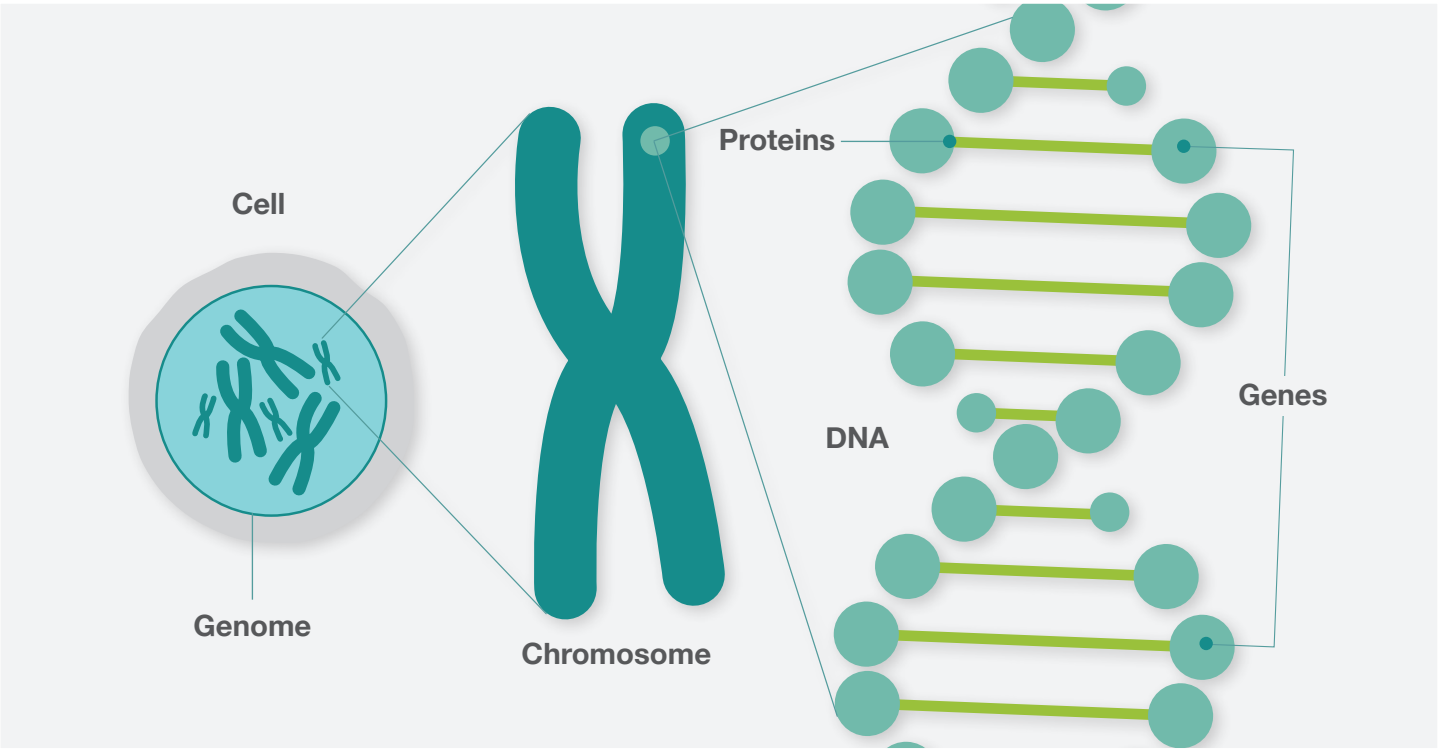
Background in DNA

All living things can be distinguished by a very specific fingerprint held within the cells that make up our bodies – DNA.

Similar to how a computer code is a binary sequence of 0's and 1's, living things are defined by a life code of four letters called bases: A (Adenine), T (Thymine), G (Guanine) and C (Cytosine).

DNA contains our life code consisting of 3.2bn pairs of these bases from two strands twirled into a double helix structure.

Segments of DNA are called genes. Genes are responsible for making proteins that make up the structures within the body such as organs and tissue; but these also control reactions and carry signals between cells. The entire collection of genes, made from DNA, is known as the *genome*, hence the genome is our full human programming code.



The length of DNA from one cell if you were to stretch it out… 2 metres

Number of years it would take if you typed out the entire genome of 3.2bn base pairs by hand… 50 years

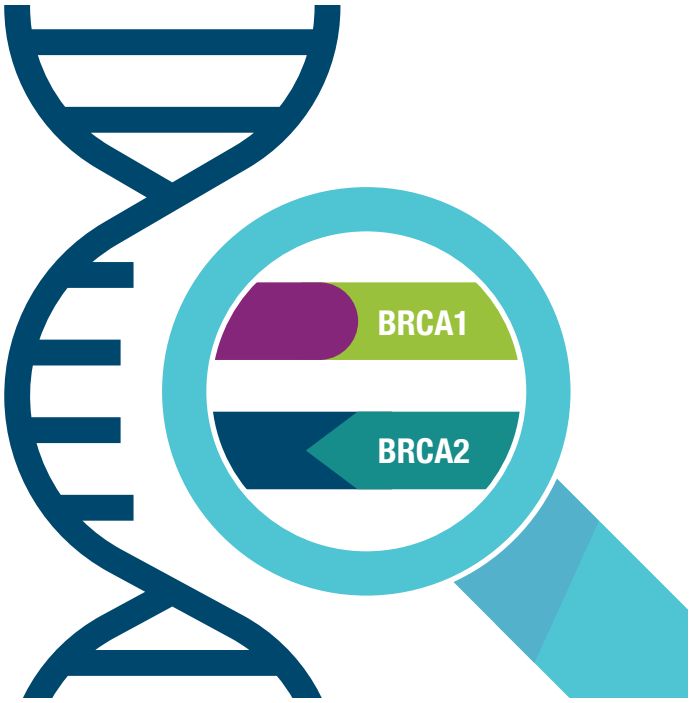
A salamander has a genome 10x the size of a human genome. Salamanders have the capability to regrow lost limbs and repair some internal injuries, somewhere in all that data is the code for regeneration!

Linking Disease to Genes

We mostly inherit our genetic makeup from our parents. This includes features such as hair, eye colour and height, but also includes genetic (hereditary) conditions such as cystic fibrosis and Huntington's disease. As research shows, genetics play a much greater and more intricate role in many medical conditions than just its direct link to genetic diseases.

DNA is constantly replicating within the body, as cells are shed and new ones formed, but occasionally mistakes occur in the DNA copying process. Policing enzymes can usually repair errors because if one side of the DNA is incorrect, it can extrapolate data from the other side – a handy feature of the double helix structure. However, sometimes errors pass by the enzymes and replicate causing a mutation to occur. Mutations occur naturally but also from environmental factors such as radiation and pollution.

These DNA mutations are incredibly important to understand as they are responsible for one of the world's deadliest killers, cancer.



Altering the DNA within a cell can stop it from behaving normally, such as uncontrollable replication in a cancerous tumour. The Cancer Genome Project found that on average a cancerous cell has 60+ mutations compared to normal DNA. Some of these mutations we can inherit, thereby predisposing us to cancer. Many mutations need to occur for a cell to become cancerous, but if some genes are inherited, the pathway to cancer is shortened.

Mutations to genes known as BRCA1 and BRCA2 are prevalent examples linked to breast cancer. On average 12% of women will get breast cancer[1], however if a woman has a harmful mutation of the BRCA1 or BRCA2 gene, the likelihood of breast cancer increases to 60% and 45% respectively by the age of 70.[2]

Linking disease to genes goes much further than just cancer, however. Other genes and mutations have been linked to a multitude of diseases and conditions: Parkinson's, diabetes, obesity, and epilepsy are a few examples. The figure below shows genes associated with diseases coloured by type of disease. As you can see, it's more connected than just cancer.

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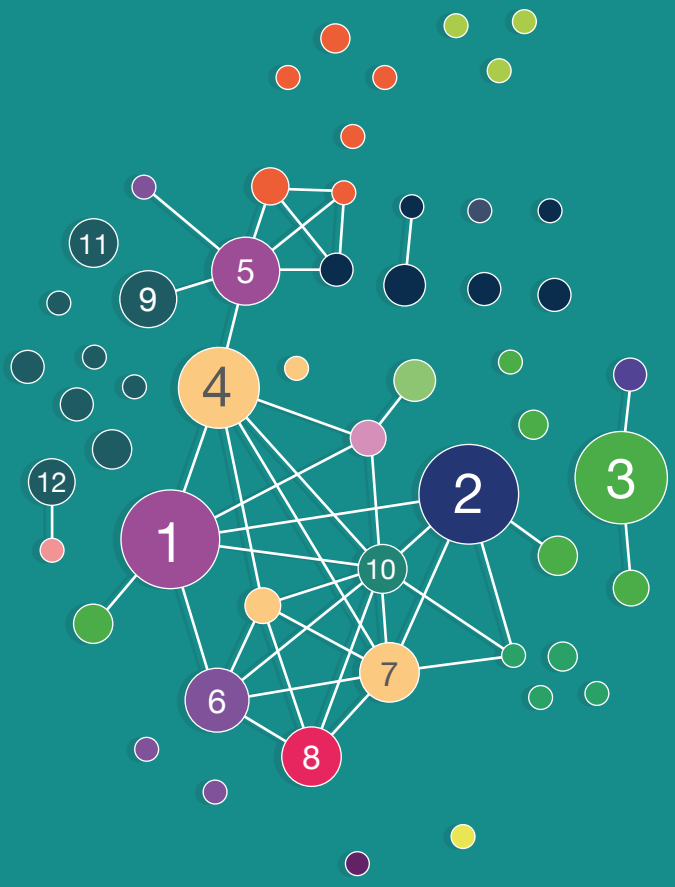
[1] Howlader N, Noone AM, Krapcho M, et al. (eds). SEER Cancer Statistics Review, 1975-2014, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2014/, based on November 2016 SEER data submission, posted to the SEER website, April 2017.

