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Syncona: gene and cell therapy overview

synconaltd.com

Image Freeline labs, Stevenage

An established leader in cell and gene therapy

Syncona has an early first mover advantage in the space - first investment in 2014

- Globally leading cell and gene therapy platform companies
- Strategically assembled, world class companies backed by leading academics
- Rapid development enabled by depth of team expertise and fully integrated platforms

Cell Therapy

Autolus

ACHILLES THERAPEUTICS

Cell therapy: companies covering key cell types

QuellTX

Resolution Therapeutics

T-cell biology & immuno-oncology

ANAVEON

neogene THERAPEUTICS

Gene Therapy

nightstar THERAPEUTICS

Gene therapy: companies covering the key tissue compartments

GYROSCOPE VISION FOR LIFE

FREELINE

SwanBio THERAPEUTICS

Purespring

What is cell and gene therapy?

Offering the potential for cures for a range of intractable diseases

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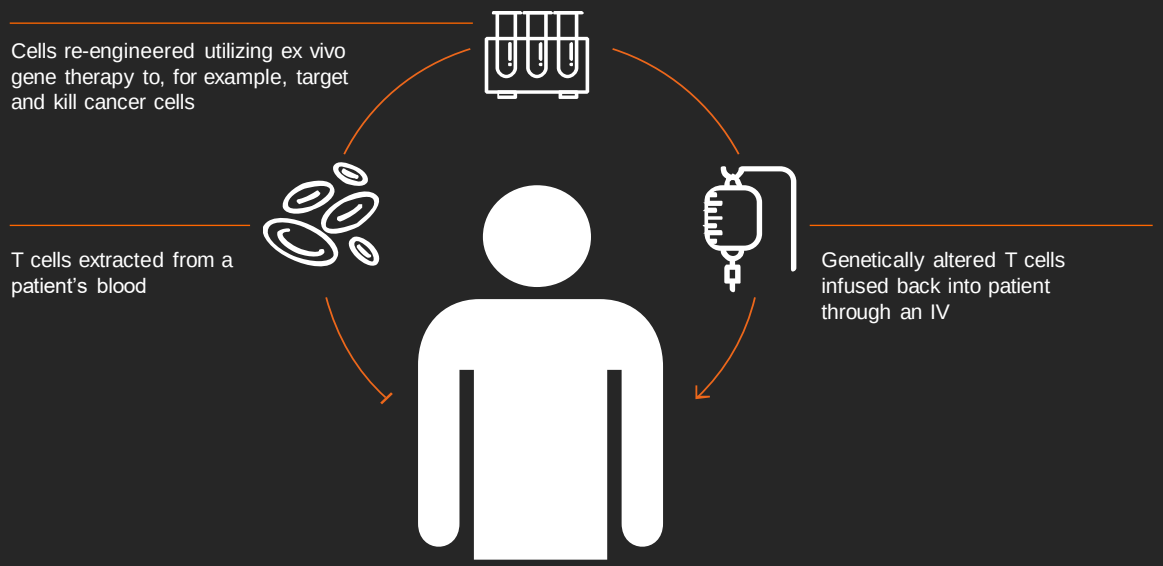
Autologous cells

Cells are removed, restored or altered, and given back to that same person to treat disease.

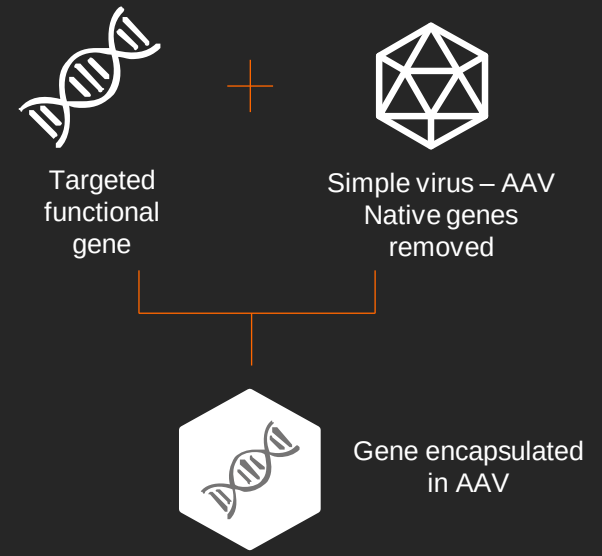
Ex vivo gene therapy

Uses host cells engineered to express a gene of interest which are then transplanted into the body.



