Sector Review

Personalised Medicine

23 April 2019

This time, it's personal!

Esteemed futurologist Dr Ian Pearson believes that if you make it past 2050 healthy with money in the bank, you could choose to be immortal. This is the effect of Artificial Intelligence, Machine learning, Quantum Computing and personalised medicine.

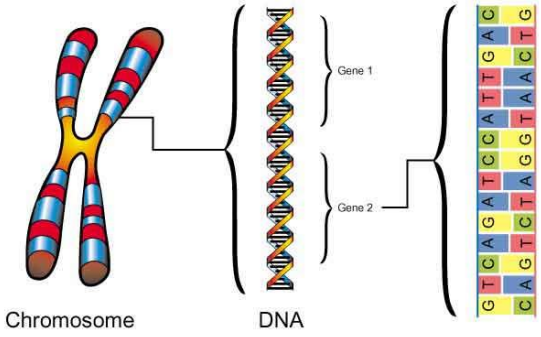
The term "personalised medicine" itself needs to be defined as this determines future fields of actions and responsibilities. Most work is based on the definition of personalised medicine given in the European Council Conclusion on personalised medicine for patients (2015/C 421/03). It states "that it is widely understood that personalised medicine refers to a medical model using characterisation of individuals' phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention."

However, there can be an argument that medicine has always been personalised. Each medical doctor who takes his or her work seriously will try to find the best possible solution for the patient at hand. What is new is the vast amount of different kinds of data that add to the direct medical data, which have the potential to support diagnosis and treatment decisions or even allow for prevention strategies. The goal of personalised medicine is to make this happen.

Source: http://www.labtestingmatters.org/personalized-medicine-part-2-the-role-of-the-laboratory/

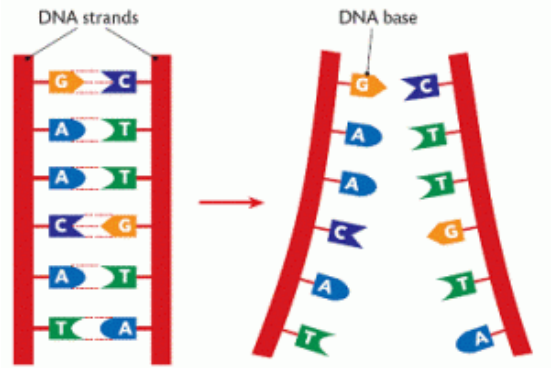
We are already seeing the benefit of these approaches, mostly in the cancer field. For example, molecular markers can define subgroups of patients that respond differently to a certain kind of treatment. In the long term, the vision is to use the full power of each individual's environmental and molecular characteristics to improve health care.

Gene Structure



Source: https://tinycards.duolingo.com/decks/2LwxEqsp/genes-chromosomes-and-inheritance

Source: https://www.23andme.com/en-gb/gen101/genes/



Source: https://www.23andme.com/en-gb/gen101/genes/

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What is Personalised Medicine?

Personalised medicine is special because it is a cross-cutting field that can only succeed if expertise and data from very different disciplines and sectors are brought together. In addition, the implementation of personalised medicine approaches has effects on all people and patients in our societies across Europe and beyond. A concerted effort is needed to make progress. Therefore, not only national, and regional governments, but also European institutions are dealing with questions on how to best govern and implement personalised medicine in our health care systems.

The main areas of personalised medicine have been within Gene and Cell therapy, which include the following:

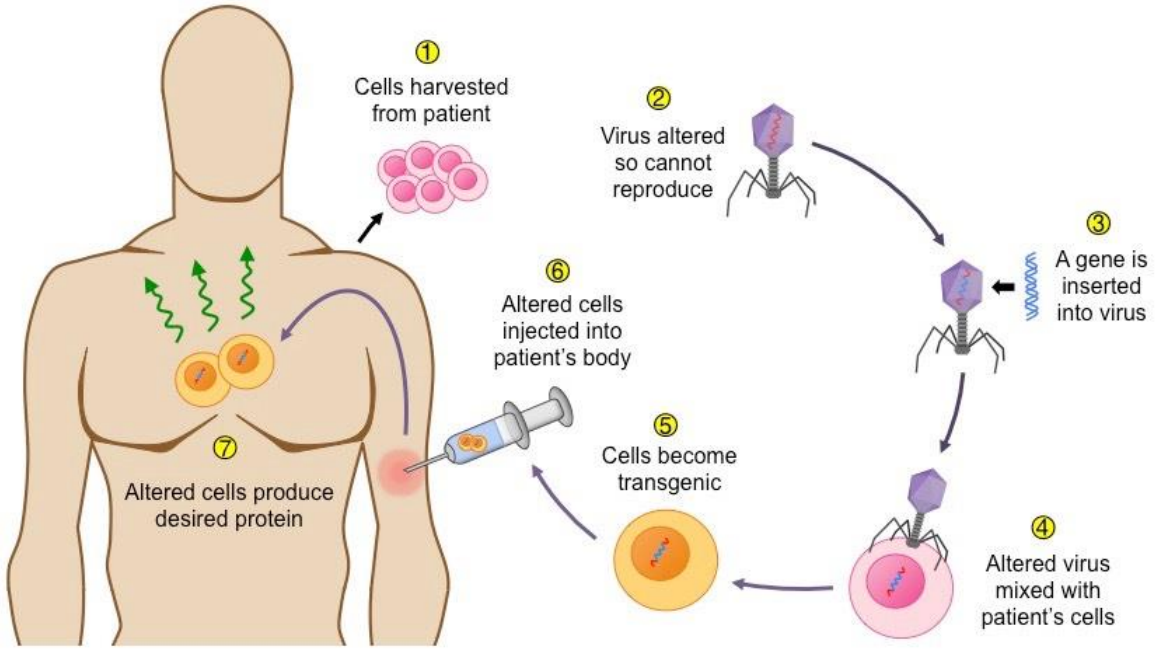
- Gene Therapy (including gene sequencing and rug development)
- Cell Therapy (including immunotherapy)
- Reagents and Services
- Diagnostics
- AI and connected health

What is Cell and Gene therapy?