[2] Kuchenbaecker KB, Hopper JL, Barnes DR, et al. Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. JAMA 2017; 317(23):2402-2416.

Disease Gene Network

The bigger the circle, the more genes that are associated with the particular disease. Interlinking of the circles indicates a connection of a gene with another disease.



1. Type 1 diabetes (36)
2. Multiple sclerosis (36)
3. ADHD and conduct disorder (33)
4. Crohn's disease (27)
5. Type 2 diabetes (22)
6. Celiac disease (19)
7. Ulcerative colitis (17)
8. Systemic lupus erythematosus (17)
9. Prostate cancer (17)
10. Rheumatoid arthritis (13)
11. Breast cancer (12)
12. Lung cancer (11)

Source: https://journals.plos.org/plosone/article/figure?id=10.1371/journal.pone.0008090.g001

Technology the Enabler

Genetic research is thriving – this is due to two key enablers:

First, the cost of genome sequencing, which records all the code (bases) of the genome, has fallen significantly since it began. The first full genome took around four years and cost billions of dollars; now it can cost less than $1,000 and takes around a day.

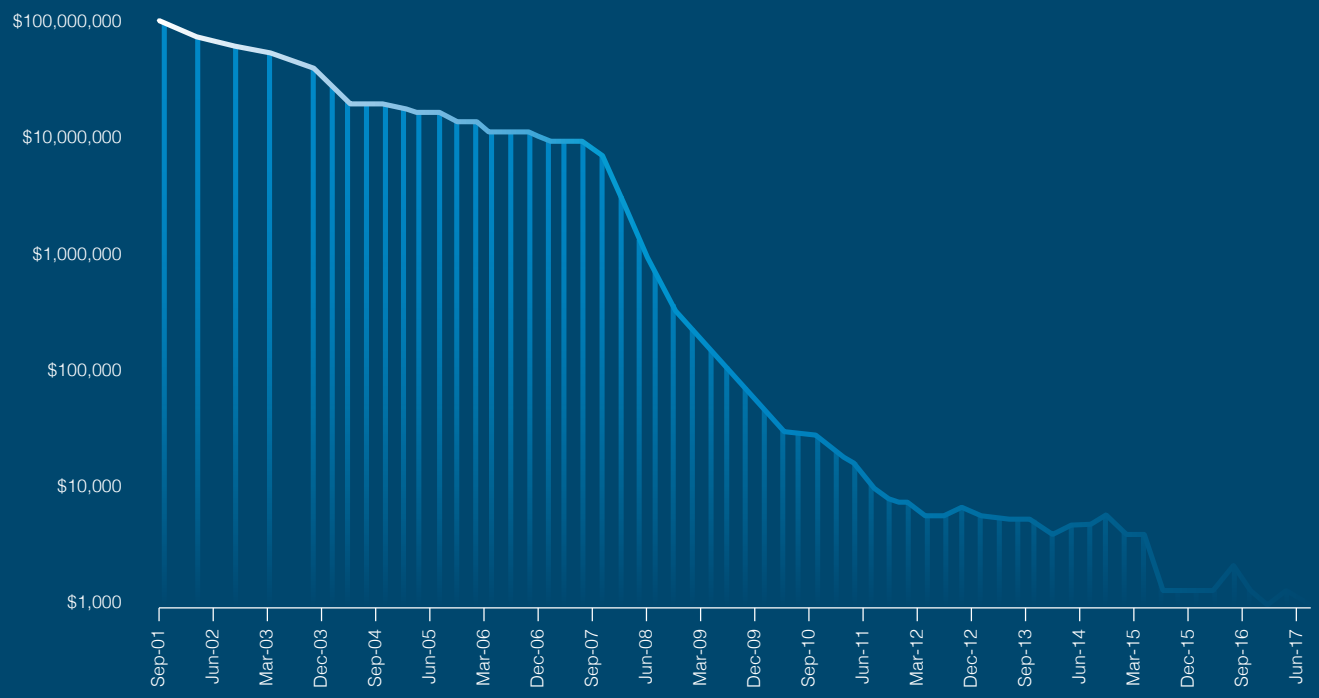
Second, the 3.2bn bases in the human genome will produce around 4GB of data. In practice however, this is typically repeated ~30 times to ensure accuracy.

Overall a whole human genome produces about 120GB of data[3]. That's equivalent to about nine of the highest capacity 1st generation iPhones!

As a result, sequencing genomes requires considerable data storage. However, over the past few decades, data storage has increased in capacity and shrunk in physical size and cost. The modern capability of cloud computing to store data for just £0.01 per gigabyte removes these barriers.

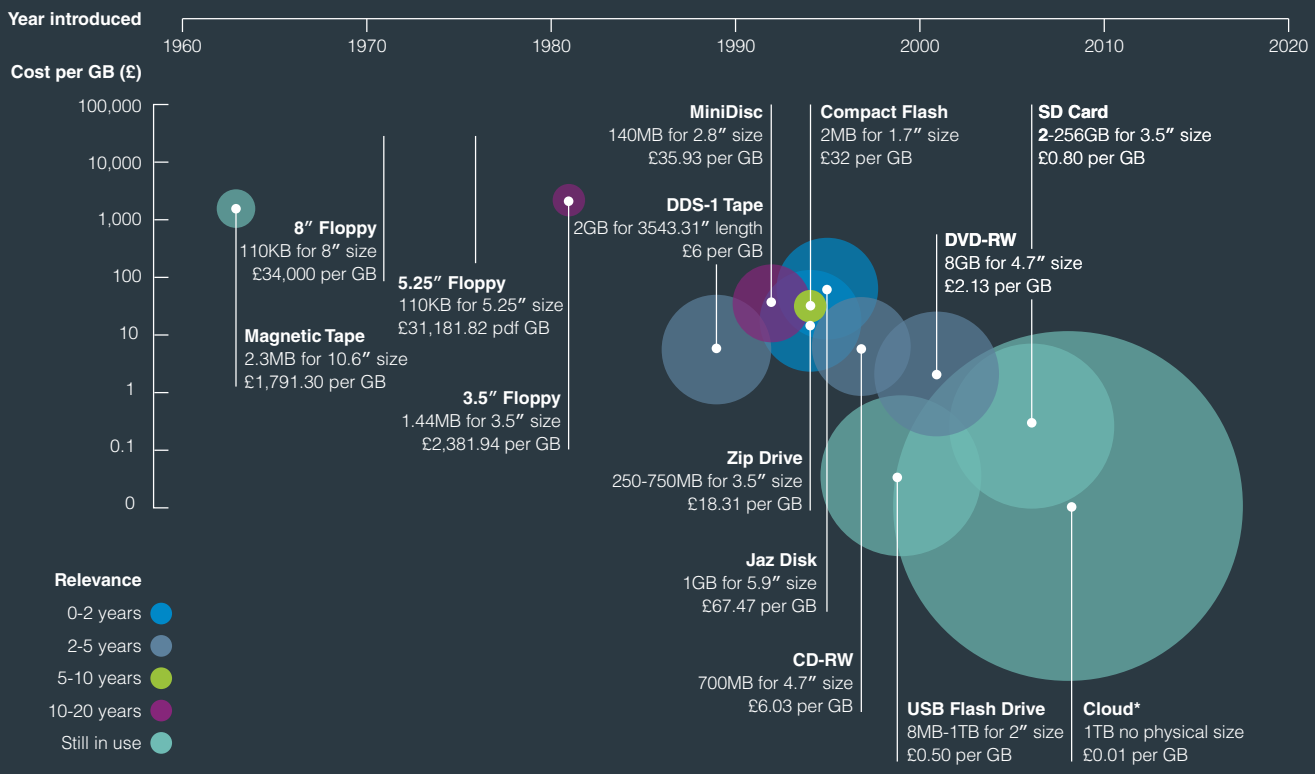
[3] https://www.strand-ngs.com/support/ngs-data-storage-requirements

Cost of Sequencing Per Genome



Source: National Human Genome Research Institute

The Evolution of Data Storage



* Based on Dropbox Cloud

Data on capacity, purchase price and price per GB are calculated based on the most commonly used types of respective storage media

Case Studies

Sequencing pioneer

Illumina (not held in Amity Funds)

Illumina is the market leader within gene sequencing and has a dominant market share of over 50%. Illumina was the first company to commercialise fully gene sequencing after purchasing Solexa in 2007, which originated out of Cambridge University. Illumina specialises in high quality and high throughput lab sequencing. The initial outlay cost for a top of the range sequencing machine (NovaSeq 6000) is c$1 million, but recurring revenue from consumable 'flow cells' (a glass slide coated with chemicals required for sequencing) makes this economic.

