The global healthcare market is continuing to grow

Ageing and growing populations, greater prevalence of chronic diseases, exponential advances in innovative, but costly, digital technologies—these and other developments continue to increase health care demand and expenditures.

Deloitte – Global health care outlook

22%

Global population over 60 by 2050, up from 12% in 2015

Global healthcare spending forecast to continue to increase

5%

compound annual growth rate 2019-2023

10.2%

forecast global healthcare spend as a share of GDP to 2023

1 billion

expected increase in the world's population by 2025

300 million

of that increase is predicted to come from those aged 65 or more

Deloitte Insights, 2020 global health care outlook, Laying a Foundation for the Future

Despite advances in technologies, there remain many incurable or intractable diseases

In Focus: Cancer in the UK in 2020

Cancer survival is improving and has doubled in the last 40 years in the UK, but still we face many challenges and unknowns. One of Syncona's key areas of focus is to contribute towards effective new treatments for this set of diseases.

Diagnosis

Every two minutes someone in the UK is diagnosed with cancer

Cases

367,167

New cases of cancer, 2015-2017, UK

Deaths

164,901

Deaths from cancer, 2015-2017, UK

Survival

50%

Survive cancer for 10 or more years, 2010-11, England and Wales

Source: Cancer Research UK

The promise of precision medicine

Enables faster development for patients, smaller, more capital efficient clinical trials and targeted commercial roll-out

Traditional drug development can lead to ineffective drug development; it assumes all patients respond similarly

Precision medicine can enable more effective therapies; genetics revolution has enabled greater insight into choosing potentially lower risk targets and selecting patients that will respond

Many chronic diseases impacting millions of patients have genetic sub-drivers, permitting targeted drug development

30-60%

A traditional drug may only be 30-60% effective[1]

3x

Medicines targeted at defined patient groups 3x more likely to succeed than conventional drugs[2]

+50%

Trials initiated in 2018 using some form of genetic based selection[3]

1 https://www.england.nhs.uk/healthcare-science/personalisedmedicine/
2 Informa Pharma Intelligence's Biomedtracker and Amplion Inc.'s BiomarkerBase.
3 According to Informa's Trialtrove

The Third Wave in healthcare

The arrival of the Third Wave of healthcare

The 'Third Wave' of healthcare has seen the arrival of advanced therapies harnessing the power of genetics and the patient themselves to treat disease. With its potential to address areas of high unmet medical need and transform outcomes for patients, our belief is that we are still in the early stages of the Third Wave and it has the potential to power healthcare innovation for decades to come.

"First Wave"

1950's

Small molecule drugs, market dominated by large pharmaceutical companies.

01

"Second Wave"

1990's

Large molecule (antibody therapies and enzyme replacement therapies).

02

The "Third Wave"

Today

Advanced biologics and genetic medicines such as gene therapy and cell therapy and DNA/RNA medicines.

03

10k

Monogenic diseases, fewer than 50 with treatments

9

Third Wave therapies approved in the US

6/9

Of Syncona's portfolio companies in Third Wave

10

'Third Wave' programmes taken into clinic by Syncona founded companies

"We understand and appreciate the tremendous impact that gene therapies can have on patients by potentially reversing the debilitating trajectory of diseases. These therapies, once only conceptual, are rapidly becoming a therapeutic reality for an increasing number of patients with a wide range of diseases, including rare genetic disorders and autoimmune diseases."

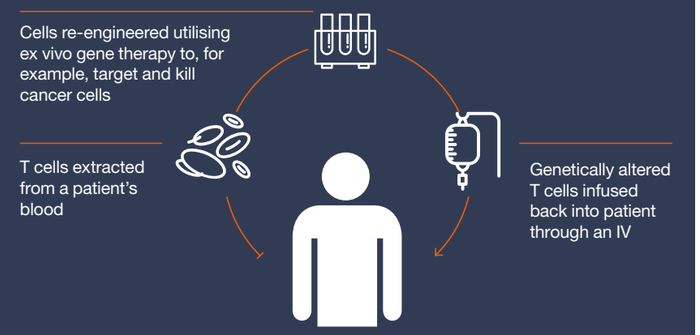
US FDA Commissioner Stephen M. Hahn M.D

Great promise for intractable disease

Gene therapy
The introduction of genetic material into cells to replace missing or defective genes. Introducing a normal copy of a gene may be able to treat or prevent disease on a permanent basis.