In vivo gene therapy

The insertion of genes via a carrier, like an AAV virus, into target tissue to replace a mutated gene which has caused a disease.



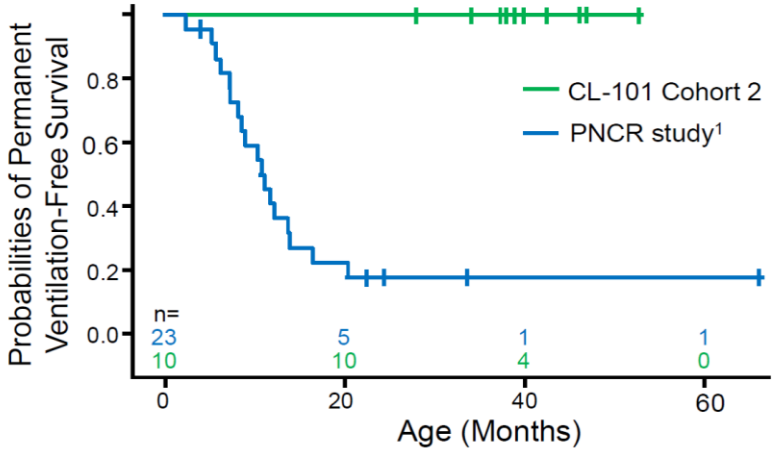
Potential to transform the lives of patients

Ability to treat and even potentially cure many intractable diseases

- Cell and gene therapies are designed to halt a disease or reverse its progress
- Approved products and data to date has shown the transformational impact and potential of these products
- Significant number of diseases where gene therapy is applicable – 10,000 monogenic diseases[1]
- Often one-time treatments vs conventional medicines which are taken on a continual basis

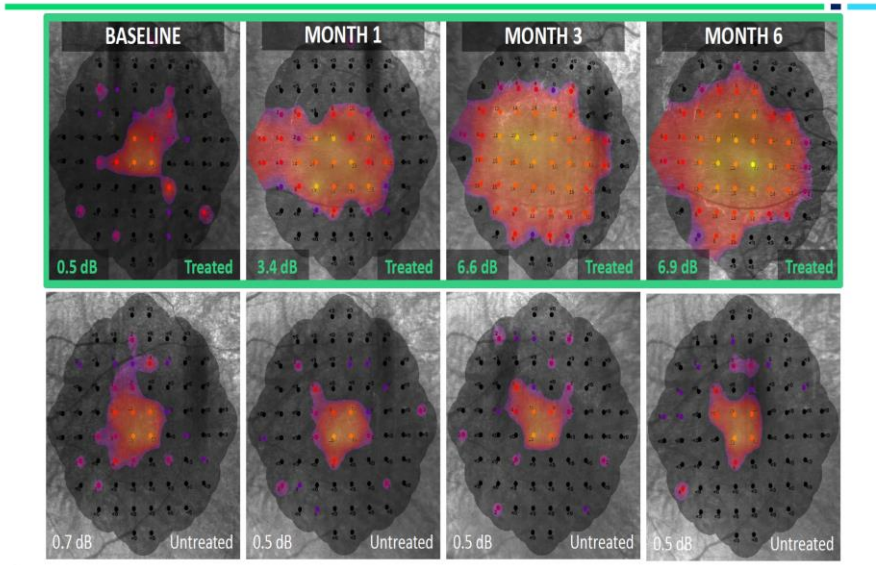
Novartis/AveXis: one-time therapy addressing spinal muscular atrophy