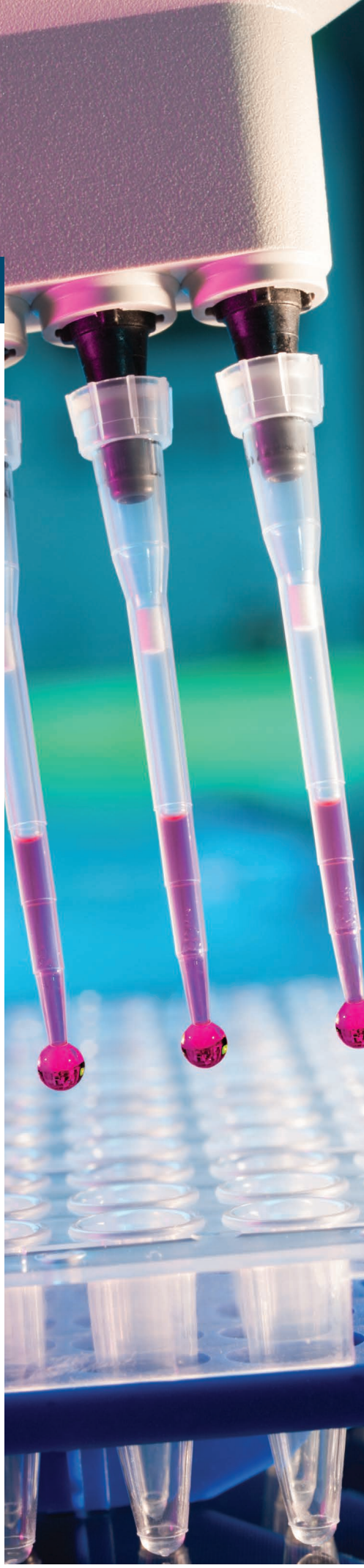
Future of sequencing

Oxford Nanopore
(IP Group held in Amity UK and Amity International)

Oxford Nanopore is a holding of Intellectual Property Commercialization Group (IP Group), and their largest holding, constituting around 20% of the portfolio. Oxford Nanopore has a niche position in making smaller, portable and cheaper sequencing devices which 'reads' in real-time, unlike Illumina's technology. These qualities make the devices ideal for infield sequencing research.

For example, they were used to sequence the recent Ebola outbreak in West Africa which caused almost 12,000 deaths in 2014-16. Genome sequencing is desirable to understand the infectious agent and its evolutionary rate. It also allows identification of 'signatures' of host adaptation. Oxford Nanopore technology was used in 2015 to devise a genomic surveillance system, allowing results to be generated within 24 hours.

Some of Nanopore's devices are smaller than a mobile phone and have a cost range in the low hundreds of pounds. Other uses for these smaller, cheaper sequencing devices could one day include biometric security, food safety and superbug detection.

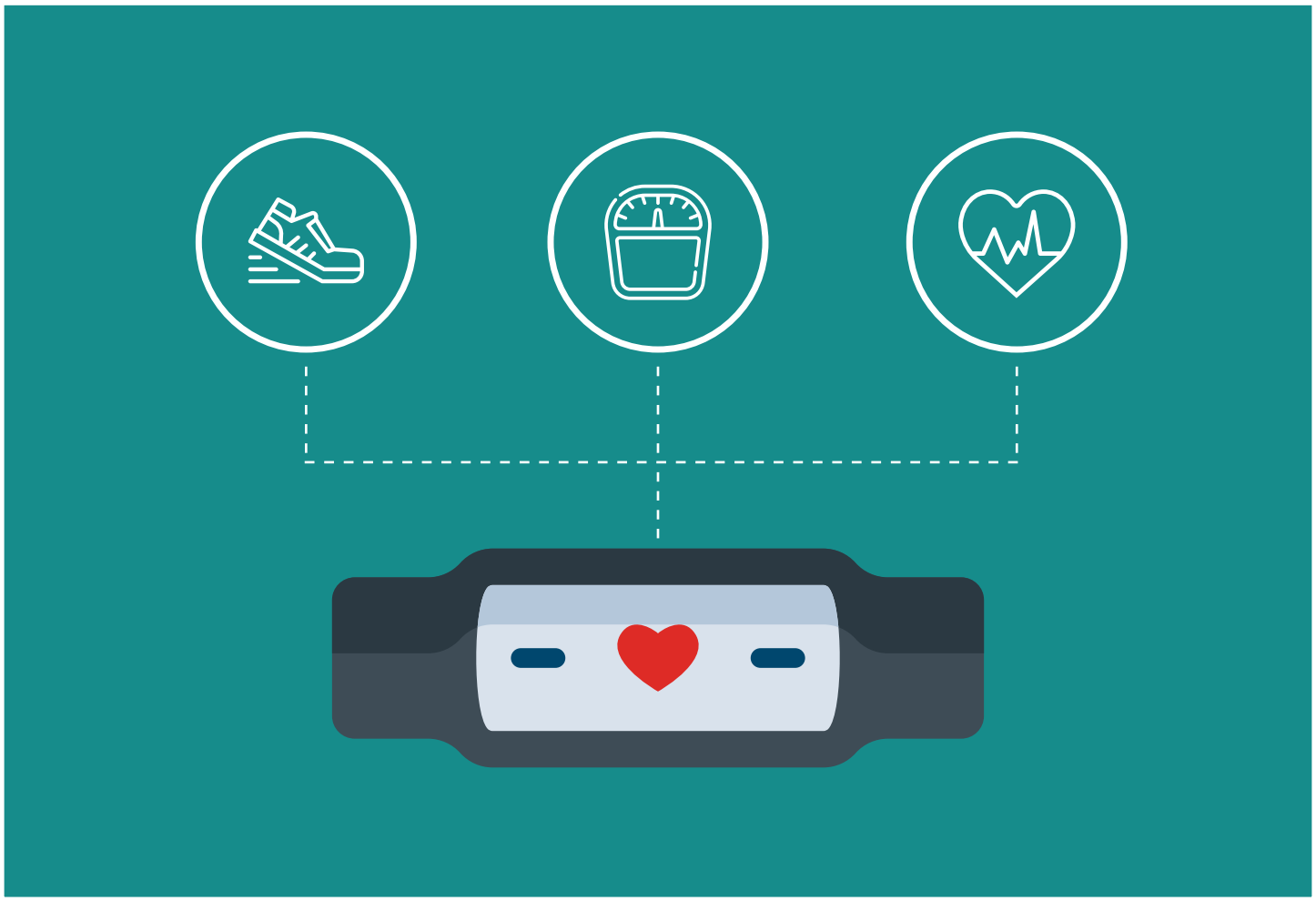


Preventative Medicine

Linking genes to predispositions to a multitude of diseases will assist medicine to become more proactive by:

- Enabling screening of individuals predisposed to a high genetic risk of certain diseases;
- Informing individuals about their genetic risks so as to empower informed lifestyle choices;
- Encouraging more responsibility for individual health.

Wearable technologies are becoming a common addition to our increasingly connected lives. Activity trackers that promote fitness and heart health have evolved into a new generation of wearable technology. The latest devices for instance, are capable of performing FDA-approved electrocardiograms (ECG) that measure heart activity and irregularities.



Personalised Medicine

Whilst medicine advanced spectacularly over the course of the 20th century, the number of patients that find prescribed drugs ineffective remains shockingly large.

Cancer drugs, regrettably, are among the worst offenders. A study by the British Medical Journal (BMJ) reviewed 48 cancer medications that had been approved by the European Medicines Agency in the period 2009-2013, and found only 10% had any measurable effectiveness and that 57% provided no benefits at all![4]

For many medical conditions, drugs are prescribed on a trial and error basis; this may seem surprising given each patient's unique genetic situation. Research into genes is beginning to decipher the mysteries of how drugs interact with the body on an individual basis to answer different types of question:

- How drugs work exactly and which genes they interact with;
- Why treatments are effective for some and not others;
- Why some experience adverse side effects and others do not.

Given developments utilising artificial intelligence (AI), this may well help interpret the wealth of information stored in our unique DNA to recommend drugs on a personalised basis. A world in which treatment is prescribed on a targeted and individual basis has better health economics:

- Less time and money will be wasted on ineffective treatment;
- Quicker recovery time and better outcomes based on genomic access to effective treatment;
- Better anticipation of negative side effects.

Within the major pharmaceutical companies, return on research and development (R&D) has been under significant pressure for the past decade or more.

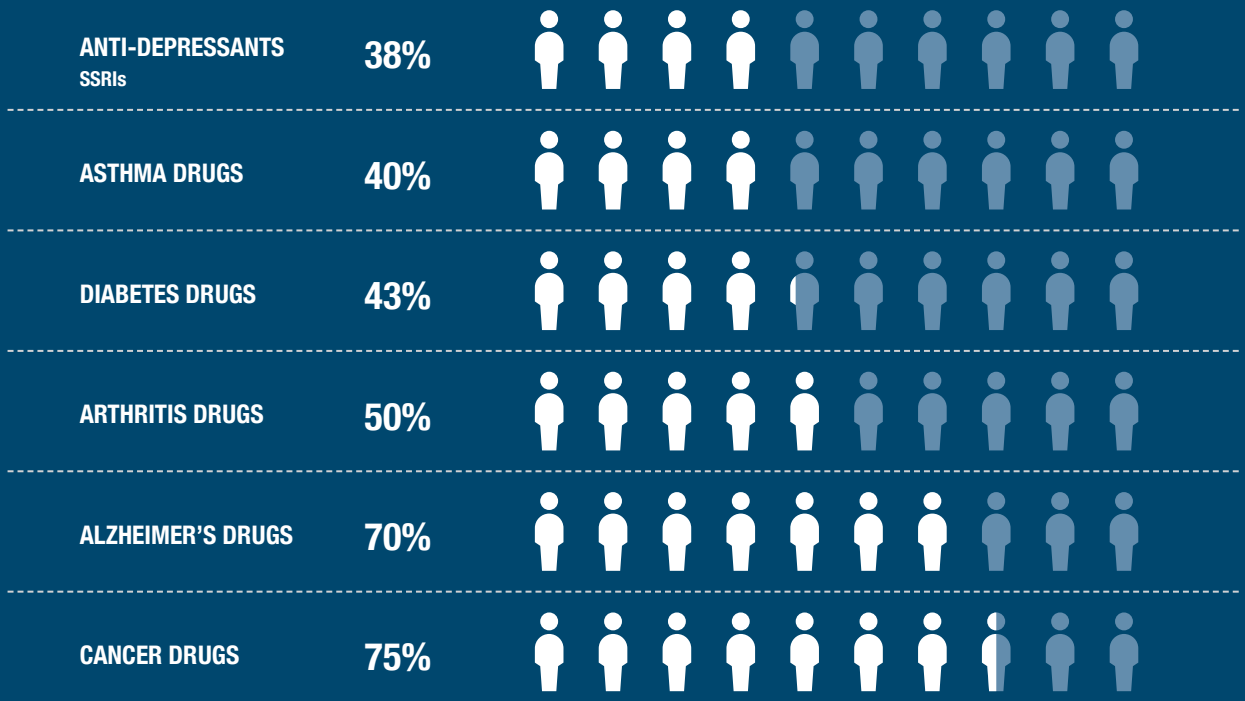
Between 2010 and 2017, the average cost of bringing a new treatment to market increased by 68%; concurrently, projected peak sales of that treatment decreased by 40%. Large pharmaceutical companies are now frequently partnering with others in an effort to 'de-risk' drug development by acquiring small or mid-sized companies in order to develop their pipelines.