The potential of Cell and Gene therapy is only just beginning to emerge as a transformative new category of medicine. Most treatments available today are chemical compounds like the cancer drug Herceptin, taken by injection, paracetamol tablets, or biologics. These medicines mostly prolong our healthy life-span and help address many serious conditions such as cancer. However, most of these drugs are one size fits all as we usually all take the same pill or injection for a particular condition. These treatments are produced in a standardised fashion, and most are relatively short-lived within the body, but cell and gene therapies are different. They involve extracting cells, protein or genetic material (DNA) from the patient (or a donor), and altering them to provide a highly personalised therapy, which is re-injected into the patient. Cell and gene therapies may offer longer lasting effects than traditional medicines.

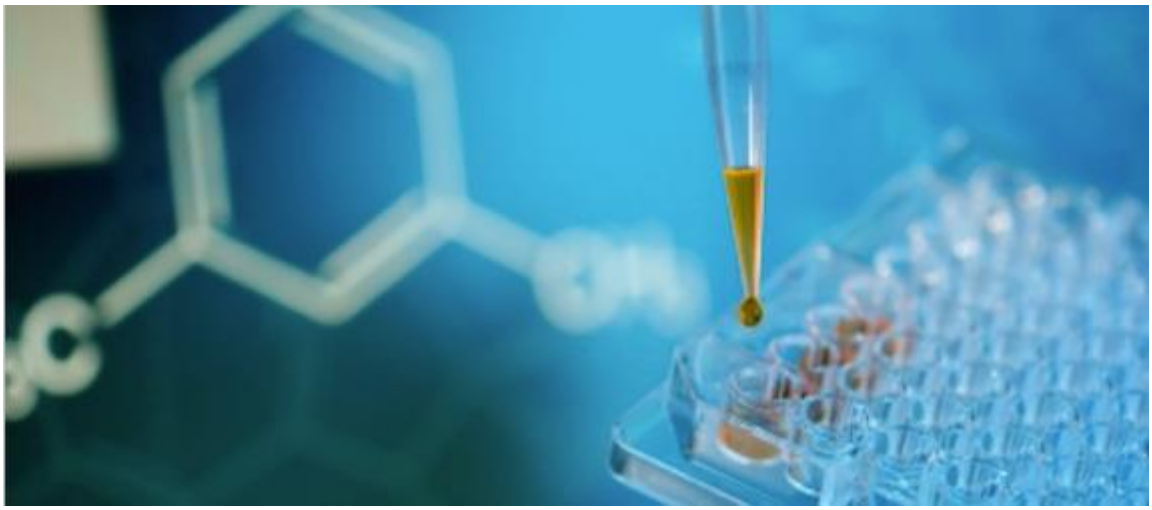
They have the potential to address complex diseases, such as motor neurone disease, and many rare disorders for which there are no effective treatments. In their simplest form, gene therapies work by replacing a faulty or missing gene that causes an inherited condition, such as sickle cell anaemia or cystic fibrosis. Scientists have developed molecules that can deliver a repaired copy of the faulty gene

for the appropriate cells, enabling those cells to function correctly again, alleviating some or all the symptoms of the disease.



Source: http://ib.bioninja.com.au/standard-level/topic-3-genetics/35-genetic-modification-and/gene-therapy.html

The difference between gene and cell therapy is gene-based therapies involve corrected copies of DNA that repair or replace faulty genes. Cell-based therapies rely on modifying both genetic material and cells. For example, some of the most exciting new cell therapies involve extracting and re-programming immune cells found within each of us, to equip them to more effectively fight disease from within.



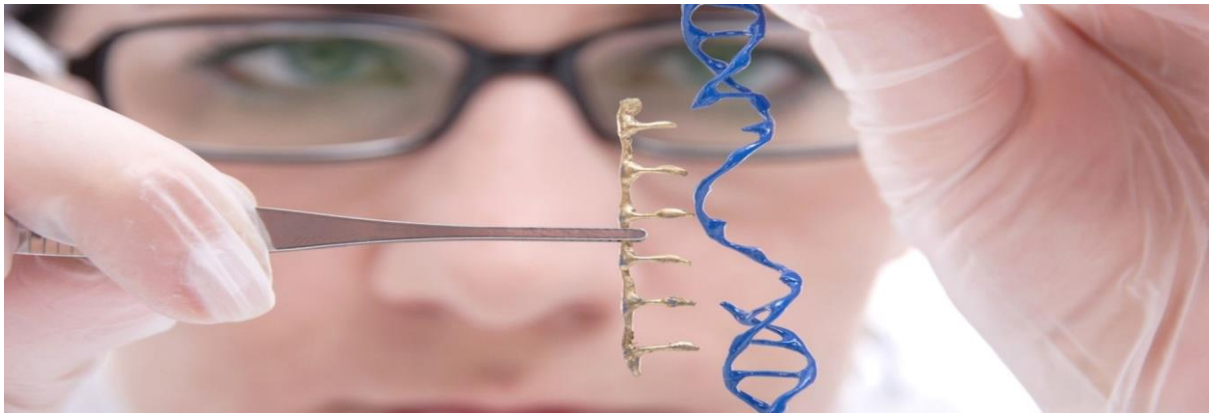
Source: http://drcurtiscripe.blogspot.com/2016/09/what-everyone-should-know-about.html

In these new medicines, a certain type of patient's own immune cells, called T-cells, are re-programmed to make them better at detecting and killing cancerous cells. Genetic material is inserted into the T-cells, coding for a receptor molecule that can easily spot a protein found on the surface of some kinds of cancer cells. The modified T-cells are then re-infused into the patient and can kill the cancer more effectively. These modified T-cells are known as CAR-T cells, short for "chimeric antigen receptor T-cell". CAR-T cell-based medicines include both a gene therapy element (the new receptor molecule) and a cell therapy element (the cells injected back into the patient). Enabling all the parts to work together and get to the right places requires other biological tools, some of which are being developed by UK companies.

Biological engineering is used for gene and cell therapy to improve the immune system's capacity to fight disease, while sparing healthy tissues in the body. For example, there are antibody-based therapies (antibodies are another kind of immune system warrior cell) that can make T-cells more effective by increasing their interactions with cancer cells. Other modifications – like adding complexity to the CAR-T and cancer cell interaction – can further sharpen T-cells' cancer-targeting ability, reducing damage to normal cells.