Cell therapy
The introduction of selected cells into a patient to treat disease. For example, in immunotherapy, pictured below, T cells capable of fighting cancer cells may be injected in order to treat the disease.

Cell therapy – a personalised approach to treating cancer



Syncona has established a global leadership position in the Third Wave

Autolus

T-cell therapy targeting a pipeline of cancers, initially focused on blood cancer

SwanBio Therapeutics

Gene therapy targeting diseases of the central nervous system

Achilles Therapeutics

T-cell therapy targeting solid tumours, initially focused on melanoma and lung cancer

Freeline

Gene therapy focused on systemic disease

QuellTx

T-reg Cell therapy, focused on autoimmune and inflammatory disease

Gyroscope Therapeutics

Gene therapy targeting the retina

Building platforms

Barriers to entry are high

Engineered cells or viruses are highly technical
They require complex manufacturing, delivery and supply chains, with no existing global capacity at commercial scale.

Highly modular, scalable opportunity
While First and Second Wave products generally required individual product platforms, Third Wave pipelines can be delivered by a single commercial scale platform once established.

Syncona is a leader in building Third Wave platform companies

Having built deep expertise in the Third Wave, we ensure our companies are set up to succeed, investing in building commercially scalable platforms from day one. Our companies focus on:

- **Manufacturing**
- **Supply chain**
- **Delivery**
- **Capsid**
- **Commercial lead programme**
- **Deep and differentiated pipeline**

Platform companies in the Third Wave are commercially valuable

Avexis
$8.7bn
Acquisition price, an 88% premium

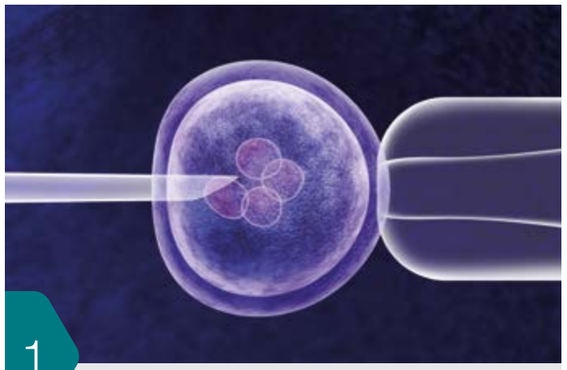
Spark Therapeutics
$4.3bn
Acquisition price, a 122% premium

Audentes
$3.0bn
Acquisition price, a 110% premium

Recent M&A premiums paid for relatively early stage Third Wave gene therapy companies demonstrate the demand for integrated platforms with commercial scale and compelling pipelines.

The potential to transform lives

The Third Wave offers a new paradigm for the treatment and cure of intractable disease. Examples of potentially life changing treatments under development or recently approved include:



1

B-cell acute lymphoblastic leukemia

Disease symptoms

B-cell acute lymphobastic leukemia (ALL) is a type of blood cancer which occurs when B cells (a white blood cell in the immune system) become cancerous and grow out of control. Untreated, the disease is terminal.

Previous standard of care

Approximately 20 per cent of patients with B-cell ALL don't have success with initial treatments. At this point, the standard of care was chemotherapy, radiation or stem cell transplant, with varying levels of success.

Third Wave impact

In 2017, KYMRIAH, a CAR-T immunotherapy treatment, was approved for patients up to age 25 with relapsed or refractory B-cell ALL whose previous treatments had not kept their cancer in remission. A cutting edge treatment, it uses the power of the immune system, engineering patients' own cells and reinjecting them into the body, to treat the cancer. In clinical trials, more than 8/10 patients went into remission, and of those in remission nearly 100% had no detectable signs of cancer at three months. At month 24, they still had a 62% chance of being in remission.

https://www.hcp.novartis.com/globalassets/eg-plus-assets59/kymriah/hcp/ped-all/kym-1222084-aya-digital-core-patient-brochure.pdf

2

Spinal Muscular Atrophy

Disease symptoms

Spinal Muscular Atrophy (SMA) is a progressive, rare genetic disease, caused by a missing or faulty gene (SMN1) which means that the body can't make enough survival motor neuron (SMN) protein. Motor neuron cells are responsible for telling our muscles to work properly. In the most severe cases, SMA leaves babies with a life expectancy of rarely more than two years.