- SMA is a genetic disease caused by a lack of a functional survival motor neuron 1 gene, resulting in the rapid and irreversible loss of motor neurons [2]
- Most often impacts babies and children
- Zolgensma now an approved product based on profound data



Nightstar: maintaining and restoring vision in blinding retinal diseases

- X-linked retinitis pigmentosa: progressive photoreceptor degeneration – no treatment options[3]
- Effects can impact patient's work, school and social interactions
- Primary goal was to maintain visual function but in phase I/II study positive efficacy signal seen



Sources can be found on slide 14

Platforms have strategic value in cell and gene therapy

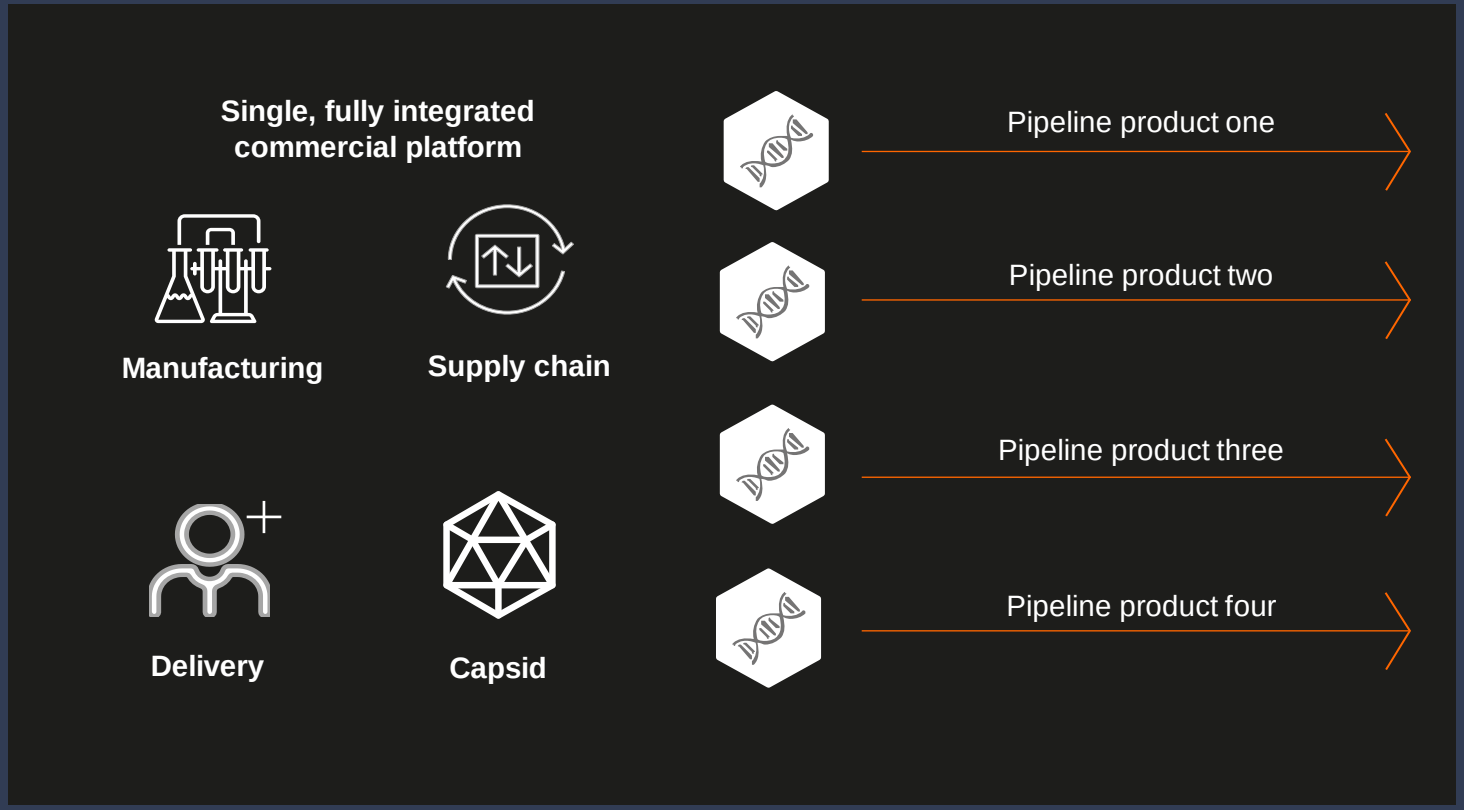
Barriers to entry are high

Engineered cells or viruses are highly technical

Complex manufacturing, delivery and supply chain – no existing global capacity at commercial scale

Highly modular, scalable opportunity

Small and large molecule drugs required individual platforms; cell and gene therapy pipelines can be delivered by a single platform once established



Syncona is a leader in building fully integrated cell and gene therapy platform companies

A strategic approach to building our gene therapy platform

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Syncona has founded companies by creating leading and scalable platforms within key tissue compartments

Retinal	Systemic	Central nervous system	Renal
nightstar THERAPEUTICS GYROSCOPE VISION FOR LIFE	FREELINE	SwanBio THERAPEUTICS	Purespring

- Strategically assembled, world-class, domain-focused companies backed by globally leading academic founders
- Commercial lead programmes with patient populations of scale and high quality pipelines
- Core capabilities in manufacturing and delivery built and funded at the outset – key to establishing a critical path to on-market product
- Aiming to address the most prevalent diseases in each tissue compartment – i.e. Gyroscope, Purespring

A world leading platform for patients breaking out of rare diseases

Building scale in cell therapy

A globally leading cell therapy platform focused on key cell types