Scientists are working on ways to expand the kinds of cancer markers that can be detected using the CAR-T cell approach, and the types of immune cell used to do the job. For example, several UK companies are working with a sub-set of T-cells found in the blood, skin and other tissues that can rapidly detect local abnormalities and recruit other immune-system players to the site. They're helped by a huge range of sophisticated tools for analysing and editing genetic material, including many from UK companies.

Regenerative medicine is another important branch of cell therapy. It enables human tissues – such as muscle, skin or cartilage – to be repaired or replaced, using appropriate cells and the molecules needed to keep them alive. Regenerative medicine may even one day allow entire organs to be grown in the laboratory – though we are not there yet. Stem cells are very important in regenerative medicine and across cell and gene therapy. These cells, found in the bone marrow of children and young adults, and in the cord blood of new-born babies, have the potential to differentiate into any cell-type – heart, skin, nerve, blood, muscle, connective tissue and immune cells. Scientists can also extract stem cells from patients with genetic disorders that affect multiple physiological functions (for instance, the immune system, muscle, and nerve function).



Source: http://www.biotechlogic.com/therapeutic-gene-editing-an-american-society-of-gene-cell-therapy-white-paper/

Correcting the defective or missing gene in the extracted stem cells tackles the root cause of the condition. Thus, re-infusing the repaired stem cells into the patient may alleviate or even eliminate many or all disease symptoms. For example, scientists are close to treating patients with beta thalassemia, an inherited disorder that affects the production of a protein in the blood that carries oxygen around the body. They harvest stem cells from the patients and edit the cell genomes to produce a foetal form of the missing protein. The stem cells are then reinfused back into the patient to restore oxygen transport.

Researchers are also developing 'off-the-shelf' stem cell (and non-stem cell) -based therapies. These don't require a patient's own stem cells to be extracted and corrected. Instead, they involve using genetically uniform, appropriately programmed cells, expanded from a single starting stem cell, under safe and sterile conditions.

These approaches may ultimately be used to treat a variety of diseases, including bone degeneration, organ failure, neuro-degenerative diseases such as Alzheimer's, and Chronic Obstructive Pulmonary Disease (COPD). For now, cell and gene therapies are highly specialised treatments that are either experimental, or available only to specific patient populations. They are complex to manufacture and administer, and very expensive. That will change as the techniques and support services underpinning cell and gene therapy Research and Drug development become more sophisticated and practical.

UK companies are among those working on new ways to design, manufacture and safely administer cell and gene therapies, driving next-generation approaches. These tools include efficient cell harvesting methods, more precise gene editing, advanced manufacturing and purification processes, cell and tissue preservation techniques, and more. These technologies are already changing healthcare – including as tools to discover and test other kinds of medicines. They also offer potential in other sectors, from agriculture to energy, industrial production and beyond.

The UK Research Landscape

The UK is recognised as a world-leader in the discovery and development of cell and gene therapies and an ecosystem capable of operating at the scale required to manufacture and deliver these therapies to patients is now beginning to emerge. As part of the broader life science endeavour, efforts to develop cell and gene therapies benefit from the UK's well-established strengths in scientific research and its commercialisation. However, in recent years there have been several additional initiatives aimed specifically at establishing and supporting a thriving cell and gene therapy industry in the UK.

The state of the industry in the UK

- There are 64 advanced therapy developers in the UK – more than any other European country
- £1.6bn has been raised by UK cell and gene therapy companies since 2013
- The UK cell and gene therapy industry employs 1,500 people
- By 2035, the cell and gene therapy industry could be worth £10bn and provide 18,000 jobs.

  * Figures as per the Cell and Gene Therapy Catapult Annual Review 2018

As part of the broader network of Catapult centres across the UK, the Cell and Gene Therapy Catapult (CGT Catapult) aims to bridge the gap between scientific research and full-scale commercialisation. It was established in 2012, with funding from Innovate UK, the business-focused arm of the UK's national funding agency, UK Research and Innovation (UKRI), to grow the UK cell and gene therapy industry. Its vision is for the UK to be a global leader in the development, delivery and commercialisation of cell and gene therapies, where businesses can start, grow and confidently develop advanced therapies, delivering them to patients rapidly, efficiently and effectively.

Source: https://ct.catapult.org.uk/manufacturing-centre

One way the CGT Catapult intends to realise this ambition is by increasing the UK's cell and gene therapy manufacturing capabilities. In April 2018, the CGT Catapult opened its state-of-the-art manufacturing centre in Stevenage, with £60m of investment from government as part of the

Industrial Strategy Challenge Fund. The new facility will enable companies to manufacture therapies at the scale required for late phase studies and commercial supply, complementing the UK's existing manufacturing facilities that cater for early stage clinical trials.

On the 10th of August 2018, the UK government announced a £780m investment into Catapult. Over the next five years, the £780m investment will allow the Catapult network to help thousands of businesses across the UK conduct cutting-edge R&D and train hundreds of apprentices and doctoral students in technical skills in high-demand from industry. This will be alongside investment from the industry, which is expected to be well over £1.5bn in R&D over the next five years. By transforming innovation in their sectors, the Catapult network will help deliver the Grand Challenges of the Industrial Strategy and will play a critical role in helping the UK achieve its ambition to raise investment in R&D to 2.4% of GDP by 2027.

The 5th of March 2019 marked the official start of RESTORE – Health by Advanced Therapies, entering the preparatory phase to become a Large-Scale Research Initiative. Advanced Therapies are new treatment modalities (e.g. cell and gene therapy, tissue engineering) that aim to consign the never-ending treatment of chronic ailments to the past and instead offer sustained improvement and even cures. To enable Europe to become a competitive leader in this field, RESTORE is defining an Advanced Therapies roadmap 2021-2030 for Europe which CGT Catapult are part of.