Precision-targeted drugs may act as a 'disrupter technology' and threaten the traditional 'blockbuster' drug business model since potential patient groups shrink if they are 'filtered' based on genetic groupings.

However, this has also provided opportunities for pharmaceutical companies. For instance, companies have been able to resurrect drugs once developed but which failed during trials. Retesting with an informed understanding of whether these will be effective within a genetic subset of patients has opened new pipeline possibilities (see across). Secondly, if a drug is targeted at those with (or without) certain gene dispositions, they have a higher probability of being effective, even within a smaller subset of patients, and thence can be charged at a premium.

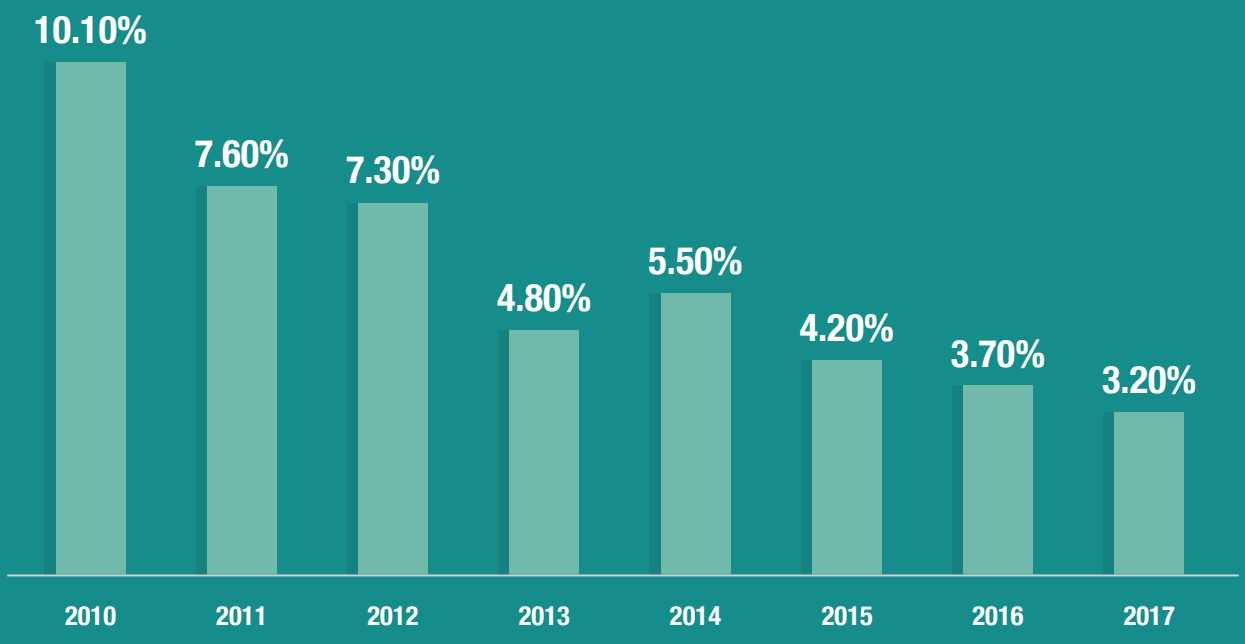
[4] https://www.bmj.com/content/359/bmj.j4528

Percentage of patients for whom a drug is ineffective, on average



Source: Brian B. Spear, Margo Heath-Chiozzi, Jeffrey Huff, *Clinical Trends in Molecular Medicine*, Volume 7, Issue 5, 1 May 2001, pages 201 - 204.

Average large cap biopharma returns on R&D



Source: Deloitte

Case Studies

Therapeutic example

Merck KGaA (Amity International and Amity European)

Erbitux, licenced to Merck KGaA, is an example of a drug where gene sequencing greatly improves effectiveness by ensuring it reaches the right patients. Erbitux is a treatment for advanced bowel cancer. It works by attaching to the growth receptors found on some cancer cells, blocking them and stopping growth. However, research has shown that if a person has a mutation in their KRAS gene, the treatment is ineffective; approximately 40% of those with bowel cancer have a mutation in this gene. As a result, patients are tested for a normal KRAS gene before this treatment path is followed, significantly increasing efficacy and economic value where a course of Ebitux costs ~$50,000.

Diagnostics

In order to ensure targeted treatment is followed, a new diagnostic arena has emerged: companion diagnostics.

Diagnostic companies have partnered with pharmaceutical companies to provide a companion diagnostic, or Next Generation Sequencing (NGS) test for new drugs. These test for specific genes rather than reading the full sequence e.g. the case of Erbitux (Merck KGaA) test on the KRAS gene.

Companion diagnostics are tests that:

- Identify patients who are most likely to benefit from a particular treatment;
- Identify those at high risk of serious side effects.

A Cautionary Tale: Myriad Genetics

The diagnostic test for breast cancer linked genes was once a monopoly held by Myriad Genetics. However following a court ruling in 2013, the patent blocking other tests was dissolved, opening up the competition and destroying Myriad's intellectual property.

Whilst a protected patent portfolio and monopolistic ownership appears to be a strong model for patient outcomes, the ethics of owning a crucial genetic test could also be a threat in the wrong hands!

Genetic Editing in ‘Reactive’ Medicine

Our understanding has reached much further than just reading and interpreting genes. Scientists can now physically change and edit genes thanks to a newly developed technique called CRISPR-Cas9, also known as ‘molecular scissors’. Whilst genetic editing may seem like a distant ‘weird’ science, the technique is already in place and being used commercially.

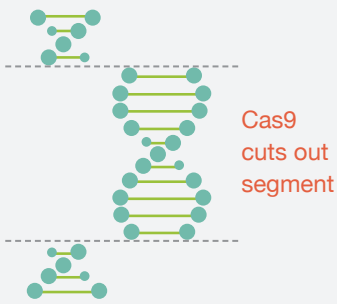
Changes to somatic cells (all cells bar reproductive ones) will only affect the individual being treated and are not handed down to future generations. Luxturna, a treatment pioneered by **Spark Therapeutics – *‘A world where no life is limited by genetic disease’* – (not held in Amity)**, is the first FDA-approved gene therapy for a genetic disease. It’s a one time treatment for those with a genetic eye disease that causes eventual blindness due to a single faulty gene and where no traditional palliative solution exists. Spark’s therapy edits out and replaces the faulty gene with a healthy alternative.

Genetic editing offers significant hope for genetic diseases linked to specific genes that had previously been untreatable, for instance in inherited diseases such as haemophilia or lysosomal storage disorder and a range of neurodegenerative conditions.

Editing Human DNA

The gene-editing tool CRISPR/Cas9 can target and modify DNA with a great deal of accuracy, changing the way we think about treating diseases.

1. DNA contains all of the information in the human genome, including physical traits as well as mutations.



2. Scientists use the Cas9 enzyme to cut out a specific segment of DNA.

3. Scientists insert an amended segment of DNA that corrects the mutation *(e.g. vision gene)*.

Source: University of California Berkeley

Case Studies

Genetic Editing – Research Enabler

Horizon Discovery (Amity UK)

Horizon Discovery uses its expertise in genetic editing to create the perfect ‘patient in a test tube’. They have a range of cell lines that can be edited to include or exclude certain genes. This creates a useful tool by producing targeted genetic cohorts for drug discovery and testing. The company has a vast library of created cells, but also offers extensive services for custom projects, preparing samples and gene editing using CRISPR technology. Horizon also produce reference standards for diagnostic/genetic testing.