Previous standard of care

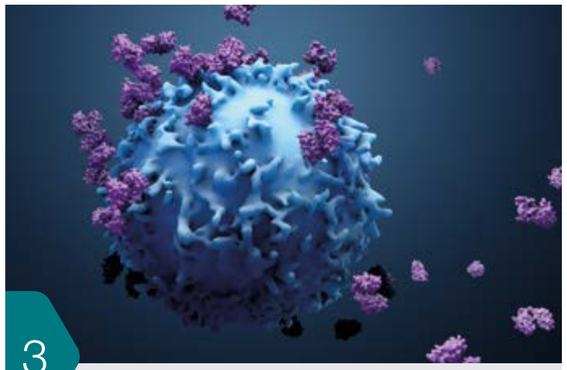
Treatments were historically focused on managing symptoms. In 2016 a new drug, Sprinraza, was approved and improved the production of SMN protein for many SMA patients.

Third Wave impact

In 2019, Zolgensma®, a gene therapy, was approved to treat paediatric SMA patients as a one off treatment designed to target the genetic root cause of SMA by replacing the function of the missing SMN1 gene. In the STR1VE clinical study of children with SMA Type 1, about 91% (20/22) of patients were alive and did not need permanent breathing support as of March 2019. In the natural history of SMA, patients with SMA Type 1 are not able to sit without help and about 25% are alive without permanent breathing support at 14 months of age.

The new gene tells motor neuron cells to produce more SMN protein. Motor neuron cells need SMN protein to survive and support muscle functions.

www.zolgensma.com; www.nhs.uk/conditions/spinal-muscular-atrophy-sma/treatment/



3

Haemophilia A

Disease symptoms

Haemophilia A is a genetic disorder caused by missing or defective factor VIII, a clotting protein. People with haemophilia A often bleed longer than other people, and bleeds can occur internally or externally.

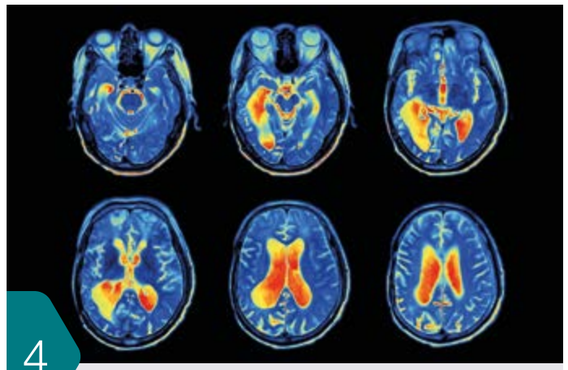
Current standard of care

The main medication to treat haemophilia A is concentrated factor VIII product, called clotting factor or simply, factor. These factor therapies are infused regularly intravenously through a vein in the arm or a port in the chest. This regular treatment involves a significant cost for healthcare systems over the course of a patient's life, and does not result in stable levels of protein for patients.

Third Wave potential

Gene therapies currently in clinical trials have the potential to address the cause of the disease with a single dose to replace the missing gene and allow the body to begin producing factor VIII. This could potentially offer a cure for these patients if they bring factor VIII into the 'normal' expression range, transforming quality of life for patients and reducing costs to the healthcare system.

https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/; https://www.biomarin.com/products/pipeline/bmn-270/ Hemophilia-A



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Dry Age-Related Macular Degeneration

Disease symptoms

Age-related macular degeneration (AMD) is the largest cause of sight loss in the developed world, affecting more than 1 in 5 people in the UK by the age of 90 and more widely in the developed world. AMD is made up of wet and dry AMD. Dry AMD is a slow deterioration of the cells of the macular, as the retinal cells die off and are not renewed. The disease progresses over many years.

Current standard of care

There is currently no treatment for dry AMD.

Third Wave potential

Investigational gene therapies are seeking to treat dry AMD effectively by restoring balance to a part of the immune system called the complement system, which causes inflammation and damages eyes when it is overactive. The studies are designed to stimulate a person's cells to create Complement Factors, a protein that is key to regulating the alternative pathway of the complement system. The goal is to slow, or possibly stop the progression of dry AMD.

https://www.macularsociety.org/what-age-related-macular-degeneration