The UK is also addressing the challenge of how to deliver cell and gene therapies to patients in the NHS. Unlike traditional pharmaceutical medicines that can be taken outside a clinical setting without supervision, the administration of cell and gene therapies will need to be performed by an experienced clinician and carefully tracked to ensure traceability and to identify potential adverse events. The UK now has a network of Advanced Therapy Treatment Centres, the first of their kind in the world, that will develop these new systems and processes. They will work together to establish best practice for the safe and effective delivery of cell and gene therapies, positioning the UK as a global leader in terms of patient access to these treatments.

UK Pioneers

Oxford BioMedica Plc (LON: OXB) 732p, market Cap: £484m

FY Dec 18

- EBITDA – £12.29m
- EPS – 10.90
- PE Ratio – 67.22
- Revenue – £66.78m

Source: https://www.yahoofinance.com

Oxford BioMedica is a world leading gene and cell therapy Company that has also built a platform called LentiVector which enables cutting edge technologies and capabilities based on a lentivirus base vector. They have two independent Good Manufacturing Practice (GMP) approved bioprocessing facilities and state of the art research facilities. In its final year results, the gene and cell therapy Company posted a pre-tax profit of £5m, reversing its £11.8m loss the year before. Oxford BioMedica's gene delivery technology lies at the heart of an emerging class of transformative gene and cell therapies. It is a key component of Novartis' KymriahTM, a pioneering immune cell-based therapy approved for certain aggressive blood cancers. It is also central to efforts to develop gene therapies for Parkinson's disease, ocular diseases, immunological diseases and cystic fibrosis. Safe and accurate gene delivery is one of the key challenges of cell and gene therapies.

Oxford BioMedica's technology exploits mechanisms used by certain kinds of viruses, called lentiviruses, to integrate their DNA into that of a host cell. The Company has adapted and fine-tuned lentiviruses (the best known of which is the HIV virus) to include only the components necessary for efficient gene delivery and integration, removing pathogenic and other unwanted parts of the viral genome. Cell lines enable more accurate predictions about which patients are likely to respond to current and future treatments, furthering progress toward personalised medicine.

Oxford BioMedica's technology is involved in several partnered products, including Sanofi, Novartis, Bioverativ (part of the Sanofi group), Boehringer Ingelheim/UK Cystic Fibrosis Gene Therapy Consortium and Orchard Therapeutics and several in the clinic. These generate development milestones and potential royalty payments. In mid-2018, US-based Axovant (NASDAQ: AXGT) paid $30m up front and promised over $800m in potential development milestones for worldwide rights to Oxford BioMedica's Parkinson's disease programme.

Cell Medica

Cell Medica is one of Europe's best-funded private biotech companies, with a total of €150m raised in private funding since its foundation in 2006. The Company develops personalised cell immunotherapies for infectious disease and cancer. Their most advanced treatment, currently in Phase II trials, employs natural T cells to target viral proteins in patients with non-Hodgkin lymphoma, whose cancer is associated with infections of the Epstein-Barr virus (EBV). Tweaking the body's own immune cells to better fight cancer is a proven, highly promising approach. Two newly-approved therapies, Novartis' Kymriah and Gilead/Kite's Yescarta, involve engineering patients' own T cells (a type of immune cell) with a specific receptor molecule that homes in on certain cancers.

London-based Cell Medica's scientists are among several groups around the world seeking to improve on this first-generation of CAR-T cell therapies, potentially broadening their reach into solid tumours, as well as making these complex treatments more convenient to make and administer. The Company's AlloCAR platform is a next-generation CAR-T, utilising a specialised class of T cells called natural killer T-cells (NKT) cells, for off-the-shelf therapies to treat multiple types of solid and haematological malignancies. Cell Medica's ambition is to be a leader in allogeneic (off-the-shelf) CAR-T therapies. The specialised class of NKT cells they work with have properties that make them ideally suited to this. This opens the door to potentially transformative therapies that face far fewer logistical hurdles than autologous CAR-T treatments.

Oncimmune (LON: ONC) 105p, market Cap: £66m.

HY Nov 18

- EBITDA – £-7.31m
- EPS – -12.30
- PE Ratio – -N/A
- Revenue – £0.24m

Source: https://www.yahoofinance.com

Oncimmune is a leader in the development, manufacture and commercialisation of personalised immunodiagnostics for the screening, detection and care of cancer. Oncimmune is changing how clinicians, researchers and patients view, diagnose and treat cancer. Their technology detects evidence of the body's natural response to cancer, enabling detection four years or more before standard clinical diagnosis. Tests facilitate clinical decision-making and are complementary to diagnostic technologies, making them valuable additions to established and new care pathways. They

partner with leading developers and distributors with an aim to make their technology available globally.

Oncimmune was founded in 2002 and launched its platform technology in 2009, followed by its first commercial tests, ***Early*CDT—Lung** and ***Early*CDT—Liver**. To date, over 155,000 tests have been performed for patients worldwide and ***Early*CDT—Lung** is being used in the largest-ever randomised trial for the early detection of lung cancer using biomarkers, the National Health Service (NHS) ECLS study of 12,210 high-risk smokers in Scotland. They are headquartered in Nottingham, UK with a CLIA lab in Kansas, US and offices in London, UK and Shanghai, China. Oncimmune joined the AIM in May 2016 under the ticker ONC.L

Immunocore

Immunocore is a private biotech Company that has developed a new class of immuno-oncology agents that have the potential to overcome some of the challenges stated. Most are expensive and time-consuming to manufacture and administer and face constraints around mode of administration and dose-control as they have shown limited clinical efficacy in solid tumours.

ImmTAC (Immune mobilising monoclonal TCR against cancer) molecules are small, soluble molecules formed by an engineered T-cell receptor (TCR) fused to a CD3-antibody fragment. The TCR portion acts as a highly tuned detector that seeks out and targets cancer antigens – molecules that signal the cancer's presence. The CD3-antibody fragment engages, re-directs and activates T-cells to kill the cancer cells. The result is a targeted immune system attack on cancerous cells.

Solid tumours, such as those in lung, skin, breast or prostate, build multiple physical and physiological barriers to avoid detection by the immune system. For instance, they reduce the number of danger-signalling antigens presented on the surface of tumour cells. Since ImmTAC molecules are small and soluble, they are better able to penetrate solid tumours than larger, cell-based therapies. Moreover, the TCR component of ImmTAC molecules can recognise a much wider range of cancer antigens than CAR-T cell therapies and other antibody-based therapies by recognising intracellular antigens that are processed and presented as small peptides on the surface of the cancer cells. Thus, TCR-based therapies such as ImmTAC molecules could open many more doors into the solid tumour.