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CAR-T	TILs	T-Reg	Macrophage
Autolus	ACHILLES THERAPEUTICS; neogene THERAPEUTICS	QuellTX	Resolution Therapeutics

- World-class cell therapy companies backed by globally leading academic founders
- Cell therapies have been shown to have transformational impacts and durable responses for patients
- Core capabilities in manufacturing and delivery built and funded at the outset – complex products, ability to manufacture therapies at scale key to delivery of value to patients and investors

A world leading portfolio of cell therapy companies addressing areas of high unmet medical need

Broader innovation in genetic medicines

Highly innovative, specific, personalised and patient led technology gaining commercial and regulatory traction

Gene editing

- Gene editing is a type of genetic engineering in which DNA is inserted, deleted, modified or replaced in the genome of a living organism
- The first genome editing technologies were developed in the late 1900s
- A new genome editing tool called CRISPR, invented in 2009, has made it simpler to edit DNA

Ribonucleic acid therapies

- RNA therapeutics are a class of medications based on ribonucleic acid
- Messenger RNA (mRNA) transfers the instructions stored in DNA to make the proteins required in every living cell
- **3** approvals of these therapies in rare genetic disorders

Freeline - a focus on manufacturing from the outset

Manufacturing platform delivers high quality and potency at attractive cost of goods

Strategic control of supply chain

- Single manufacturing platform meets demand from tox to commercial

High quality for safety and potency

- Quality built into product using proprietary technology and supported by analytics leading to high quality standardised product

Commercial scale and costs of goods

- iCellis is a commercial platform that allows adherent systems to scale, enabling large patient population and lower cost of goods

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First employee – Markus Hörer – Founder and Chief Technology Officer (2016)

State of the art CMC Development and Analytical Labs acquired in Munich (2016)