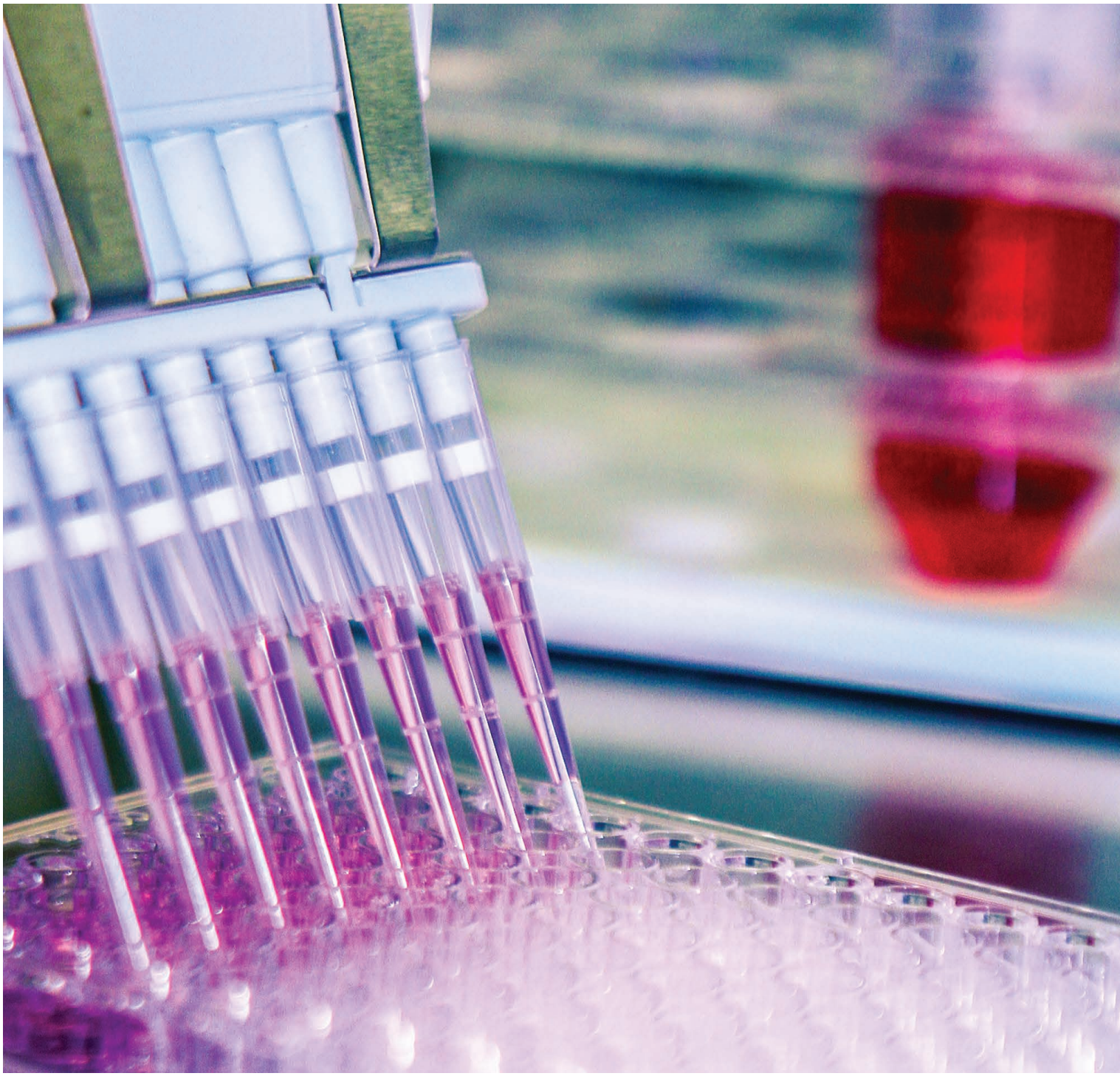
Groundbreaking cancer treatment

Novartis (Amity European, International and Global Equity)

Kymriah, by Novartis, is the first regulatory-approved CAR-T therapy (Chimeric Antigen Receptor-T cell). This combines immuno-oncology, gene therapy and cell therapy by training a patient’s own immune system to recognise and target a protein found in most blood cancers and to kill the cancer cells.

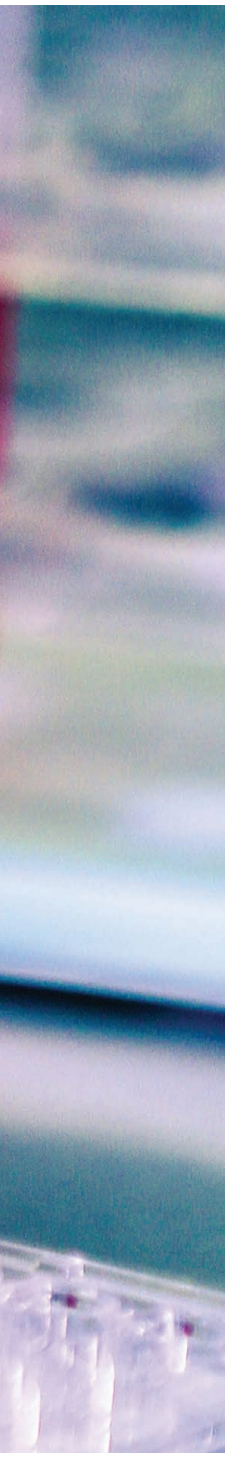
The treatment costs an estimated ~$475,000 per patient and is approved in England by the NHS for use with children with hard-to-treat blood cancers where multiple prior treatments have failed. The treatment, genetically targeted, has been seen as a ‘miracle cure’, as patients with only a short expected life-span have recovered, and 83% have achieved complete remission after three months.

Ethical Implications for Responsible Investors



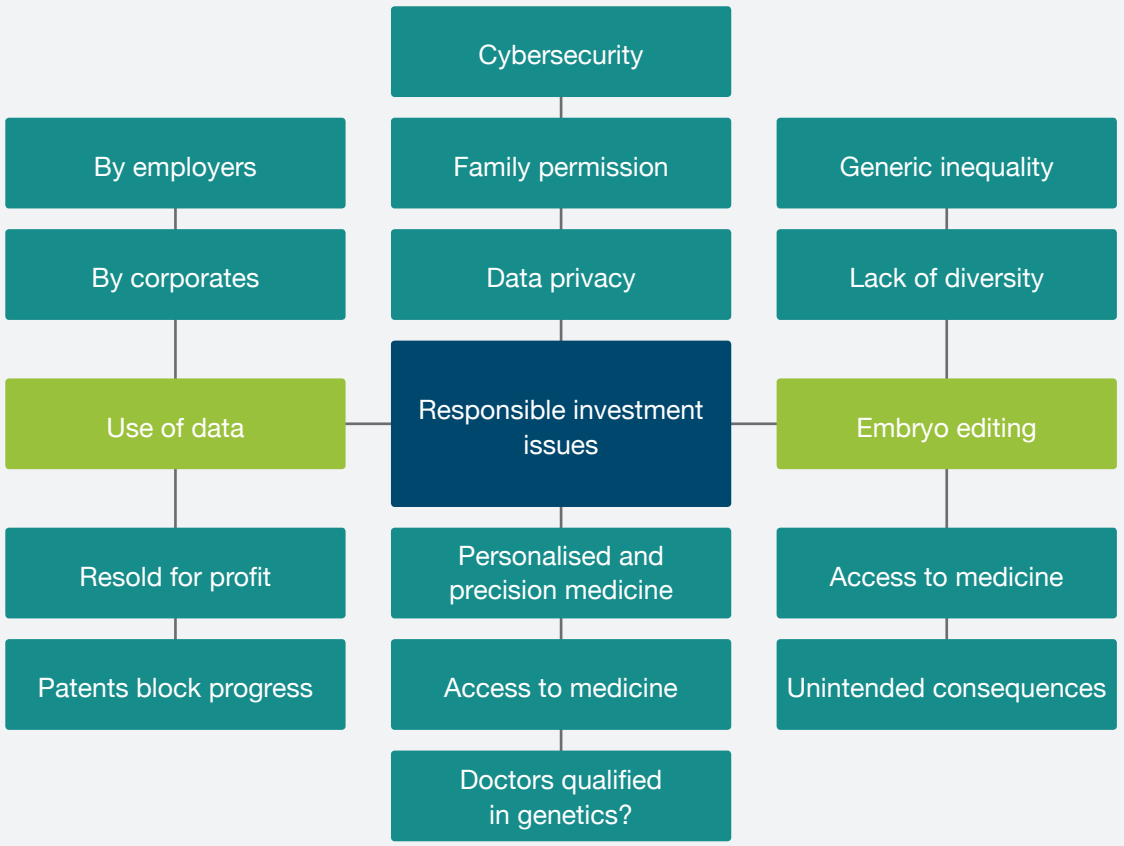
Given the cutting edge nature of the technology outlined in this Amity Insight, the ethical implications for responsible and sustainable investors are broad and deep.

Some of these challenges touch on the nature of life and what it means to be human.



Unsurprisingly, given the nature of scientific advancement, regulation, ethics and public policy thinking are failing to keep pace! Whilst we do not have all of the answers, we scope here some of the ethical risks and challenges.

In this Insight we look at risks surrounding the use (and potential misuse) of patient data, life-ethics challenge around embryo editing and the consequences of personalised medicine as 'the survival of the richest'.