Soluble ImmTAC molecules are available as 'off-the-shelf' reagents unlike cell therapies such as CAR-T cells, which require extraction and manipulation of the patient's own immune cells prior to treatment. ImmTAC molecules also offers more flexible dosing options and better control in the instance of adverse events. Immunocore has several other proprietary and partnered oncology programmes. These include a study in metastatic cutaneous melanoma with AstraZeneca using

IMCgp100 combined with checkpoint inhibitors, a type of targeted cancer treatment, as well as multi-target collaborations with GlaxoSmithKline, Roche and Eli Lilly.

A second ImmTAC programme partnered with GSK is due to enter the clinic targeting the NYESO antigen for treatment of diverse indications, including Non-Small Cell Lung Cancer (NSCLC), urothelial carcinoma and synovial sarcoma. Immunocore is headquartered at Milton Park, Oxfordshire, UK, with an office outside Philadelphia, USA. The Company is privately held by range of international investors.

Angle Plc (LON: AGL) 66p, market Cap: £95m

HY Oct 18

- EBITDA – £-8.67m
- EPS – -6.80
- PE Ratio – N/A
- Revenue – £0.73m

Source: https://www.yahoofinance.com

Angle develops products for use in rare cell diagnostics that enable early, accurate identification of an individual's condition for the prevention, treatment, and monitoring of disease. They have a clear strategy to commercialise its Parsortix™ technology. The cell capture and harvesting technology consists of a cell separation cassette together with an automated system to run blood samples through the cassette. There is extensive intellectual property protection around key elements of the system.

Successful evaluation of the system by major cancer research centres has already been achieved and a major part of Angle's current efforts relate to further deployment with key opinion leaders in the field. Regulatory authorisation for the clinical use of the system is currently CE Marked while the process of FDA clearance has been initiated and is currently ongoing in the USA. Widespread adoption of the Parsortix™ system in the clinical market is crucially dependent upon how information about the product is presented to key opinion leaders.

To reach this goal, they aim to:

- Undertake pilot studies assessing clinical applications for CTC's
- Select the most promising applications
- Undertake larger patient studies providing fully documented evidence of how the system should be used for patient applications in routine treatment

- Convert key opinion leader support and peer reviewed publications into widespread adoption of the Parsortix™ system in routine patient care

Freeline Therapeutics

Freeline is a private leading clinical-stage biotechnology Company that focuses on development and commercialisation of innovative gene therapies, mainly to create better lives for people suffering from chronic, debilitating disease. They are developing functional cures for a wide range of liver-based diseases which have previously been underserved and incurable.

Their gene therapy uses AAV technology to deliver safe and effective gene replacement to the liver to produce sustained therapeutic protein expression for diseases like haemophilia B and Fabry. Treatment builds on the renowned pioneering work of their founder and CSO, Amit Nathwani, Professor of Haematology at UCL. His award-winning scientific research was the first to show successful and sustained correction of bleeding symptoms in patients with severe haemophilia B.

PsiOxus Therapeutics

PsiOxus is seen as a world leading private cancer gene therapy Company delivering medicines of value to patients with cancer. PsiOxus focuses on discovering and developing innovative gene-based immuno-oncology treatments for solid tumours a their proprietary intravenously administered T-SIGn virus platform. Its portfolio of differentiated gene therapy products are all delivered systemically but act locally within the tumour.

PsiOxus is advancing its internal early and clinical stage candidates and establishing strategic partnerships with immuno-oncology leaders to bring cancer gene therapy products to patients. It focuses on discovering and developing innovative gene-based immuno-oncology treatments for solid tumours using a proprietary intravenously administered T-SIGn virus platform

Horizon Discovery (LON: HZD) 164p, market Cap: £247m

FY Jun 18

- EBITDA – £-2.11m
- EPS – -6.40
- PE Ratio – N/A
- Revenue – £49.52m

Source: https://www.yahoofinance.com

Horizon Discovery's technologies and services help scientists better understand genes and gene function. This in turn enables and accelerates drug discovery, through more rapid, effective identification of promising molecular targets and drug candidates. Horizon's suite of gene-editing tools is enhanced by some of the very latest techniques, including CRISPR (clustered regularly interspaced short palindromic repeats). CRISPR is based on a natural gene editing system used by bacteria as a defence against viruses. The CRISPR mechanism, along with a scissor-like protein, enables scientists to cut out efficiently and rapidly particular genes or DNA sequences from a cell or organism. This helps them probe the specific function of those genes, for example, knocking out certain genes and observing the downstream effects can help to elucidate which genes are responsible for a disease.

Horizon also offers CRISPR-based approaches that allow scientists to reduce, rather than completely shut off, the expression of particular genes. They can also amplify gene expression, or indeed add in new DNA sequences to understand gene function. These manipulations can help identify viable drug targets and drug candidates. For instance, they might uncover which genes contribute to drug toxicity, or for cell and gene therapy explain sensitivity to experimental therapies.

Horizon's gene-editing technologies can alter an increasingly wide range of gene sequences within human cells and several different species of mammalian cells. Horizon also offers a wide range of engineered cell lines. These families of identical cells, designed with particular genetic characteristics, are another important tool for gene- and cell-based therapy discovery. Cell lines provide a platform on which to study the effect of gene-edits, including those made using CRISPR. They are also powerful in vitro models for genetically-based diseases, allowing scientists to uncover, for instance, how particular mutations impact drug activity, drug resistance, and patient responsiveness.

Finally, cell lines also enable more accurate predictions about which patients are likely to respond to current and future treatments, furthering progress toward personalised medicine. Horizon can engineer a very special kind of 'master' cell known as an induced pluripotent stem cell (IPSC). These cells can turn into any cell type within the body, such as liver cells, heart cells or neurons. They offer scientists a way to isolate and study the effects of individual genetic mutations that drive disease, with minimum background genetic variability. The IPSC platform is particularly useful in the development of new therapies.