88/236 employees in CMC

Commercial scale
Attractive COGS
Aiming to lead the industry in quality

In-house manufacturing capability

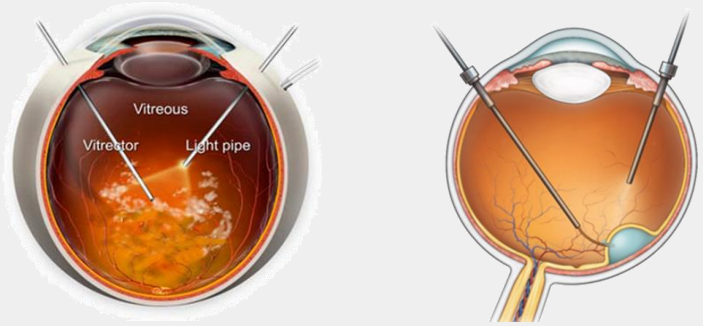
Gyroscope – moving into polygenic diseases

Scaling delivery to large patient populations

Current subretinal delivery requires a vitrectomy

Potential drawbacks include:

- Potential for retinal tears, retinal detachment, cataracts
- Uncertainty of dose delivered, loss of valuable product, lack of scalability.



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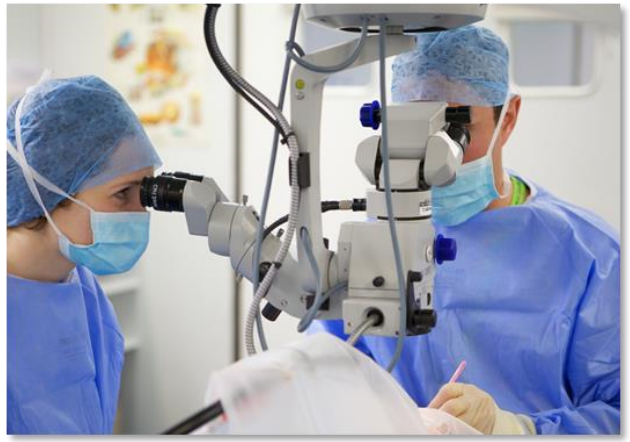
Syncona drove acquisition of Orbit SDS device; designed to protect the structure of the eye

- Optimised surgical procedure could lead to consistent clinical outcome
- Extensive proprietary in-house surgeon training capability
- Seeking to partner with cell and gene therapy companies to establish a gold standard for delivery to the subretinal space

The device shown is not approved for human use



Orbit device innovation developed to enable retinal gene therapy to scale

Cell therapy: manufacturing and logistics

Manufacturing and logistics are central to the success of cell therapy

Manufacturing of personalised medicines poses complex challenges:

- Variability of starting product
- Multi-step process over a number of weeks
- Proximity of manufacturing to patients key to reduce supply chain complexity
- Significant personnel expertise required in relatively new field
- Standardization has not yet developed across the supply chain

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Autolus developed manufacturing facilities in CGT Catapult (UK) and in Maryland (US), now reading for commercial manufacture

Achilles developing an automated and fully closed end-to-end process – focused on commercial manufacture ability early

Quell appointed Bernd Schmidt as Head of Product Delivery to leadership team in first 12 months

neogene THERAPEUTICS

Synthetic biology approach offers advantages with respect to standardization and scalability

Significant opportunity for innovative cell and gene companies

Developing and commercialising breakthrough therapies in areas of high unmet medical need

Significant momentum and an increasingly supportive regulatory environment	$188bn	Total biopharmaceutical global sales in 2017; of which monoclonal antibodies were >65%[4]	c100	Clinical trials testing monoclonal antibodies in 1997[5]	c1000	Cell and gene therapies in clinical trials in 2020; nearly 600 in oncology[6]
Commercial potential being realised and commercial recognition of the value of platforms	10	Approved cell and gene therapy products in the US[7]	$2.1m	Price per treatment of Zolgensma developed by Avexis[8]	$3bn	Raised by cell and gene therapies in NASDAQ IPOs in 2020; up 210% over 2019[9]

Sources for all data can be found on slide 14

What's next for cell and gene therapy?

Fast evolving fields with significant opportunity ahead

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Monogenic diseases to polygenic disease

Increasing the precision of delivery through optimised capsids

Autologous or allogeneic therapies

Appendix

Sources

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