Source: EdenTree Investment Management

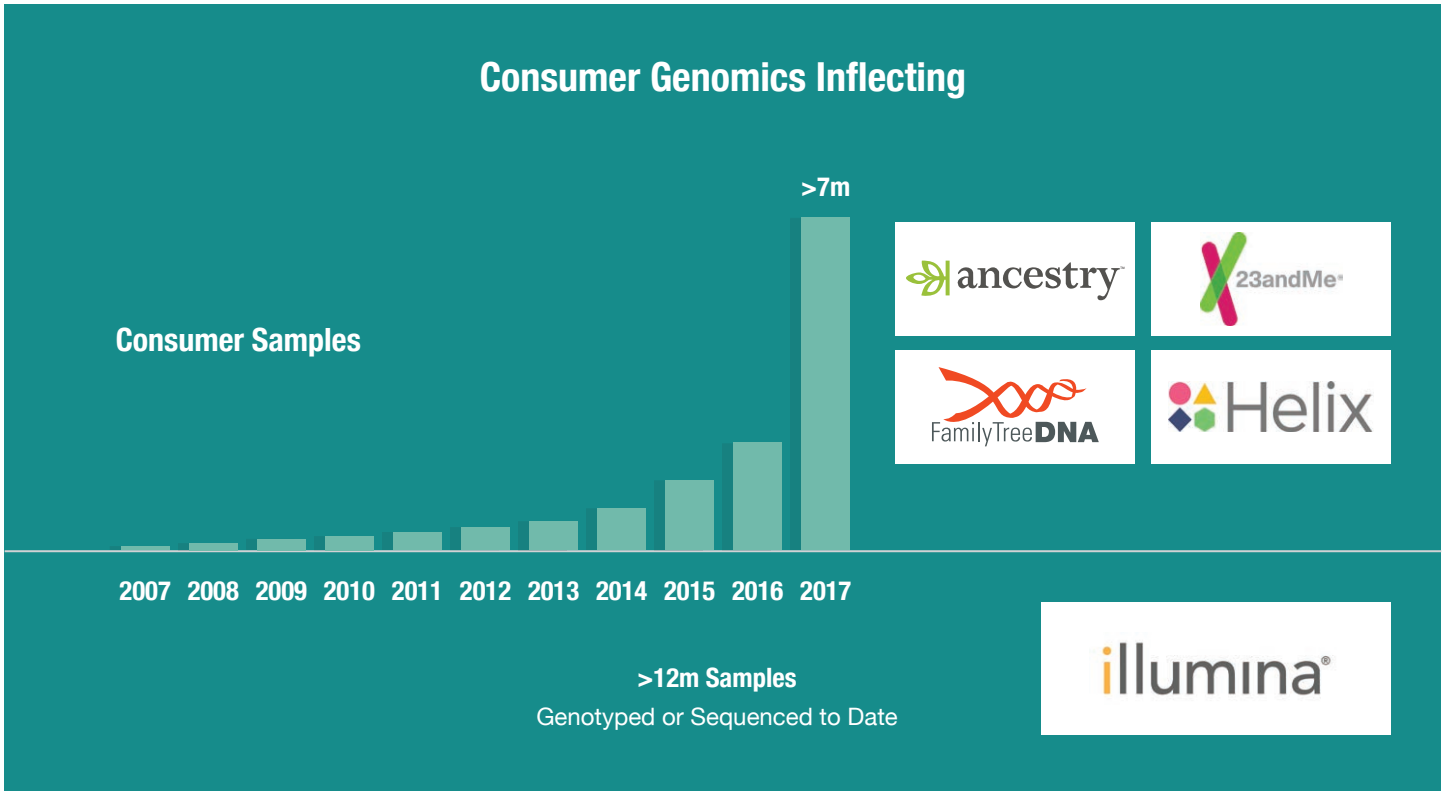
Data Risk – Privacy Ownership

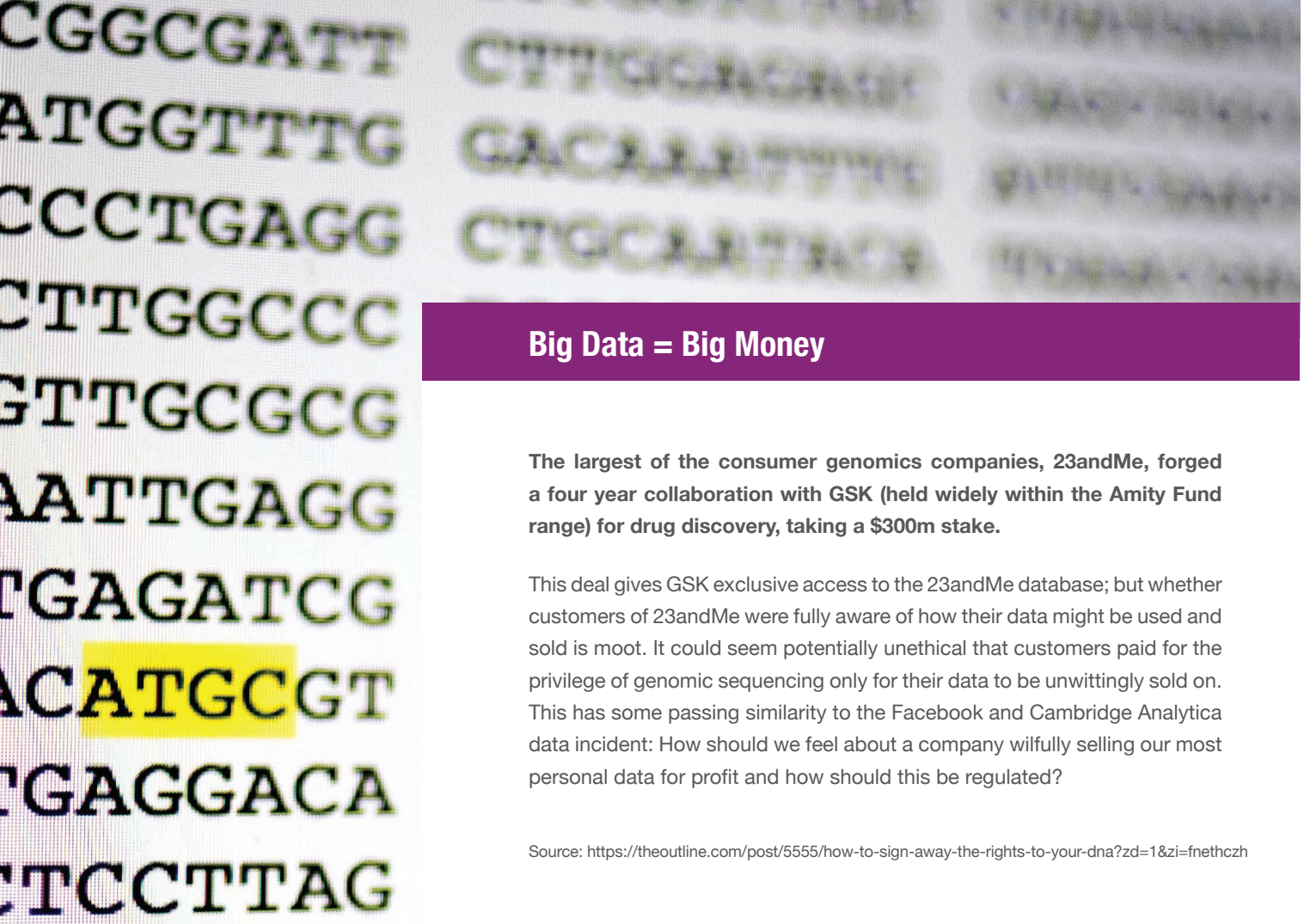
Whilst we have demonstrated the medical efficacy of targeted prescription based on genetic testing, increasing access to individual health data carries risks.

A rising area is 'consumer genomics' where an individual – at a cost – can send away a DNA sample to find out more about their genetic make-up and ancestry, including carrier status for selective genetic conditions and genetic risk factors. The largest commercial companies offering this service are **23andMe**, **Ancestry**, **FamilyTreeDNA** and **Helix,** where combined around 12million genetic samples have been sequenced to date.

Genetic information is extremely personal and potentially highly valuable information, for instance to insurance companies (the next black box technology?) or to employers who could use it discriminatingly.

A booming number of companies with access to this data is therefore a potent area for data security risk.





Big Data = Big Money

The largest of the consumer genomics companies, 23andMe, forged a four year collaboration with GSK (held widely within the Amity Fund range) for drug discovery, taking a $300m stake.

This deal gives GSK exclusive access to the 23andMe database; but whether customers of 23andMe were fully aware of how their data might be used and sold is moot. It could seem potentially unethical that customers paid for the privilege of genomic sequencing only for their data to be unwittingly sold on. This has some passing similarity to the Facebook and Cambridge Analytica data incident: How should we feel about a company wilfully selling our most personal data for profit and how should this be regulated?

Source: https://theoutline.com/post/5555/how-to-sign-away-the-rights-to-your-dna?zd=1&zi=fnethczh

Survival of the Richest –

Denying access to medicine for all?

We have shown how genetic therapies may shrink target patient groups; a one-time discreet treatment also presents a challenge to business and investor models that depend on repeatable income from incurable or chronic maladies.

These more efficient, complex drugs are accompanied by premium price tags. The one-time drug for a genetic eye condition – Luxturna mentioned previously – is thought to be the most expensive treatment cleared by the FDA at around ~$850,000 for the treatment to both eyes. Whilst arguably a one-time treatment that cures will save a host of other ongoing and long-term treatments, very few healthcare models will be able to afford the $850,000 price tag if the drug is not covered by health insurance or viewed as widely efficacious.

> **Gene therapy companies are exploring different pricing models, such as payments spread over many years and outcome based models with rebates if it is not as successful as expected.**

Nevertheless, for those without generous health insurance and for many in lower income countries, this treatment is not accessible regardless of outcome. Whilst Luxturna has been approved for use within the EU by the European Commission, it has not been approved for use within the NHS by NICE (National Institute for Health and Care Excellence).

Despite the extraordinary potential benefits, gene therapy also holds out the prospect of lottery medicine at its most extreme, with large parts of the world likely to be left behind in favour of very selective treatment groups based on ability to pay.

Genetic Editing –
Limiting the Creator?