The Company is also applying its gene editing and cell line engineering expertise to improve the efficiency of biopharmaceutical production. Many biopharmaceuticals (including antibody drugs) are made using Chinese hamster ovary (CHO) cells in large, stainless steel fermenter tanks. The process is expensive, and relatively low yield. Horizon is using CRISPR-based gene editing to boost CHO yields. This may one day allow more rapid, lower-cost production of this growing class of medicines. Horizon

Discovery is based at the UK Cambridge Research Park, with offices in the US. Its customers include biopharma and diagnostics companies, research institutes and contract manufacturing organisations.

UK Smaller Caps

Silence Therapeutics (LON: SLN) 53p, market Cap: £37.7m
FY Dec 18

- EBITDA – -20.17m
- EPS – -26.20
- PE Ratio – N/A
- Revenue – N/A

Silence Therapeutics is the only European biotech developing a new generation of medicines based on RNA interference, which makes use of a natural cellular process to block the expression of disease proteins. Their proprietary technology can selectively inhibit any gene in the genome, specifically silencing the production of disease-causing proteins. Using their enabling delivery systems, they deliver therapeutic RNA molecules exclusively to target cells. Silence's proprietary RNA chemistries and delivery systems are designed to improve the stability of molecules and enhance effective delivery to target cells, providing a powerful modular technology well suited to tackle life-threatening diseases.

The first of this type of therapies, developed by US-based Alnylam, might be in the market as soon as this year. Silence's licensee Quark Therapeutics is now running Phase II/III trials testing the RNAi technology in patients with acute kidney injury and delayed graft function.

Oxford Biodynamics (LON: OBD) 124p, market Cap: £115m
FY Sep 18

- EBITDA – -2.27m
- EPS – -2.20
- PE Ratio – n/a
- Revenue – £1.19m

OBD is a revenue-generating biotechnology Company focused on the discovery and development of novel biomarkers for use within the biotechnology and pharmaceutical industries. Its proprietary technology, EpiSwitch™, has multiple, immediate applications across several therapeutic areas and indications, including oncology, autoimmune disease, immunotherapy, metabolic and neurodegenerative conditions and can be used on an industrial scale to:

- Reduce time to market, failure rates and the costs at every stage of drug discovery, from pre-clinical through to clinical development;
- Gain significant insights into disease mechanisms for drug discovery and product re-positioning programmes, as well as for the creation of predictive, diagnostic and prognostic tests; and
- Personalise therapeutics to patients in the context of challenging pricing environments where improved clinical outcomes are critical

Its strategic aim is to become the biomarker discovery technology platform of choice.

4d pharma (LON: DDDD) 110p, market Cap: £72m

FY Jun 18

- EBITDA – -23.81m
- EPS – -29.50
- PE Ratio – N/A
- Revenue – N/A

4d's aim is to be pioneers in understanding and utilising the functionality of bacteria as a revolutionary new class of medicines – called live biotherapeutics. The bacteria which colonise the human gastrointestinal tract – known as gut microbiome – have emerged as one of the most promising targets in medicine. More than just aiding in the digestion of food and production of vitamins, they are important in the development and regulation of our immune system, and it is also thought in the maintenance of our central nervous system.

It is understood that the bacteria of the gut microbiome have an important function in health and disease, but importantly – how they function, and how they could be used as potential new therapies. Understanding how they function means that their live biotherapeutics will potentially provide new and effective treatments for IBS and Crohn's Disease and game-changing treatments for cancer, asthma and autoimmune conditions such as rheumatoid arthritis and multiple sclerosis.

The live biotherapeutics they develop have the potential to transform the way in which many challenging diseases are treated.

Sareum Holdings plc* (LON: SAR) 0.725p, market Cap: £20.9m

FY Dec 18

- EBITDA – -1.79m
- EPS – -0.1000
- PE Ratio – N/A
- Revenue – N/A

Sareum discovers and develops innovative drug candidates aimed at cancers and autoimmune diseases. Its drug development programmes aim to improve outcomes for patients with serious medical conditions and where current therapies are inadequate. Sareum's most advanced development programme (Chk1) was developed in collaboration with the Institute of Cancer Research and the CRT Pioneer Fund. It is undergoing two Phase 2 clinical trials, being conducted by licence partner Sierra Oncology, with a further two trials planned. With other development programmes in the pipeline. The Chk1 programme could generate up to $88 million in milestone payments, plus sales royalties to Sareum, as SRA737 advances over the coming years. Whilst the current clinical program is focussed on monotherapy and a low dose chemotherapy combination, recent preclinical data relating to the drugs capability of enhancing immunotherapy has been extremely compelling. A combination of SRA737 +Low Dose Gemcitabine with anti-PD-L1 in a mouse model showed that 10/10 examples showed tumour regression at the end of the 21-day treatment period and 8/10 showed sustained complete response after a further 39 days without further treatment.

Sareum's earlier stage TYK2 /JAK1 inhibitor SDC 1802, the stablemate of SDC 1801 investigating autoimmune conditions, has also been the subject of evidence of preclinical data investigating its immunotherapeutic effects, suggesting it can modulate the host's immune system to block tumour cell proliferation in disease models of certain kidney, colon, skin and pancreatic cancers.

Fluid analytics

Fluidic Analytics, a private Company, envisions a world where information about proteins and their behaviour transforms our understanding of how the biological world operates and helps all of us make better decisions about how we diagnose diseases, develop treatments and maintain our personal well-being. Proteins form the structure of cells, regulate cellular activity and carry out the biochemical processes that underpin function in every living organism. Just as DNA

tells us what could happen over lifetimes, proteins and their behaviour tell us what is happening now. By building the world's best tools, software and services for protein characterisation and making them universally accessible in the lab, in the clinic or at home, they are making this vision a reality not just for a small group of expert users, but for everyone who can benefit.

These products are based on a fundamentally new technology platform developed at the University of Cambridge with investors like Draper Esprit (GROW.L). This platform enables the rapid characterisation of proteins based on the physical properties that determine their function. And because proteins are characterised in solution and in their natural state – without the need for surfaces, matrices or ionisation – this platform gives their customers access to unique quantitative insights into protein behaviour that are not accessible using other approaches. Their platform 'The Fluidity One' helps scientists in the lab determine protein folding, aggregation, and degradation in a rapid, convenient workflow that consumes just microlitres of sample.

The Fluidity One is just the first in a series of products that will make it easier for Fluid Analytics customers to extract unprecedented insights for an ever-expanding range of applications.

Physiomics plc* (LON: PYC) 3.46p. Market Cap: £2.5m

FY Dec 18

- EBITDA – -0.15m
- EPS – -0.1000
- PE Ratio – n/a
- Revenue – £0.74m

Physiomics is a leading oncology consultancy which uses the Company's proprietary state of the art Virtual Tumour™ technology and other tools to predict and better understand the effects of cancer treatments. It works with partners developing cancer drugs to help them save time and money and achieve better outcomes during pre-clinical and clinical development. It is also developing AI tools to support cancer treatment in real world settings. Currently dosing of docetaxel in prostate cancer is based on population averages, leading to effective under or over dosing in a significant number of patients. Their tool could, if approved, provide information that could assist clinicians in adapting chemotherapy dosing for individual patients. This offers the possibility of enhancing both the safety and efficacy of an existing standard of care without the costs typically associated with a new pharmaceutical product.

Physiomics' vision is to transform oncology drug development. It helps its partners develop great cancer drugs and to apply them optimally in real-world settings. Based in Oxford in the United Kingdom, Physiomics' specialist oncology services are used by global pharmaceuticals as well as small biotech companies to support oncology R&D. Physiomics' advanced capabilities leave it very well positioned to benefit from the growing interest in personalised medicine. Virtual Tumour has been the key driver of recent growth at Physiomics which saw revenue leap 161% and operating losses halve in HY Dec 2018.

The path towards point of care personalised treatment solutions has a longer time horizon, but could ultimately net a larger prize, with the prostate cancer dosing tool only one example of the sort of product Physiomics may seek to develop.

Genedrive (LON: GDR) 23.5p, market Cap: £8m

FY Dec 18

- EBITDA – -4.53m
- EPS – -29.20
- PE Ratio – N/A
- Revenue – £2.14m

Genedrive is a molecular diagnostics Company developing and commercialising a low cost, rapid, versatile, simple to use and robust point of need molecular diagnostics platform for the diagnosis of infectious diseases and for use in patient stratification (genotyping), pathogen detection and other indications. We are passionate about the opportunity to not only build a sustainable business around molecular diagnostics, but to play an important role in the diagnostic and treatment challenges presented by global health issues.

Genedrive® development has been validated through a range of applications and external independent evaluations. The Genedrive® HCV-ID test has received CE-IVD Certification and has been launched in Africa and the Asia Pacific region. Genedrive has distribution agreements with subsidiaries of Sysmex Corporation for the distribution of the Genedrive® platform in the EMEA and selected countries of the Asia Pacific region, and with ARKRAY Healthcare pvt Ltd for the distribution of the Genedrive® HCV ID Kit and Genedrive® platform in India. The Company also has an active development programme underway for tuberculosis detection and drug resistance assessment.

Genedrive is based in Manchester, United Kingdom. The business was floated on the London AIM market in 2007, trading as Epistem Holdings Inc. With a historical founding in the provision of contract research services to Pharmaceutical and Biotech companies, the business was renamed Genedrive in July 2016 to reflect the new direction of the Company targeting molecular diagnostic requirements at the point of need. The legacy contract research services divisions were divested in June 2018.

Oxford Genetics

Oxford Genetics is a private leading synthetic biology Company focused on developing novel technologies to overcome the challenges associated with the discovery, development and production of biologics, gene therapies, cell therapies and vaccines. Its proprietary genomic system enables the precise engineering of DNA, which in combination with automated platforms, drives the rational design of complex biologics and their associated production processes, with the overarching aim of increasing predictability, robustness, and scalability, while lowering cost and human error. Oxford Genetics was founded on the belief that there was a better way to create biologics with investment from Mercia Technologies (MERC.L).

RenalytixAI (LON: RENX) 142.50p, market Cap: £77m

HY Dec 18

- EBITDA – N/A
- EPS – N/A
- PE Ratio – N/A
- Revenue – N/A

RenalytixAI is a developer of artificial intelligence (AI) enabled clinical diagnostic solutions for kidney disease, one of the most common and costly chronic medical conditions globally. The Company's solutions are being designed to make significant improvements in kidney disease risk assessment, clinical care, patient stratification for drug clinical trials, and drug target discovery.

The Company's technology platform will draw from distinct sources of patient data, including systems containing extensive electronic health records, predictive blood-based biomarkers and other genomic information for analysis by high-performance, learning computer algorithms (machine learning). The

Company intends to build a deep, unique pool of kidney disease-related data for different AI-enabled applications designed to improve predictive capability and clinical utility over time.

In May 2018, the Company secured a cornerstone collaboration with the Icahn School of Medicine at Mount Sinai, the medical school of the Mount Sinai Health System, for product development and intended commercialisation by the Company beginning in 2019. As part of the collaboration, Mount Sinai became a shareholder in the Company and has made a further equity investment. They believe that its current business model of collaborating with major medical centres whose patients are most likely to benefit from its products will provide an effective opportunity to commercialise its products. The Company intends to enter further collaborations beginning in 2019. RenalytixAI was quoted on AIM on the 6th November 2018 after a successful raise of £22.25m.

Diaceutics (LON: DXRX) 95p, market Cap: 66m

FY Dec 18

- EBITDA – 1.52m
- EPS – -3,076
- PE Ratio – 0.03
- Revenue – £10.37m

Diaceutics is a data analytics and implementation services Company which services the global pharmaceutical industry. It has established a suite of data-driven products and implementation services powered by the data held in its proprietary database. Its products and services are not quite personalised medicine but are similar with a focus on optimising its clients' strategies for the development and launch of precision medicines and specifically, the diagnostic testing required to guide selection of such medicines. The Group currently provides services to 20 of the 30 largest global pharmaceutical companies.