In addition to gene therapies creating a 'survival of the richest' barrier, a further area with the potential to create ethical polarisation in healthcare is genetic editing.

Genetic editing techniques are already used to create therapies that treat existing conditions, but they could also be deployed to edit an embryo to remove and prevent specific medical conditions. When these cells are edited, changes made to the DNA are passed down to all future generations. The ability to remove faulty hereditary disease genes at the embryo level and thereby reduce prevalence for current and future generations might appear a positive medical advancement. However, as this touches on the nature of life itself, the dignity of the individual and the value placed upon all life, it is fraught with ethical questions and dilemmas.

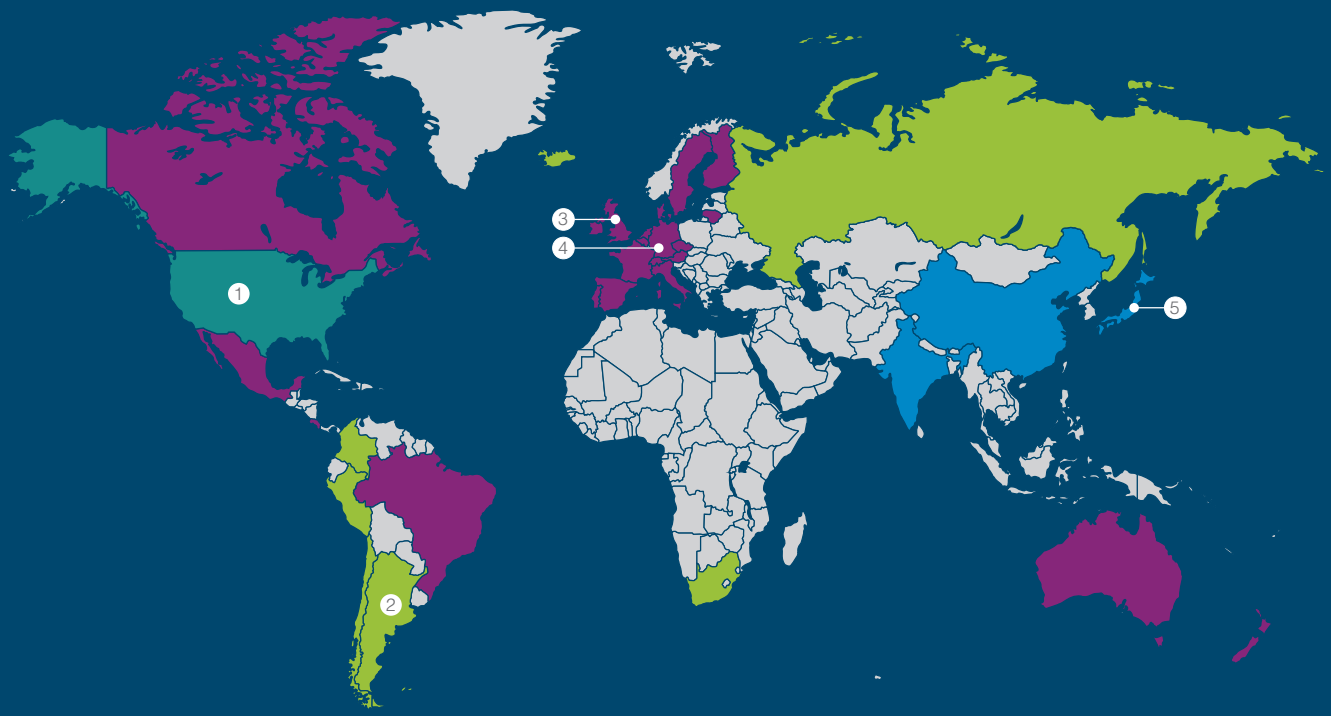
In theory, genetic editing of the embryo could create an exclusive area of medicine, reserved for the richest or the unscrupulous that would widen the healthcare divide and bear witness to strong intervention and steer in the creation process itself. These are questions regulators and ethical panels will need to grapple with so that *'all that can be done should not necessarily be done'*, is placed at the forefront of thinking. It is a debate at the heart of who we are and what kind of society we want to be that must exercise theologians and scientists alike!

- Will eradicating genetic diseases increasingly lead to removing genetic predispositions to conditions such as diabetes and obesity?
- Will this one day go further into the realm of designer babies, prescribing characteristics such as taller, smarter or more athletic?
- Could the wealthy create a 'super sub-species' of near perfect, disease resistant, physically superior individuals?
- If genetic possibility starts to decree what a human should and should not be, where would the line properly be drawn between medical desirability and man (or doctor) playing God?

Whilst these scenarios may seem somewhat difficult to envisage, law and regulation surrounding genetically editing embryos with the latest CRISPR methods are globally not robust. Many countries have guidelines around the topic, but in reality outright bans are few.

Let's not perfect these technologies ahead of a conversation about whether we should allow this technology.

Edward Lanphier, Founder of Sangamo Biosciences



CRISPR Embryos and the Law

1. **The United States** does not allow the use of federal funds to modify human embryos, but there are no outright genome-editing bans. Clinical development may require approval.

2. **Argentina** bans reproductive cloning, but research applications of human-genome editing are not clearly regulated.

3. **The United Kingdom's** independent Human Fertilisation and Embryology Authority may permit human-genome editing for research, but the practice is banned in the clinic.

4. **Germany** has strict laws on the use of embryos in assisted reproduction. It also limits research on human embryos, and violations could result in criminal charges.

5. **Japan**, like China, India and Ireland, has unenforceable guidelines that restrict the editing of a human embryo's genome.

Source: bit.ly/CRISPRbaby

EdenTree Approach

This Amity Insight sets out an area of science that is fast-developing, innovative and at the cutting edge of redefining treatment prescription.

As we have seen, whilst genetic sequencing holds out the prospect of personalised, targeted treatment, in some ways it is also fraught with ethical challenges. As with all innovative areas, we scope the issue carefully, conduct robust due diligence and apply our rigorous approach to responsible and sustainable investing.

There remain many ethical implications and unanswered questions about this area of science which heavily touch on the most personal questions about what it means to be human. Notwithstanding the uncertainty, we see this as an exciting area of investment potential and one in which we have expertise and exposure.

As a House, we have a strong commitment to Health & Wellbeing as one of our responsible and sustainable themes, with exposure across the healthcare spectrum. This area of genetic therapeutics fits well with our interest in innovation, targeted medicine and the avoidance of unknown side effects for the patient. Whilst genetics may not have universal application, the value chain is sufficiently broad for us to gain exposure via one of the channels outlined in the Insight. Overall we remain positive on this area of science given:

- Treatments can be selected on an individual 'best match' approach thereby reducing waste and targeting the person rather than the condition;
- The improved health economics through better patient outcomes and reduced costs;
- Our understanding of how genes play a critical role in determining disease predisposition, creating a new age of drug discovery;
- Our understanding more about personal health and risk. This will increase targeting of high risk individuals, catching serious diseases sooner;
- The opportunity to treat and 'cure' genetic diseases.

As a thought leader, EdenTree strives to bring new and emerging areas of thinking that highlight investment opportunities as well as emerging ethical risks.

Genetic therapeutics is a novel topic with many outstanding, unanswered questions with which society will need to grapple.

With these caveats, EdenTree seeks to support the beneficial and therapeutic aspects of this area of science as a strong enabler of the next 'age of medicine'. We are positive on sequencing, research, diagnostics and personalised medicine, and extremely cautious on embryo editing. We hope this Insight will have provoked much thought and perhaps more questions; our aim has been to introduce the concept of *The Life Code* as a suitable area for investment – albeit one with serious ethical implications.

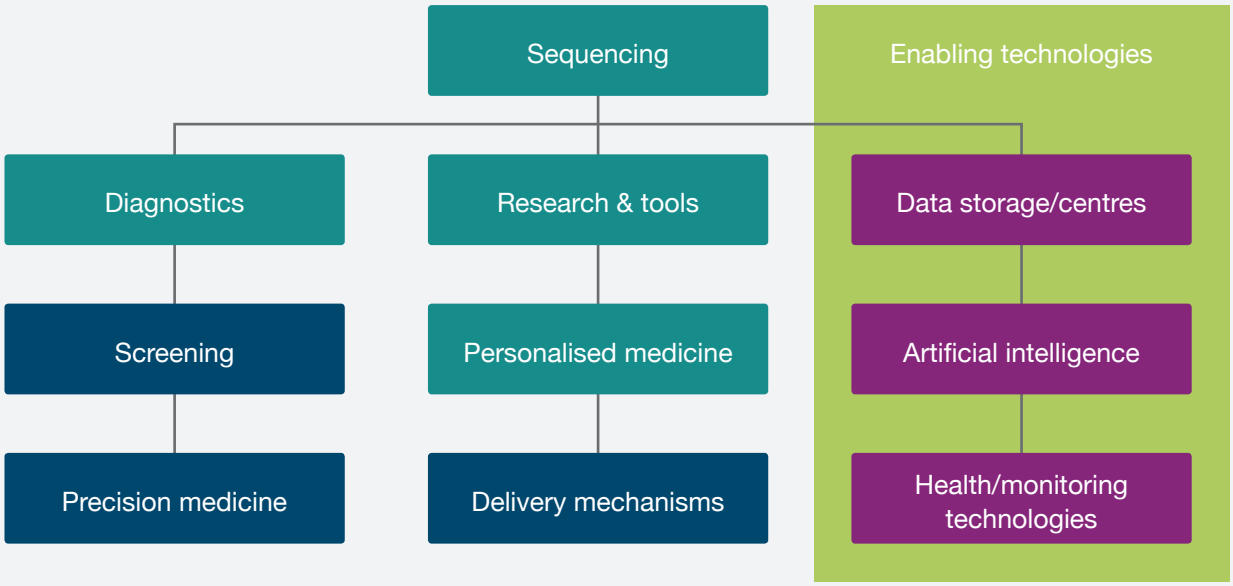
Our previous Amity Insight *'Cyber Security'* (2016) is relevant in terms of its discussion of issues around data security and data privacy whilst our House views on healthcare more generally can be seen in *Healthcare: Life Ethics Explored* (2015).