Precision medicines (or therapies) are a class of drug tailored to individual patient groups dependent on molecular or genetic factors of the individual. Today, they are used for treatment in oncology as well as other disease areas such as multiple sclerosis and rheumatoid arthritis. The increasing use of precision medicines results from the fact that some drugs have demonstrated significant positive clinical results in some patients but have been shown to be less effective or less safe across the entire patient population.

Growth in the precision medicine market is evident, with major pharma companies such as AstraZeneca confirming that approximately 90 per cent of their clinical development pipeline is currently driven by precision therapeutics. This growth is being led by technological advances in genetics and improved understanding in molecular diagnostic techniques, enabling better prospects of the successful development of precision therapeutics. Leading pharma companies working in precision medicine include Novartis, Roche/Genentech, AstraZeneca, Pfizer, BMS, Merck and Amgen. Given the specific nature of precision therapeutics, the successful roll-out of these medicines by a pharmaceutical company is increasingly reliant on having effective and widespread testing available for doctors and patients from launch. Diaceutics floated on AIM on the 21st March 2019 and raised£17m.

Arix Bioscience (LON: ARIX) 151.50p, market Cap: £190m

FY Dec 18

- EBITDA – 37.97m
- EPS – -28.70
- PE Ratio – 5.28
- Revenue – £52.2m

Arix Bioscience is a global venture capital Company focused on investing in and building breakthrough biotech companies around cutting-edge advances in life sciences. They collaborate with entrepreneurs and provide the capital, expertise and global networks needed to help accelerate their ideas into important new treatments for patients. As a quoted company, they can bring this exciting growth phase of the industry to a broader range of investors.

Arix provides public market investors access to game changing life science innovation across a range of therapeutic areas and geographies. They take a board seat and play an active role to support companies grow, also, providing scientific and commercial experience to help navigate clinical and operational hurdles. Partnerships, such as Fosun, Takeda, UCB and Ipsen provide access to extensive R&D insights and due diligence capabilities.

ReNeuron (LON: RENE) 228p, market Cap: £72m

HY Sep 18

- EBITDA – -17.25m

- EPS – -42.30
- PE Ratio – N/A
- Revenue – £0.9m

ReNeuron has used a unique stem cell technology to develop cell-based therapies for significant disease conditions where the cells can be readily administered “off-the-shelf” to any eligible patient without the need for additional drug treatments. Its lead stem cell therapeutic candidate is a therapy for the treatment of patients left disabled by a stroke. It has announced positive Phase II data with a therapeutic candidate and is pursuing plans to commence a Phase IIb trial in patients who are living with disability post-stroke.

The Company’s hRPC stem cell candidate is being developed for the treatment of retinal diseases. Clinical development of this candidate in retinitis pigmentosa, a blindness-causing disease of the retina, has commenced in the US and is expanding the hRPC programme to target a further retinal disease, cone-rod dystrophy. The Company is also progressing pre-clinical development of an exosome nanomedicine platform.

What next?

As with all areas of scientific innovation, there is a risk that the exciting science underpinning personalised medicine (especially cell and gene therapies) will out-pace society's ability and willingness to adopt its outputs. The UK must ensure it has the right infrastructure, systems and people in place to remain internationally competitive in the field, and subsequently fully reap the economic and societal benefits of a thriving cell and gene therapy industry.

The previous section demonstrated the UK's capabilities in manufacturing for advanced therapies. However, additional capacity is required. Traditional medicines are usually produced using a common manufacturing process or platform, meaning multiple products can be made at one site and in batches large enough to meet anticipated demand. This is not the case for cell and gene therapies. These treatments are far more varied in terms of their format and how they are administered, and they are often manufactured in response to an individual patient's need. This results in many different manufacturing and logistical processes, making it challenging to manufacture cell and gene therapies at scale.

As a growing number of companies approach late stage clinical trials and commercial supply, there is a risk that the manufacturing supply chain in the UK could become a bottleneck. In addition, issues around manufacturing capacity in the UK could be exacerbated by a shortage in skills. While this challenge is not unique to the cell and gene therapy sector – in fact it is common across all STEM fields – the projected growth of the industry suggests the problem could be particularly acute. In 2016, a joint industry-government taskforce was established to consider what measures are needed to make the UK the go-to destination for international investment in advanced therapies manufacturing. As part of this, the taskforce developed an end-to-end talent plan for the sector, which is now being implemented with financial support from Innovate UK.

Summary

To retain its competitive edge the UK should not only address its capacity to develop and manufacture cell and gene therapies, it should also ensure there is a viable and extensive market for them in the NHS. Indeed, another question is around how the NHS will pay for these treatments. Cell and gene therapies present difficulties for Health Technology Assessment bodies (HTAs), such as the National Institute for Health and Care Excellence (NICE), which are responsible for assessing the value of medicines and whether they should be made routinely available to patients. Due to the personalised nature of cell and gene therapies they are generally expensive to manufacture and administer and there may be a lack of data available to assess their cost and clinical effectiveness because of small patient populations. In addition, cell and gene therapies tend to be one-off treatments but they have the potential to deliver substantial long-term health gains, meaning large up-front costs for the NHS. This is very different to how the NHS currently pays for its medicines.

New payment models will therefore be needed to ensure patients can access these treatments. In March 2016, NICE conducted a mock assessment for a CAR-T cell product and concluded that their appraisal methods could be applied to cell and gene therapies. Nonetheless, industry still has concerns, especially given NICE's increasing reliance on cost-effectiveness thresholds. One positive was to see the deal announced between NHS England and Novartis to grant young patients access to the CAR-T treatment Kymriah. However, as therapies continue to come to market, NHS England, NICE and industry will need to continue to work together and remain flexible to ensure NHS patients do not miss out.

The risk is high for these personalised medicines to make it to market, however, if they do manage to pass through trials the rewards could be great. It is very dependent on the specific medicine as it is personalised so if the number of patients with the cancer or medical issues are small it may not reach the revenues that some other oncology or immunotherapy drugs can.

Despite these challenges, the future for personalised medicine in the UK looks promising. What is clear from the issues discussed is that commitment from all parts of the ecosystem is needed to address potential barriers to the growth of the industry and to ensure that these treatments reach patients quickly and are administered safely and effectively.

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