Investing in the Life Code

The investible universe associated with the themes explored in *The Life Code* is very broad, but we view the core areas to be (i) sequencing, (ii) research & tools, (iii) diagnostics and (iv) precision & personalised medicine.

Given the nature of the science, many companies developing technologies in the field of therapeutic genetics are small or have emerged out of academic establishments as incubator enterprises.

Examples where we see opportunity across the value chain include:



Sequencing

Investment case:

- Sequencing has broken the £1,000 per genome barrier
- Crucial in understanding disease and treatment response
- Central to personalised and more accurate treatment

Sequencing is the engine for genetic discovery, it has vast applications within healthcare and fuels a new age of personalised and more accurate treatment. EdenTree invests in IP Group, an IP commercialisation company with its largest holding in Oxford Nanopore. Nanopore is most renowned for inexpensive portable sequencers using a different underlying technology than peers. IP commercialisation companies are a good way to access early stage companies by spreading the risk profile. Illumina is the market leader.

illumina · ThermoFisher SCIENTIFIC · PACIFIC BIOSCIENCES · Oxford NANOPORE Technologies

Research & Tools

Investment case:

- Critical for understanding the link between genes and disease
- Research is at a new stage of advancement fuelled by sequencing
- Research adds value in providing the link between genes and drug development

Research and development provides an interface with pharmaceutical and other healthcare actors in reducing R&D investment. Given the fast pace of development, competition, and constraint on R&D, pharmaceutical companies for the most part cannot afford to build out specific expertise internally and will seek to partner or acquire.

EdenTree holds Horizon Discovery which aids drug development and testing essentially creating 'perfect patients' with selected genetic trials.

horizon INSPIRED CELL SOLUTIONS · Thermo SCIENTIFIC · Agilent Technologies · OxfordBioMedica

Diagnostics

Investment case:

- Responsible for identifying groups of patients that will respond to a treatment
- Assesses side-effect risk
- Early diagnosis is better for ultimate outcomes – this is the principle driver

Diagnostics are a highly responsible and sustainable approach to medicine, as early detection greatly improves outcomes, particularly in life-threatening conditions such as cancer. Selecting the right treatment for the right patients improves outcomes and removes needless trial and error approaches. EdenTree holds Roche across four of our retail and charity funds, however we view diagnostics as a robust long term investment theme and we may seek further exposure.

Roche · Agilent Technologies · sysmex · QIAGEN · Abbott · Thermo SCIENTIFIC

Precision & Personalised Medicine

Investment case:

- Precision medicine is more likely to succeed than 'one size fits all' treatment
- Oncology and genetic illnesses respond best to personalised medicine
- Dominated by large pharmaceutical companies and nippy start-ups

Precision and personalised medicine is bringing forward a new era of disease treatment processes. Personalised medicine has the potential to 'cure' genetic diseases where previous 'trial and error' approaches could only abate symptoms. New, targeted drugs are having the most immediate impact in oncology treatments and will be a game changer in genetic medicine and other serious diseases. Novartis and Roche are comparatively advanced in this space and are held in the Amity Funds. Small biotechnology companies are emerging with highly concentrated portfolios and early stage treatments and may follow a boom or bust trajectory.

NOVARTIS · Roche · Autolus · Spark THERAPEUTICS · nightstar THERAPEUTICS · Intellia THERAPEUTICS · REGENERON · MaxCyte

View from the top

By Ketan Patel, CFA

Fund Manager

This Insight examines complex issues, raising more questions than answers for investors who are facing a highly fluid landscape where technology and healthcare are combining continually to push the boundaries.

As responsible and sustainable investors, we are tasked to navigate this ever changing environment to find businesses that are delivering goods and services which benefit consumers and society at large. We welcome the potential health economic benefits that personalised and preventative medicine bring, which could help alleviate the pressure on global healthcare systems that are already under considerable financial pressure.

The ethical issues outlined in this Insight will for the most part remain difficult to resolve in the short-term, more so as the pace of innovation will likely present more dilemmas and also hopefully some solutions. Data privacy and gene editing will top the concerns of many investors, but a wider concern is the potential widening of inequality in access to cutting-edge treatments, which may exclude large parts of society who will not be able to fund their current and future healthcare needs.

The eye watering costs of some innovative treatments will only increase the financial strain on healthcare payers who are faced with a fast-growing patient pool that is living longer with myriad complex and chronic diseases. Access to healthcare and affordable medicine are among the biggest challenges facing governments and policymakers in the 21st century and will be more pronounced in the developing world which is well on the way to mimicking the higher levels of chronic diseases that are so well entrenched in the Developed World.

The investment themes highlighted are both deep and broad, with EdenTree's holdings being well represented in the sequencing, research & tools, diagnostics and precision & personalised medicine sectors. Whilst some areas will always be niche and difficult to access, there are plenty of high quality and well established businesses for investors to access through a pooled vehicle like IP Group or Arix Biosciences, or directly across a range of market capitalisations. The larger companies like Novartis and Roche, both widely held across our funds, are well represented in diagnostics which we think will be the main beneficiary of greater innovation in sequencing and research & tools.

This will enable healthcare professionals to intervene much earlier in disease management, benefitting both the patient and the healthcare system.

Health and Wellbeing remains a strong theme for our Amity fund range and we continue to find exciting opportunities to invest in whilst being highly cognisant of the challenges of becoming shareholders in businesses that are at the forefront of the next 'age of medicine'.

Our People

Sue Round

Chief Executive Officer

Sue joined EdenTree in 1984 and has been central to the growth of the business and also the wider profile of responsible and sustainable investing in the UK over the last 3 decades. Today she is also the Director of Group Investments at EdenTree and has successfully managed the Amity UK Fund since its launch in 1988.

Robin Hepworth

Chief Investment Officer

Rob started his career with EdenTree as an Analyst in 1988. He figures in Citywire's selection list of top fund managers over the last decade, is an FE Trustnet Alpha Manager and a member of their 'Hall of Fame' for consistent performance. Robin is best known for his contrarian approach, as well as for his skill in tactical asset allocation and switching.

Neville White

Head of Responsible Investment

Neville leads on strategy, policy and corporate governance and oversees strategy on research and engagement. He previously managed ethical and socially responsible investment for a number of church and charity investment managers, was secretary to the Church of England Ethical Investment Advisory Group and the Church Investors Group, and has acted as a consultant on ethical investment to the Central Finance Board of the Methodist Church in Great Britain.

Chris Hiorns

Senior Fund Manager

Chris has worked at EdenTree since 1996. He started as a Graduate Trainee and worked as an Investment Analyst before being appointed as the Fund Manager for the Amity European Fund in 2007 and co-manager of the Amity Sterling Bond Fund in 2008.

Ketan Patel

Fund Manager

Ketan joined EdenTree Investment Management in 2003 as a Research Analyst. He began his career at JP Morgan, before moving to Insight Investment as a Global Healthcare & Biotech Analyst. He is co-manager on the Amity UK Fund, Amity Global Income Fund and UK Equity Growth Fund. He has been a CFA Charterholder since 2009, and holds a post-graduate degree in both Geography and Economic History from the University of London.

David Katimbo-Mugwanya

Fund Manager

David joined EdenTree in 2015 and possesses over a decade of investment expertise across sovereigns, corporate debt and money markets. Along with a BSc in Economics from the University of Essex, David holds the IMC and is a CFA Charterholder. His previous experience at Epworth Investment Management saw him excel at managing portfolios for a diverse clientele via designated mandates and/or bespoke solutions.

Philip Harris

Fund Manager

A graduate from Southampton University with a degree in modern history, politics and economics, Phil started his career at Albert E Sharp in Birmingham as a Private Client Executive and Analyst before being internally promoted to work on their small companies and UK general funds. Subsequently he has worked at Threadneedle, Credit Suisse, Hermes and RWC before coming to EdenTree as a Fund Manager on the UK Equity Growth Fund.

Thomas Fitzgerald

Fund Manager

Tom joined EdenTree in 2011 as a Research Analyst where he focussed on global equity analysis and the technology sector. His Amity Insight report on Cybersecurity was 'highly commended' at the Investment Week Research Awards in 2017. Tom continues to contribute investment ideas to other funds, as well as co-managing the Higher Income Fund and the Amity International Fund.

David Osfield

Fund Manager

David joined EdenTree in July 2016 as joint Fund Manager on the Amity International Fund after beginning his career at Alliance Trust in 2002. David is passionate about sustainable investing and has completed a course in Sustainability Leadership at the University of Cambridge Institute. He has a 1st class BA (Hons) in Business Finance from Durham University and is a CFA Charterholder.

Esmé van Herwijnen

Responsible Investment Analyst

Esmé holds a Master's degree from Toulouse Business School where she specialised in Sustainable Business and gained experience in ESG research from Sustainalytics and PIRC. She supports our Responsible & Sustainable Investment Team with company screening, proxy voting and engagement.

How to contact us

We hope you have found this Amity Insight interesting and useful. If you have any questions, or would like to know more about our responsible investment, in-house research and analysis, please get in touch.

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